18/1

National Institute of Mental Health

NEWARK PUBLIC LIBRARY

MAR 2 3 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

Psychopharmacology Bulletin

Vol. 18, No. 1
January 1982

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

HE 20. 8109:

Contributions and inquiries should be sent to:

Allen Raskin, Ph.D.
Editor-in-Chief

Lillian Altman
Managing Editor

Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

The *Psychopharmacology Bulletin* is available on subscription from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402. Subscription price $11.00 per year for the United States. All other countries add $2.75 for postage. Please make check or money order payable to the Superintendent of Documents. An annual subscription for four quarterly issues begins with the next issue following receipt of the order. Single copies and back issues may also be ordered from the Superintendent of Documents. The expiration date is printed on the top line of the address label. Change of address and complaints about non-receipt of issues should be sent to the Superintendent of Documents, and should include the old address, preferably a mailing label, as well as the new address.

ORDER FORM Mail To: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Enclosed is $______ ☐ check,
(U.S. Currency Only)
☐ money order, or charge to my
Deposit Account No.
☐☐☐☐☐☐☐–☐

Order No.__________

Credit Card Orders Only

Total charges $______ Fill in the boxes below.

Credit Card No. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Expiration Date Month/Year ☐☐☐☐

Please enter my subscription to: **PSYCHOPHARMACOLOGY BULLETIN** [*PSBU*]
@ $11.00 domestic, @ $13.75 foreign.

Name—First, Last

Street address

Company name or additional address line

City **State** **ZIP Code**

(or Country)

PLEASE PRINT OR TYPE

For Office Use Only.

	Quantity	Charges
Enclosed		
To be mailed		
Subscriptions		
Postage		
Foreign handling		
MMOB		
OPNR		
UPNS		
Discount		
Refund		

Psychopharmacology Bulletin

CONTENTS

Vol. 18, No.1 **January 1982**

Page

Meeting Announcements 1
Books Received 1

Brief Report—

Tardive Dyskinesia: Inter- and Intrarating Scale Comparisons—*Mary Ann Richardson and Thomas J. Craig* 4

Annual NCDEU Meeting (1981)—Abridged Proceedings—

NCDEU Update—

Neurotransmitter Precursors for the Treatment of Depression—*Alan J. Gelenberg, Candace J. Gibson, and Joanne D. Wojcik.* 7

Dosage and Treatment Strategies in Schizophrenia and Affective Disorders—

Low-Dose Neuroleptics in Outpatient Schizophrenics—*John M. Kane, Arthur Rifkin, Margaret Woerner, and Gerard Reardon.* 20
Early Intervention vs Continuous Pharmacotherapy of Schizophrenia—*William T. Carpenter, Jr., Joseph H. Stephens, Alix C. Rey, Thomas E. Hanlon, and Douglas W. Heinrichs* 21
Routine Use of Psychotropic Plasma Levels in Medically Ill Psychiatric Patients—*Richard Dorsey and Ann Bahrani* 23
Assessing the Effects of Electroconvulsive Therapy (ECT)—Critical Research Issues—*Jack D. Blaine* 27
Evaluation of the Central Nervous System Risks of ECT—*Richard D. Weiner, Helen J. Rogers, Jonathan Davidson, and Robert D. Miller* 29
Efficacy of ECT in the Treatment of Depression—Wave Form and Electrode Placement Considerations—*Charles A. Welch, Richard D. Wiener, Douglas Wier, Jane F. Cahill, Helen J. Rogers, Jonathan Davidson, Robert D. Miller, and Michel R. Mandel* 31
ECT Combined with Neuroleptics in the Treatment of Schizophrenia—*Joyce G. Small, Victor Milstein, Marietta Klapper, Jeffrey J. Kellams, and Iver F. Small* 34

Current Issues in the Treatment of Anxiety States and Disorders—

Predictability of Treatment Response to Diazepam at Several Points During the Course of a 6-Week Drug Trial—*Robert W. Downing and Karl Rickels* 37
Issues in Long-Term Treatment with Diazepam—*Karl Rickels, George W. Case, and Robert W. Downing* 38
Behavioral Assessment of Drug Effects in Obsessive-Compulsive Disorders—*Samuel M. Turner* 41

Clinical Trials of Neuropeptides in Psychiatric Disorders—

Effect of Des-Tyr-γ-Endorphin in Schizophrenia—*Herbert Y. Meltzer, Daniel A. Busch, John Lee, and Yiannis Papacostas* 44
Vasopressin Studies in Alzheimer's Disease—*Carol A. Tamminga, Raymon Durso, Paul Fedio, and Thomas N. Chase* 48

Psychoactive Drug Treatment in Retarded Populations—

Effects of Phenytoin Withdrawal on Matching to Sample and Workshop Performance of Mentally Retarded Individuals—A Brief Report—*Vicky J. Davis* 51

Effects of Neuroleptic Drugs on the Intellectual and Habilitative Behaviors of Mentally Retarded Persons—*Donald G. Ferguson* 54

An Applied Dose-Response Curve of Thioridazine with the Mentally Retarded: Aggressive, Self-Stimulatory, Intellectual, and Workshop Behaviors—A Preliminary Report—*Stephen E. Breuning* 57

An Analysis of Institutionalized Retarded Residents Using DIS-CO—*Robert L. Sprague* 60

Tardive Dyskinesia in Mentally Retarded Children, Adolescents, and Young Adults: North Carolina and Michigan Studies—*C. Thomas Gualtieri, Stephen E. Breuning, Steven R. Schroeder, and Dana Quade* 62

Neuroleptic Serum Levels in Mentally Retarded Boys—*James C. Harris, Larry E. Tune, Michael Kurtz, and Joseph T. Coyle* 65

Free Communications—Session A—

Efficacy of Mianserin in Mildly Depressed Patients—*Jonathan W. Stewart, Frederic M. Quitkin, Patrick J. McGrath, Michael R. Liebowitz, and Donald F. Klein* 68

The Effect of Mianserin on Cardiac Conduction: A Controlled Study—*Patrick J. McGrath, Frederic M. Quitkin, David Blood, Michael R. Liebowitz, Jonathan W. Stewart, Abby Fyer, and Donald F. Klein* 71

Double-Blind Comparison of Bupropion vs Amitriptyline in Depressed Outpatients—*Nancy Harto-Truax, Joanne Van Wyck Fleet, and Warren C. Stern* 72

Wellbutrin Studies—*Baron Shopsin and Gregor Laakmann* 76

Atypical Depressives: A Preliminary Report of Antidepressant Response and Sleep Patterns—*Frederic M. Quitkin, David Schwartz, Michael R. Liebowitz, Jonathan R. Stewart, Patrick J. McGrath, Frieda Halpern, Joaquim Puig-Antich, Elaine Tricamo, Edward J. Sachar, and Donald F. Klein* 78

Biological and Clinical Studies of Tardive Dyskinesia—*Robert C. Smith, Richard Allen, Jack Gordon, Chandra Misra, Joseph Schoolar, Judith Wolff, and Beng T. Ho* 80

Results from a Prospective Study of Tardive Dyskinesia Development: Preliminary Findings over a 2-Year Period—*John M. Kane, Margaret Woerner, Paul Weinhold, and James Wegner* 82

Impairment of Swallowing, Tardive Dyskinesia, and Anticholinergic Drug Use—*Thomas J. Craig, Mary Ann Richardson, Nigel M. Bark, and Roman Klebanov* 84

Lecithin Treatment of Tardive Dyskinesia—A Progress Report— *Brian G. Anderson, Dean Reker, Miodrag Ristich, Eitan Friedman, Miriam Banay-Schwartz, and Jan Volavka* 87

Effects of AMPT on Tardive Dyskinesia and Psychosis—*Henry A. Nasrallah, Robert E. Smith, Frederick J. Dunner, and Mona McCalley-Whitters* 89

Receptor Sensitivity Modification in the Treatment of Tardive Dyskinesia—*Murray Alpert, Florence Diamond, and Arnold J. Friedhoff* 90

Free Communications—Session B—

Combination Choline/Piracetam Treatment of Senile Dementia—*Steven H. Ferris, Barry Reisberg, Eitan Friedman, Michael K. Schneck, Kathleen A. Sherman, Pervez Mir, and Raymond T. Bartus* 94

Development and Prediction of Postsynaptic Depression in Neuroleptic-Treated Schizophrenic Patients—*Joanne B. Severe, Michel R. Mandel, and Nina R. Schooler* 95

Plasma Levels of Thiothixene by Radioreceptor Assay and Clinical Outcome—*Theodore van Putten, Philip R.A. May, Stephen R. Marder, and Jeffrey N. Wilkins* 99

The Effects of Psychotropic Drugs on Informed Consent—*Barbara Stanley, Michael Stanley, Eric Peselow, Adam Wolkin, Steven Deutsch, Laura Platt, Julie Speicher, Lynn Golash, and Michael Kaufman* 102

Page

Research Use of the Early Clinical Drug Evaluation Unit Data Bank—*John E. Overall and Howard M. Rhoades* 105

Diagnostic and Statistical Manual-III and the Children's Psychiatric Rating Scale—*Betty Pfefferbaum and John E. Overall* 107

Haloperidol in Autistic Children: Effects on Learning, Behavior, and Abnormal Involuntary Movements—*Magda Campbell, Lowell T. Anderson, Ira L. Cohen, Richard Perry, Arthur M. Small, Wayne H. Green, Lillian Anderson, and William H. McCandless, Jr.* 110

A Controlled Study of Methylphenidate in Combination with Academic Instruction—*Rachel Gittelman* 112

Methylphenidate in Adults with Minimal Brain Dysfunction—*Jeffrey A. Mattes, Lane Boswell, and Herman Oliver* 114

Cumulative Index—Psychopharmacology Bulletin—1981 117

Psychopharmacology—A Recurring Bibliography—

Subject Section S-1

Author Section A-59

Meeting Announcements

The **Society of Behavioral Medicine**, formerly located at 600 North Wolfe Street, Baltimore, Maryland, is pleased to announce that its national office has moved to Knoxville, Tennessee. The Society's new address is:

The Society of Behavioral Medicine
P.O. Box 8530, University Station
Knoxville, TN 37916
Phone No. 615 974-5164

In addition, the Society's Third Annual Meeting will be held in Chicago, Illinois on March 3-5, 1982 at the downtown Chicago Marriott. This year's meeting will include courses in the fundamentals of behavioral medicine, numerous workshops, practica, symposia, and short courses, and a debate on the "Dangers and Benefits of Exercise." There will also be an invited address by Chandra Patel, M.D., of London, England entitled "A New Dimension on Coronary Heart Disease Prevention."

Inquiries about the Society and the upcoming meeting should be directed to Judith C. Woodward, Administrative Director, at the above address.

* * * *

The **International Conference on Alcoholism** will hold its meeting on March 30-April 4, 1982, in Oxford, England. For information write to: Philip Goldring, Broadway Lodge, Oldmixon Road, Weston-super-Mare, BS24 9NN, Avon, England.

* * * *

The **American Psychological Association** meeting will be held August 23-27, 1982 in Washington, D.C. For information write to: Adelbert H. Jenkins, c/o Candy Won, American Psychological Association, 1200 17th Street, N.W., Washington, D.C. 20036.

* * * *

The **International Congress on Alcoholism and Drug Dependence** will meet on October 9-15, 1982, in Tangier, Morocco. For information write to: International Council on Alcohol and Addictions, P.O. Box 140, CH-1001 Lausanne, Switzerland.

* * * *

An **International Evoked Potentials Symposium** will be held on October 18-20, 1982, in Cleveland, Ohio. For information write to: International Symposium Office, Cleveland Clinic Educational Foundation, 9500 Euclid Avenue, Cleveland, OH 44106.

* * * *

An **International Conference for the Mental Health of the Elderly** will be held in Cairo, Egypt on November 22-25, 1982. Anyone interested in submitting an abstract should forward same to one of the following members of the Program Committee:

Dr. A. Ashour
Secretary General
P.O. Box 290
Heliopolis, Cairo,
Egypt

Dr. Gosta Bucht
Department of Medicine
S. 90185
Umea, Sweden

Dr. Sanford Finkel
230 North Michigan Avenue
Suite 2400
Chicago, IL 60601,
USA

Dr. D. MacLachlan
Toronto General Hospital
101 College Street
Toronto, Ontario M5G 1L7, Canada

* * * *

Books Received

The following new books have recently been received by us for review:

- **GABA and Benzodiazepine Receptors**, Vol. 26 in the series **Advances in Biochemical Psychopharmacology**, edited by E. Costa, G. Di Chiara, and G.L. Gessa. Available from Raven Press, 1140 Avenue of the Americas, New York, NY 10016; Price: U.S. $36.00; 321 pp.

- **Anxiety: New Research and Changing Concepts**, edited by D.F. Klein and J.G. Rabkin. Available from Raven Press, 1140 Avenue of the Americas, New York, NY 10016; Price: U.S. $49.50; 453 pp.
- **Phenomenology and Treatment of Psychophysiological Disorders**, edited by W.E. Fann, I. Karacan, A. Pokorny, and R.L. Williams. Available from SP Medical & Scientific Books, 175-20 Wexford Terrace, Jamaica, NY 11432; Price: U.S. $35.00; 335 pp.
- **Treatment of Migraine: Pharmacological and Biofeedback Considerations**, edited by R.J. Mathew (Proceedings of the Symposium of the Texas Research Institute of Mental Sciences, Houston). Available from SP Medical & Scientific Books, 175-20 Wexford Terrace, Jamaica, NY 11432; Price: U.S. $25.00; 170 pp.

New Journal

Archives of Gerontology and Geriatrics is a new English-language journal published in editorial cooperation with the National Institute of Geriatrics (INRCA), Rome, Italy, and F. Verzar International Laboratory for Experimental Gerontology (VILEG), Ancona, Italy, and Debrecen, Hungary.

The principal aim of the journal is to facilitate the exchange of information between specialists in research in experimental, clinical, and social studies on aging.

Experimental papers dealing with the basic mechanisms of aging at molecular, cellular, tissue, or organ levels will be published. Clinical papers will be accepted if they provide sufficiently new information and are of fundamental importance for the knowledge of human aging. Papers dealing with anti-aging pharmacological presentations in humans are welcome, as are papers on the social aspects of geriatrics. Review papers of interdisciplinary character are especially welcome.

Brief outlines should be sent to the Executive Editor for preliminary consultation:

Dr. Imre Zs-Nagy
Scientific Coordinator of VILEG
University Medical School, VILEG
Hungarian Section
H-4012 Debrecen/Hungary

Book Review

Biochemistry and Pharmacology of Ethanol (Vols. 1 and 2), edited by E. Majchrowicz and E.P. Noble, represent an extensive and scholarly compilation of subjects of interest to researchers and clinicians working in areas related to alcoholism and alcohol abuse. The aim of the editors was to provide in-depth, detailed reviews of the physiological, biochemical, and behavioral effects of alcohol and, in general, this aim has been met. The first volume is devoted mainly to discussion of ethanol metabolism, and to the effects of ethanol on metabolic pathways in peripheral organs and in brain. Detailed attention is given to descriptions of basic research on kinetic mechanisms of alcohol and acetaldehyde metabolism, and more clinically oriented accounts of the interference of ethanol with organ function are also included. In addition, several contributions deal with the often misunderstood or neglected interactions of ethanol with nutritional factors.

The second volume is more concerned with the biochemical, and particularly neurochemical, effects of ethanol. Many of the chapters discuss the possible contribution of ethanol to the important phenomena of intoxication, tolerance, and biochemical and hormonal effects of physical dependence. This volume also contains chapters on ethanol's interactions with other drugs, and discussions of currently popular areas of research, such as the fetal alcohol syndrome, as well as some more neglected but perhaps equally important aspects of alcohol exposure, such as effects on sleep. Within the second volume, several chapters are particularly well prepared. The chapter "Alterations in Neurotransmitter Function After Acute and Chronic Treatment with Ethanol" is a good example. By analysis of the methodology used in various published reports, the authors greatly clarified an area of research generally plagued with contradictory results. The above-mentioned chapter, "Fetal Alcohol Syndrome: Clinical Pharmacology", is another example of an excellent summary of an important subject area.

Although some unevenness is evident in the quality of the various contributions, in general, they are concise, informative, and substantial in their review of past and current work within each subject area. One especially useful feature for the casual reader, or one who is specifically interested in particular aspects of ethanol biochemistry or pharmacology, is the presence of summaries following each chapter. Because these volumes cover research which is relevant to so many important aspects of alcohol abuse, one wishes that attention could have been given to the psychosocial aspects of alcoholism. Perhaps this topic will be the subject of a later volume.

However, with respect to the biochemistry and pharmacology of ethanol, these two volumes will provide an excellent reference source for readers, both now and in the future.

The books may be ordered directly from the publisher, Plenum Press, 223 Spring Street, New York, NY 10013. Price: U.S.$47.50 (Vol. 1) and U.S.$42.50 (Vol. 2); 704 pp. (Vol. 1) and 574 pp. (Vol. 2).

Boris Tabakoff, Ph.D.
Alcohol & Drug Abuse
Research & Training Program
University of Illinois
Chicago, Illinois

Brief Report

Tardive Dyskinesia: Inter- and Intra-Rating Scale Comparisons

Mary Ann Richardson, M.A.,[1] and Thomas J. Craig, M.D., M.P.H.[2]

Tardive dyskinesia is an iatrogenic movement disorder that affects large numbers of psychiatric patients and as such has become a major public health concern. A multiplicity of assessment methods have been used to both define the prevalence of this disorder and determine the effectiveness of treatment modalities—the most common of these being rating scales (Gardos, Cole, & LaBrie, 1977). Several scales are currently in use which follow two main formats—multi-item scales and scales composed of several global ratings. The Simpson Tardive Dyskinesia Rating Scale (TDRS) and the Simpson Abbreviated Dyskinesia Scale (ADS) (Simpson, Lee, Zoubak, & Gardos, 1979) are examples of the multi-item approach. These scales list and define specific movements to be rated and provide scaling criteria. The Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976) illustrates the combined global rating scale format and lists body areas to be rated and examples of the types of movements to be included within a body area. The lack of uniformity in these and other rating instruments demands that inter- and intrascale data be available to the research community to make possible meaningful comparisons of study results. Unfortunately, little work has been done in this area. Chien, Jung, Ross-Townsend, and Sterns (1977), studying a small group of outpatients, performed interscale correlations on five assessment methods—direct counting, the Gerlach scale, the Crane scale, a portion of the Simpson TDRS scale, and the AIMS scale. The TDRS and the AIMS showed average correlation coefficients to the other four scales of .74 and .73, respectively. The scores of two raters, a medical student and a psychiatrist, were averaged for these analyses. Smith, Kucharski, Oswald, and Waterman (1979) reported that intrascale correlations on the AIMS computed on mean patient scores ranged from .23 to .88. The present study offered the opportunity to perform both inter- and intrascale comparisons of the ADS and the AIMS using ratings collected on a large population of psychiatric inpatients by a single rater

Method

One hundred and thirty-two inpatients were evaluated for abnormal movements using the ADS and the AIMS at one rating session per patient by a single rater. Of this group, 40 were females (30.3%) and 92 were males (69.7%). Ages ranged from 19-82 with a mean age of 40 and a median age of 34.5. The Simpson scale was modified by removing tongue tremor, eyelid tremor, the four "other" categories, and by changing the scaling to conform to the five-point scale of the AIMS. The AIMS was modified by removing the "one less" rule for activated movements. Inter- and intrascale correlations were performed using the Pearson product-moment correlation coefficient. For the ADS, intrascale correlations were obtained for the total scale (Items 1-6, 8-10, 12-14) total facial/oral (Items 1-6), total trunk (Items 8-10), and total extremities (Items 12-14). For the AIMS, intrascale correlations were obtained for the total scale (Items 1-7), global severity (Item 8), total facial/oral (Items 1-4), trunk (Item 7), and total extremities (Items 5 and 6).

---

[1] Clinical Research and Development, Information Sciences Division, Rockland Research Institute, Orangeburg, NY 10962.

[2] Clinical Research and Development, Information Sciences Division, Rockland Research Institute, Orangeburg, New York and Department of Psychiatry, New York University, New York, NY 10024.

Results

Table 1 lists the interscale comparisons. These data demonstrate highly significant correlations between the two scales on total scores, and the total facial/oral and total extremities subscales of .95769, .98096, and .87294, respectively. The total trunk on the ADS and the trunk item on the AIMS show much lower correlations with all other scores.

Table 1

Interscale Correlations*
of the ADS and AIMS

	AIMS			
ADS	Total Scale (1-7)	Total Facial/Oral (1-4)	Trunk (7)	Total Extremities (5-6)
Total Scale (1-16)	.95769 $p < .0001$	.84862 $p < .0001$	.43272 $p < .0001$	.61630 $p < .0001$
Total Facial/Oral (1-6)	.84983 $p < .0001$	.98096 $p < .0001$	.19014 $p < .029$	.27279 $p < .0016$
Total Trunk (8-10)	.37841 $p < .0001$	.29113 $p < .0007$	.56167 $p < .0001$	.10438 NS
Total Extremities (12-14)	.67399 $p < .001$	.34387 $p < .0001$	.31225 $p < .0003$	.87294 $p < .0001$

* Pearson "r"

The intrascale correlations are listed in Table 2. The ADS shows a strong correlation for the total scale with the total facial/oral (.86169) and a correlation of .68120 for the total scale with the total extremities. Again, the total trunk score correlates much less strongly with either the total scale, total facial/oral, or total extremities. The total extremities subscale, in addition, showed low correlation with the total facial/oral score.

The AIMS demonstrated a similar pattern with good correlations between the total score and the global severity and total facial/oral items (.85103 and .86971, respectively). In addition, global severity correlated with the total facial/oral score—.72006. The total extremities subscale, however, correlated at a lower level with the total score and global severity items, while the trunk item showed the lowest level of correlation with all other subscales. Despite these variations, all correlations except that between the ADS trunk and extremities subscales achieved statistical significance.

Discussion

This study demonstrates that the ADS and the AIMS correlate well and seem equally efficient in the rating of tardive dyskinesia, despite real differences in format and content. The facial/oral subscales correlate particularly well both in intra- and interscale comparisons. These subscales are perhaps better conceptualized and may possess greater validity for this disorder in this population than the trunk and extremity subscales.

There is a possibility that because these ratings were collected by a single rater at a single session, the reported correlations are somewhat inflated by a carryover effect. On the other hand, interscale correlations performed by multiple raters could be deflated by differences between raters. The lower correlations reported for the trunk and extremity subscales, however, seem to speak against a substantial carryover effect for these data.

In summary, a multi-item rating scale and a scale combining global ratings show strong correlations. The selection of which scale to use will most likely be dictated by the research design. The multi-item scale would be preferable, for example, if the demonstration of differential treatment effects on specific tardive dyskinesia movements is needed; the global approach may be more efficient, for instance, for a large-scale prevalence study where a yes/no designation is all that is required.

The findings also suggest the need for more research into the reason for the relatively low correlations found for trunk and extremity ratings. For example, are these separate manifestations

Table 2

Intrascale Correlations* for ADS and AIMS

AIMS

ADS	Total	Global Severity	Total Facial/Oral	Trunk	Total Extremities	AIMS
		.85103 $p < .0001$	.86972 $p < .0001$	.46549 $p < .0001$	.65983 $p < .0001$	Total Scale
			.72006 $p < .0001$	.34745 $p < .0001$	.63516 $p < .0001$	Global Severity
Total Facial/Oral	.86169 $p < .0001$			.22188 $p < .01$	.26945 $p < .002$	Total Facial/Oral
Total Trunk	.40905 $p < .0001$		.27139 $p < .0016$		.23713 $p < .006$	Trunk
Total Extremities	.68120 $p < .0001$		.34795 $p < .0001$	.11711 NS		
	Total Scale		Total Facial/Oral	Total Trunk	Total Extremities	
			ADS			

Pearson "r"

with little physiologic relation to the facial/oral signs representing different patterns of vulnerability (e.g., demographic or clinical) or different underlying mechanisms, or are they merely more difficult to rate? If the former is so, should separate scales be developed rather than lumping all three body areas together into a total score which may obscure significant differences? If the latter, there may need to be a sharpening of diagnostic criteria for these areas.

Acknowledgment: The authors wish to thank Joseph A. Wanderling for programming and statistical assistance, and Frances Simpson for manuscript preparation.

References

Chien, C.P., Jung, K., Ross-Townsend, A., and Sterns, B. The measurement of persistent dyskinesia by piezoelectric recording and clinical rating scales. *Psychopharmacol. Bull.*, 13(3):34-36, 1977.

Guy, W. *ECDEU Assessment Manual for Psychopharmacology, Revised, 1976.* U.S. Department of Health, Education, and Welfare, DHEW Publ. No. (ADM) 76-338, 1976.

Simpson, G.M., Lee, J.H., Zouback, B., and Gardos, G. A rating scale for tardive dyskinesia. *Psychopharmacology (Berlin)*, 64:171-179,1979.

Smith, J.M., Kucharski, M.A., Oswald, W.T., and Waterman, L.J. A systematic investigation of tardive dyskinesia in inpatients. *Am J. Psychiatry*, 136:918-922, 1979.

Annual NCDEU Meeting (1981)—Abridged Proceedings

The annual meeting of the New Clinical Drug Evaluation Unit (NCDEU) of the Pharmacologic and Somatic Treatments Research Branch (PST), National Institute of Mental Health, took place on May 26-28, 1981 in Key Biscayne, Florida.

These annual meetings are open meetings sponsored by the PST which focus primarily on recent research findings in psychopharmacology. Updates or reviews of significant issues in this field are also presented.

As in previous years, we are again publishing summaries of the papers presented. We are now listing the titles and authors of all the papers in a panel or plenary session to provide the reader with a better understanding of the content and scope of these sessions. However, in some cases, not all of the papers of a session are included because they were not received before going to press.

NCDEU Update

Chair: Robert F. Prien, Ph.D.
Pharmacologic and Somatic
Treatments Research Branch
National Institute of Mental Health
Rockville, Maryland

Neurotransmitter Precursors for the Treatment of Depression

Alan J. Gelenberg, M.D.,[1] Candace J. Gibson, Ph.D.,[2] and Joanne D. Wojcik, R.N., M.S.[3]

The two most widely held biochemical models of depression—the catecholamine (CA) and indoleamine (IA) hypotheses—explain depression as a result of deficient transmission of the CA norepinephrine (NE) or the IA serotonin (5-hydroxytryptamine, 5-HT). Until recently, all drugs used to treat depression appeared to enhance neurotransmission in one or both of these systems, which was used to explain their antidepressant actions. In fact, it was this action of these drugs that gave rise to the models themselves. Another way to increase brain levels of NE and 5-HT, and potentially to increase presynaptic activity, would be the systemic administration of the precursors of the neurotransmitters, an approach something like organic gardening in the brain. For this purpose, the 5-HT precursors tryptophan and 5-hydroxytryptophan (5-HTP), and the NE precursors tyrosine and dihydroxyphenylalanine (DOPA), have been administered to depressed patients. This paper will review some of the theoretical background and clinical experience with these substances, present a view of their current status, and hazard a few predictions regarding the course of future research in this field.

---

[1] Special Studies Clinic, Erich Lindemann Mental Health Center and Massachusetts General Hospital, Boston, MA 02114.

[2] Laboratory of Neuroendocrine Regulation, Massachusetts Institute of Technology, Boston, MA 02114.

[3] Special Studies Clinic, Erich Lindemann Mental Health Center and Massachusetts General Hospital, Boston, MA 02114.

Monoamine Hypotheses of Affective Disorders

Antidepressant Drugs

The CA and IA hypotheses of affective disorders, largely derived from the pharmacology of drugs that produce or reverse depression in humans and animals, suggest that central monoamine (MA) deficits—particularly of NE or 5-HT—may lead to depression (Maas, 1975; Schildkraut, 1965; Schildkraut & Kety, 1967). Both monoamine oxidase (MAO)-inhibitors and tricyclic antidepressants appear to potentiate the effective level of MAs at the synapse: MAO inhibitors inhibit MA degradation, increasing levels in brain; tricyclics inhibit brain MA uptake mechanisms, prolonging the action of MA at the synaptic receptor. Among the currently available tricyclic antidepressants, the secondary amine compounds (i.e., desipramine, nortriptyline, and protriptyline) are more potent inhibitors of NE-uptake in vitro and in vivo than the tertiary amines (amitriptyline, imipramine, and doxepin), which more selectively block 5-HT-reuptake (Bopp & Biel, 1974). However, all three tertiary amine tricyclics are metabolized in vivo to active secondary amines. Thus, administration of either a tertiary or a secondary amine tricyclic results in a blockade of NE reuptake. A novel approach to the treatment of depression, which is consistent with the CA hypothesis, has been the administration of a **β-adrenergic stimulating drug, salbutamol** (Lecrubier, Puech, Frances, et al., 1981).

Recently, questions have been raised about the role of uptake inhibition in the mechanism of tricyclic antidepressant action. For example, inhibition of reuptake occurs almost immediately, yet reversal of depressive symptoms typically requires several weeks of drug treatment. Despite these questions, the focus of attention remains on MA neurotransmission. Recent data suggest that following several weeks of tricyclic administration, changes may occur in the sensitivity of pre-and postsynaptic MA receptors (Maas, 1979; Sulser, Vetulani, & Mobley, 1978). Thus, via a receptor-mediated feedback mechanism, the neuronal firing rate may be altered and/or postsynaptic receptor sensitivity to the MA "message" may be readjusted. Although the advent of some newer classes of antidepressants has even thrown into question the primacy of NE and 5-HT in the genesis of depression and the action of antidepressant compounds (Gelenberg, 1980), the CA and IA theories still have considerable heuristic value and clinical relevance.

Postmortem Studies: Biochemical findings in depressed patients have provided some support of the MA theories. Postmortem findings in the brains of depressed patients who committed suicide have suggested central deficits in 5-HT. Decreased concentrations of 5-HT and its major metabolite, 5-hydroxyindole acetic acid (5-HIAA), have been found in the brainstem—particularly in the raphe nuclei, which contains cell bodies of 5-HT neurons (Birkmayer & Riederer, 1975; Lloyd, Farley, & Deck, 1974). No deficits in NE or dopamine (DA) have been found (Bourne, Bunney, Colburn, et al., 1968). A recent study, which examined brains from endogenously depressed patients who died of cardiac failure or pneumonia, reported no significant NE deficits but did find extensive decreases in levels of the major NE metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG), in 6 of 14 areas examined (Riederer, Birkmayer, Seeman, & Wuketich, 1980). This suggests that although NE levels are normal, brain NE turnover may be decreased in some depressed patients.

Cerebrospinal Fluid (CSF): Biochemically, depression may represent a heterogenous disorder, with subgroups of patients who have decreased NE function and normal 5-HT, others with decreased 5-HT and normal NE, and still others with normal values for both systems (Garver & Davis, 1979; Maas, 1975). Furthermore, this heterogeneity in biochemical measurements may underlie a possible heterogeneity in treatment response. For example, Maas has suggested that patients with NE deficits are more responsive to NE-augmenting therapies (e.g., desipramine or amphetamine), while those with 5-HT deficits will respond preferentially to 5-HT-augmenting treatment (e.g., amitriptyline, tryptophan, or 5-HTP) (Maas, 1975). Not all studies, however, support this dual-amine concept or differential drug responsiveness among patients (Ridges, Bishop, & Goldberg, 1980).

Studies of CSF MAs and metabolites have not been conclusive in confirming an MA theory of affective disorders (van Praag, 1980a, 1980b). In general, CSF levels of NE and its major metabolite, MHPG, are elevated in manics when compared with depressed patients. Reported levels in depressed patients have been less consistent —sometimes lower (Gordon & Oliver, 1971), sometimes the same as those in neurological controls (Post, Lake, Jimerson, et al., 1978; Shopsin, Wilk, Gershon, et al., 1973). These discrepancies could be due to the putative biochemical heterogeneity of depressive disorders: Decreases in CSF NE levels in a subgroup of patients might be obscured when means among a diverse group are compared to controls. Also, many of these studies do not distinguish depressives with a history of mania (bipolars) from those with no previous episodes of mania (unipolars and first-episode depressives).

As with CSF MHPG, baseline levels of lumbar CSF 5-HIAA, the 5-HT metabolite, are decreased in some, but not all depressed patients (Åsberg, Thoren, & Traskman, 1976; Papeschi & McClure, 1971; van Praag, 1980). However, in assessing 5-HT turnover in brain, a complicating factor is that a substantial portion of 5-HIAA measured in lumbar samples is derived from the spinal cord and may not reflect brain 5-HT metabolism. It seems there is a gradient of CSF 5-HIAA concentration: Levels in ventricular fluid are four to five times higher than those in lumbar fluid. When brain ventricular CSF was sampled directly, concentrations of 5-HIAA were lower in patients with endogenous depression, compared to levels in other psychiatric patients and in a neurological control group (Bridges, Bartlett, & Sepping, 1976).

A dynamic measure of central 5-HT turnover can be obtained by administering probenecid, which blocks the transport of acidic metabolites out of CSF, so that their rate of accumulation can be used as an index of 5-HT turnover (Goodwin, Post, Dunner, & Gordon, 1973). Studies using the probenecid technique report that 5-HIAA accumulation was decreased in 40 to 50% of depressed patients (Goodwin et al., 1973; van Praag, 1980). Interestingly, this same subgroup of patients has been reported to improve during treatment with the 5-HT amino acid precursor, 5-HTP (van Praag, 1980) (more about this later).

Urinary Metabolites: Studying urine to figure out what is happening in the brain has been compared to analyzing the Potomac river in an attempt to determine what the President had for lunch. Nevertheless, urinary MA metabolites are more accessible than brain, CSF, or even blood. The most studied of the urinary MA metabolites in depression is the major NE metabolite MHPG. A majority of urinary MHPG is supposedly derived from central nervous system (CNS) NE metabolism, which suggests that MHPG levels should reflect central NE turnover (deMet & Halaris, 1969). However, this remains controversial: Estimates of central contributions of MHPG to the urine pool range from 20 to 70% (Blombery, Kopin, Gordon, et al., 1980; Maas, Hattox, & Greene, 1979).

Like CSF levels of NE and MHPG, urinary levels of MHPG are also elevated in the manic phase of bipolar illness, in contrast with the depressive phase (Jones, Maas, Dekirmenjian, & Fawcett, 1973; van Praag, 1980). In bipolar patients, changes in urinary MA metabolites appear to precede mood swings (Jones et al., 1973), and there is general agreement that depressed bipolars excrete less MHPG than healthy controls (Jones et al., 1973; Jones, Maas, Dekirmenjian, & Sanchez, 1975; Schildkraut, Orsulak, Schatzberg, et al., 1978a; Schildkraut, Orsulak, LaBrie, et al., 1978b). In unipolar depressives, however, equivocal results have been obtained. Some reports indicate lower excretion in unipolar endogenous depressives as compared with healthy controls or patients with characterological depressions (Schildkraut et al., 1978a; Schildkraut et al., 1978b), but others do not (Beckmann & Goodwin, 1980). Earlier reports on this question are hard to interpret because they failed to specify depressive subtypes—e.g., bipolar or unipolar, primary or secondary, endogenous or other.

For proper design and interpretation of studies, it must be noted that the normal range of daily urinary MHPG excretion is very wide—900 to 3,500 mg daily (Hollister, Davis, Overall, & Anderson, 1978). This may be influenced by diet (Muscettola, Wehr, & Goodwin, 1977), mental state and anxiety (Sweeney, Maas, & Heninger, 1978), physical activity (Ebert, Post, & Goodwin, 1972), and state of sympathetic nervous system activity (Cymerman & Francesconi, 1975; Hollister, Prusmack, Knopes, & Kanaske, 1980; Izzo, Horwitz, & Kaiser, 1979). Furthermore, the observed MHPG decreases in unipolar patients are small: The range of MHPG excretion in unipolar depressed patients is 800 to 3,020 μg daily (Hollister, Davis, & Berger, 1980). Therefore, unless conditions such as diet, activity, and stress are carefully controlled in both subjects and healthy controls, variations within the normal range may obscure differences.

Several groups of investigators have observed a correlation between pretreatment urinary MHPG excretion and drug response. Specifically, depressed patients who excrete the lowest amounts of urinary MHPG tend to show a better response to drugs which act primarily on NE systems, compared to depressed patients with high levels of urinary MHPG (Bechmann & Goodwin, 1975; Fawcett, Maas, & Dekirmenjian, 1972; Hollister et al., 1980). However, there is not universal agreement on this point (Ridges, Bishop, & Goldberg, 1980).

Urinary 5-HIAA is even more susceptible than MHPG to environmental, dietary, and peripheral variations, and is therefore not a reliable index of central nervous system function (Nomra, Colmenares, & Wurtman, 1977).

Precursors

Biochemical Background

In mammalian brain, the CAs, DA and NE, and the IA, 5-HT, are synthesized from their amino acid precursors, L-tyrosine and L-tryptophan, respectively (Wurtman, 1980). The initial and rate-limiting steps in their syntheses are the hydroxylation of the aromatic ring of tyrosine by tyrosine hydroxylase (Nagatsu, Levitt, & Udenfriend, 1964) to form DOPA and the hydroxylation of the indole core of tryptophan by tryptophan hydroxylase (Friedman, Kappelman, & Kaufman, 1972) to form 5-HTP. Both of these amino acid intermediates—DOPA and 5-HTP—are rapidly decarboxylated by the enzyme aromatic L-amino acid decarboxylase to form the amine neurotransmitters DA and 5-HT (Lovenberg, Weissbach, & Udenfriend, 1962). In neurons that contain the enzyme dopamine-β-hydroxylase, DA is converted to NE (Axelrod, 1972).

The enzyme tryptophan hydroxylase is not normally saturated with its amino acid substrate in vivo and, therefore, the rate of brain 5-HT synthesis can be influenced by changes in brain tryptophan concentration (Fernstrom & Wurtman, 1971). Brain tryptophan concentration, in turn, varies directly with its plasma concentration and indirectly with the sum of the plasma concentration of the other large neutral amino acids (LNAA)—leucine, isoleucine, valine, phenylalanine, tyrosine—which compete with it for uptake into the brain (Fernstrom & Wurtman, 1972). Thus, tryptophan administration, or the ingestion of a carbohydrate-containing meal (which elicits insulin secretion, thereby lowering the plasma level of competing LNAAs), results in increases in brain tryptophan and, hence, in brain 5-HT.

It also has been said that the blood concentration of non-albumin-bound tryptophan determines the rate of tryptophan uptake into brain, but this remains controversial (Young & Sourkes, 1977).

Just as tryptophan hydroxylase is not fully saturated in vivo, the same holds true for tyrosine hydroxylase. Only 75% of tyrosine hydroxylase is saturated, as estimated by Carlsson and Lindqvist (1978). This means that raising (e.g., by tyrosine injection or consumption of a protein-containing meal) or lowering (by injection of a competing LNAA) brain tyrosine concentrations in rats can cause parallel changes in CA synthesis, as measured by the rate at which brain DOPA accumulates after decarboxylase inhibition (Gibson & Wurtman, 1977; Wurtman, Larin, Mostafapour, & Fernstrom, 1974). However, increases in brain tyrosine levels lead to increased NE release, as measured by the accumulation of the NE metabolite 3-methoxy-4-hydroxyphenylglycol sulfate (MHPG-SO|) (after probenecid, which blocks its egress from rat brain, or in animals subjected to cold stress, which increases NE turnover in brain) (Gibson & Wurtman, 1978).

In the basal state, DA neurons may be less dependent on tyrosine levels than NE neurons. Thus, administration of tyrosine to animals receiving probenecid does not result in further increases in the major DA metabolite, homovanillic acid (HVA). However, when DA receptors are blocked by pretreatment with haloperidol, thereby accelerating the firing rates of DA neurons, tyrosine does significantly elevate striatal HVA (Scally, Ulus, & Wurtman, 1977). Similarly, lesions that deplete DA stores and increase firing and turnover in central DA neurons also appear to increase the effects of tyrosine administration.

The response to tyrosine in NE systems also is enhanced when neuronal firing and amine turnover are increased. In hypertensive rats, tyrosine administration results in decreased blood pressure and increased concentration of NE metabolites in the brainstem (Sved, Fernstrom, & Wurtman, 1979). Presumably, NE neurons in the brainstem of these animals are deficient to start, which results in hypertension. The exisiting NE neurons are firing rapidly in a vain attempt to lower the pathologically elevated blood pressure. In this situation, tyrosine can enhance NE release, leading to increased NE transmission in the brainstem and deceased peripheral sympathetic outflow, which serves to lower blood pressure.

Probably the ability of tyrosine to accelerate CA synthesis depends quantitatively on the firing frequency of CA-containing neurons. Therefore, it is possible that in disease states characterized by deficiencies in NE or DA, in which neurons may be firing more rapidly (in an attempt to compensate for the deficiencies), there could be greater sensitivity of CA neurons to tyrosine administration.

The intermediate metabolites DOPA and 5-HTP also have been administered experimentally to increase central CA and IA activity, respectively, since they readily traverse the blood-brain barrier. Normally, concentrations of DOPA and 5-HTP in the brain are undetectable (Carlsson & Lindqvist, 1978); as soon as they are formed, they are rapidly decarboxylated to the neurotransmitters DA and 5-HT, respectively.

Although it is a precursor of the CA's DA and NE, DOPA can be transported into IA, as well as CA neurons. In DA neurons, DOPA is decarboxylated to DA and acts to replace the endogenously occurring neurotransmitter. In 5-HT neurons it is decarboxylated to DA and can displace or release 5-HT from its normal sites (Ng, Chase, Colburn, & Kopin, 1970), thus acting as a false neurotransmitter and interfering with normal 5-HT function. Therefore, DOPA administration leads to increased brain DA but decreased 5-HT; NE remains relatively unaffected (Everett & Borcherding, 1970; Karobath, Diaz, & Huttunen, 1971).

Under normal conditions, then, tyrosine may be preferable for increasing NE synthesis, while DOPA appears more specific for increasing DA synthesis. Furthermore, tyrosine administration has fewer effects on the IA system; although both may decrease brain tryptophan uptake competitively (Rieder, 1980), DOPA can also displace 5-HT from its storage sites, further decreasing brain 5-HT (Karobath et al., 1971).

Just as DOPA enhances CA activity at the expense of IA activity, the IA precursor 5-HTP creates the opposite problem. The administration of 5-HTP effectively raises brain 5-HT, but displaces NE after decarboxylation in CA-containing neurons and lowers brain NE in experimental animals (Lichtensteiger, Mutzner, & Langemann, 1967).

Compared to the intermediate precursors DOPA and 5-HTP, tyrosine and tryptophan may be more specific in increasing their respective neurotransmitters, NE and 5-HT. Their conversion depends on uptake into neurons containing the specific enzymes tyrosine or tryptophan hydroxylase, which are highly localized to those cells containing NE and 5-HT, respectively (Friedman et al., 1972; Nagatsu et al., 1964). Although they can compete with one another for uptake into brain, this effect is less than that seen with L-DOPA or 5-HTP on an equimolar basis.

The possibility has been raised that some depressed patients may have a reduced ability to convert orally administered tryptophan to 5-HTP (van Praag, 1980). It is conceivable that in such individuals, administration of the precursor 5-HTP may be more advantageous than treatment with tryptophan. Similarly, one could speculate that if a similar situation exists regarding NE, some depressed patients might respond preferentially to DOPA.

Precursor Studies in the Treatment of Depression

Unlike the biogenic amines DA, NE, and 5-HT, their precursors—DOPA, tyrosine, 5-HTP, and tryptophan—easily cross the blood-brain barrier. Thus, the precursors can be administered systemically to increase their respective amines' rates of synthesis. L-DOPA raises brain DA level, as measured by increased CSF HVA (Bunney, Brodie, Murphy, & Goodwin, 1971). L-DOPA probably has little effect on NE level and may actually decrease brain 5-HT, as observed by decreases in CSF 5-HIAA (Goodwin et al., 1973; Bunney et al., 1971). Tryptophan and 5-HTP both raise brain 5-HT levels, producing increases in CSF 5-HIAA (Goodwin et al., 1973; van Praag, 1980). 5-HTP appears to compete with tyrosine's entry into brain, which probably lowers DA activity and has been observed to produce decreased CSF HVA levels (Meyer, Welch, Deshmukh, et al., 1977). Orally administered tyrosine raises plasma tyrosine in man and increases urinary excretion of NE and MHPG (Glaeser, Melamed, Growdon, & Wurtman, 1979).

CA precursors: DOPA—Several trials of DOPA (with and without peripheral decarboxylase inhibitors) for the treatment of endogenous depression have been conducted. Results have generally been poor (Bunney et al., 1971; Carroll, 1972; Dunner & Fieve, 1975; Goodwin et al., 1971; Klerman, Schildkraut, Hasenbush, et al., 1963; Mendels, Stinnett, Burns, & Frazer, 1975; Murphy et al., 1973, Persson & Wålinder, 1971; van Praag, 1977,1980), although DOPA may activate some patients with psychomotor retardation. Among patients with prior manic episodes, periods of hypomania have sometimes been induced (Bunney et al., 1971; Goodwin et al., 1971; Murphy et al., 1973), which were alleviated by decreasing or discontinuing DOPA. Additionally, psychotic features have often been aggravated by DOPA (Goodwin et al., 1971).

It is conceivable that the clinical effects of DOPA are due to increases in brain DA, rather than NE activity. In fact, urinary and CSF levels of the DA metabolite HVA increase linearly with the administered dose of DOPA, but urinary concentrations of the NE metabolite MHPG do not increase until doses of DOPA exceed 4 g (Bunney et al., 1971; Goodwin et al., 1971). Furthermore, as noted earlier, DOPA administration can decrease central 5-HT activity, which might make some patients more depressed. In fact, some parkinsonian patients who receive high doses of DOPA actually develop severe depression (Goodwin et al., 1971). Also, some of the unwanted effects associated with DOPA have been attributed to its competition with uptake and lowering of brain levels of tyrosine and tryptophan (Lichtensteiger et al., 1967). L-DOPA is also associated with many other unwanted and toxic effects such as nausea and vomiting, blood pressure changes, and cardiac rhythm disturbances (Langrall & Joseph, 1972).

CA precursors: Tyrosine—Few trials with tyrosine have been conducted, since it had been believed that the enzyme tyrosine hydroxylase was fully saturated in vivo, and hence that no increase in CA levels could be achieved by tyrosine administration. Indeed, no change in brain NE *levels* is seen in animals treated acutely with tyrosine; however, significant increases do occur in the *rate* of synthesis (Carlsson & Lindqvist, 1978; Gibson & Wurtman, 1977; Wurtman et al., 1974). In addition, re-evaluations of the amount of saturation of tyrosine hydroxylase have suggested that normally it is 75% saturated, so that there is some leeway for increasing synthesis. Moreover, when conditions of deficient CA neurotransmitters exist, the effect of exogenous tyrosine is even more pronounced. As discussed earlier, for instance, tyrosine injection increases the level of MHPG-SO_4 in the brainstem of spontaneously hypertensive rats and lowers blood pressure by a central mechanism (Sved et al., 1979). Therefore, tyrosine may be more specific than other means for increasing brain NE synthesis, particularly if there is a preexisting deficiency. This could make tyrosine particularly useful for treating human diseases characterized by such a deficiency.

One early report on the use of tyrosine in depression failed to find an effect, but there was no indication of the dose used or the length of treatment (Carroll, 1972). In 1980, we published the results of a single-case, placebo-controlled, double-blind crossover trial (Gelenberg, Wojcik, Growdon, et al., 1980). A 30-year-old woman with primary unipolar depression had to discontinue an antidepressant drug because of unwanted effects. As an alternative, she was treated with tyrosine, 100 mg/kg/day by mouth, in three divided doses. Her depression improved markedly after 2 weeks of tyrosine therapy, and within 1 week of placebo substitution her depressive symptoms began to return. The reinstitution of tyrosine therapy was followed by a marked improvement in depression. No adverse effects were noted. Plasma tyrosine levels drawn 2 hours after a dose were approximately double those measured during placebo ingestion. Soon after, Goldberg reported symptom improvement following nonblind administration of tyrosine to two patients who had previously responded to amphetamine (Goldberg, 1980). Perhaps in these patients tyrosine was specifically correcting an NE deficiency, since amphetamine responders have been found to have relatively low levels of urinary MHPG (Fawcett et al., 1972).

We now have data on an additional six patients who have entered an ongoing double-blind, placebo-controlled pilot study. Three patients were randomly assigned to placebo and three to oral tyrosine (100 mg/kg/d, in three divided doses), for a 4-week trial. During tyrosine treatment, the mean score on the Hamilton Depression Rating Scale (HAM-D) was reduced by 55%, from a initial mean of 21.7 to a final score of 9.7 (*see* Table). In the placebo group, only a small reduction occurred, from an initial mean score of 25.7 to a final mean of 21.3. The three tyrosine-treated patients showed impressive improvement on their HAM-D scores (Table), while two of the three placebo patients had to be withdrawn from the study: One patient deteriorated and became suicidal; the other asked to be removed from treatment because of lack of improvement.

Table

Hamilton Score Changes with Tyrosine and Placebo

			Hamilton Depression Rating Scale (HAM-D)	
Patient	**Age**	**Sex**	**Initial Score**	**Final Score***
Tyrosine (100 mg/kg)				
1 (KC)	36	M	22	19
2 (FB)	41	M	20	3
3 (JS)	56	F	23	7
Mean ± SE			21.7 ± 1.5	9.7 ± 8.3
Placebo				
4 (NM)	46	M	25	18
5 (JB)	45	M	30	21
6 (DG)	51	M	22	25
Mean ± SE			25.7 ± 4.0	21.3 ± 3.5

*Final score was determined 4 weeks after beginning of treatment, except for Patients #4 and #6, who were withdrawn from the study early and evaluated at the time of withdrawal, 15 days and 7 days, respectively.

Interestingly, there seems to be a correlation between the change in HAM-D score (pretreatment vs. posttreatment) and the change in fasting plasma tyrosine level (percent change from initial level) (*see* Figure), which is similar to what has been reported during tryptophan therapy (Chouinard, Young, Annable, & Sourkes, 1979).

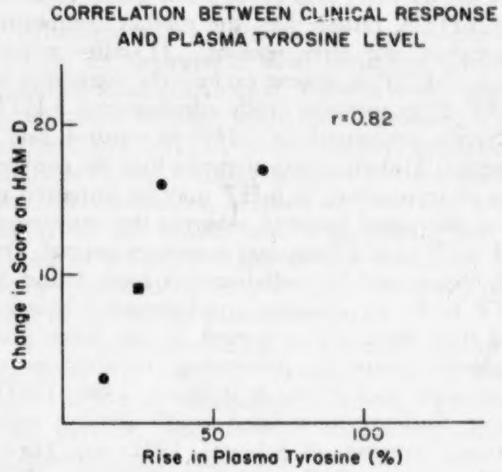


FIGURE. Correlation between clinical response and plasma tyrosine level.
● = patients receiving tyrosine
■ = patients receiving placebo

Change in score on the Hamilton Depression Rating Scale represents the initial value (Day 0) minus the final value (Day 28).

Rise in plasma tyrosine represents the percent increase in fasting plasma tyrosine level on Day 28 from the initial level on Day 0. Tyrosine was measure fluorometrically by the method of Waalkes and Undenfriend.

Other studies have suggested possible abnormalities of peripheral amino acid metabolism in depression. There are indications that peripheral tyrosine metabolism and uptake into brain may be altered in depressed patients. The normal 11 a.m. peak in blood tyrosine level is absent in the depressed phase (Benkert, Renz, Marano, & Matussek, 1971; Kishimoto & Hama, 1976), and there may be less transport of tyrosine into brain (Gaillard & Tissot, 1979). Even if these metabolic changes are not primary factors in the genesis of depression, decreases in plasma tyrosine could aggravate existing central compromises in NE function.

IA precursors: 5-HTP—The use of the intermediate precursor of 5-HT, 5-HTP, for the treatment of depressed patients was reviewed recently by van Praag (1980). His group chose to use 5-HTP, rather than the mother compound tryptophan, for three reasons: 1) unlike tryptophan, 5-HTP is almost exclusively converted to 5-HT; 2) in animals, orally administered 5-HTP is partly converted to 5-HT in central 5-HT neurons; 3) their group suggests that the conversion of tryptophan to 5-HT may be impaired in some depressed patients, whereas the conversion of 5-HTP to 5-HT appears to remain normal. Dr. van Praag and his collaborators have found 5-HTP to be an effective antidepressant acutely, and they have also reported it may have prophylactic value in preventing recurrences of depression (van Praag & deHaan, 1980; 1981). These findings have been confirmed by some (Angst, Woggon, & Schoepf, 1977; van Hiele, 1980), but not all (Brodie, Sack, & Siever, 1973; Takahashi, Takahashi, & Masamura, 1976) investigators.

Assuming the possibility that 5-HTP is an effective antidepressant, negative results may have reflected some or all of the following:

1) Study Design: Some studies used numbers of patients that were inadequate to establish significant differences from placebo. Moreover, in some, patients were treated for periods of time (1 to 2 weeks) that are too brief to test antidepressant effects.

2) Dosages: There is a probability that 5-HTP has a "therapeutic window" (van Praag, 1980). In some studies, dosages may have been inadequate; in others, excessive levels of 5-HTP could have resulted in decreases in DA and NE concentrations and activity, leading to countertherapeutic outcomes.

3) Selection of Patients: There is evidence that a subgroup of depressed patients might have a "serotonergic" depression and, in fact, patients who exhibit increased accumulation of 5-HIAA in CSF after probenecid administration have been reported to respond best to 5-HTP therapy (van Praag & deHaan, 1979). Also, there is preliminary evidence that 5-HTP may enhance the action of the serotonergic tricyclic antidepressant clomipramine and MAO inhibitor antidepressants (van Praag, 1980).

Dr. van Praag typically administers 5-HTP in combination with an agent such as carbidopa, which inhibits peripheral decarboxylase. This diminishes the conversion of 5-HTP to 5-HT outside of the brain, thereby a) increasing the amount of 5-HT that is centrally available, and b) decreasing unwanted effects. One of the most common and limiting of these unwanted effects has been gastrointestinal upset, attributed to direct effects of 5-HTP on stomach and intestinal walls. To circumvent this problem, Dr. van Praag uses an enteric-coated capsule.

IA precursors: Tryptophan—Tryptophan has undergone many trials as an antidepressant (Bunney et al., 1971; Carroll, 1972; Chouinard et al., 1979; Dunner & Fieve, 1975; Mendels et al., 1975; van Praag, 1977; van Praag, 1980), but unfortunately no consensus has emerged about its efficacy. In fact, a "weigh in" of positive vs negative data would likely be equal. Several excellent reviews over the past few years have evaluated the wide range of studies of tryptophan as an antidepressant (Cole, Hartmann, & Brigham, 1980; Cooper, 1979; Growdon, 1979; van Praag, 1980; Wirz-Justice, 1977).

As was the case with 5-HTP, we will make the assumption that tryptophan actually has some merit as an antidepressant and will attempt to explain the negative data. There is a heuristic advantage to this approach, as it can help in the design of future studies.

1) Inadequacy of study design—Similar to the case with 5-HTP, some studies with tryptophan have used inadequate patient samples for too brief periods of time.

2) Dosage—Evidence has emerged of a possible "therapeutic window" for tryptophan: in six separate studies in which tryptophan was found to be an effective antidepressant, the mean dose was 6 g/day; in seven other studies in which it was ineffective, the mean dose was 8.7 g/day (Young, Gibson, & Gauthier, in press). There is evidence that the therapeutic range may be different for bipolar compared to unipolar patients (Goldberg, 1980). There is also evidence that the co-administration of an inhibitor of tryptophan pyrrolase in

liver may shift the therapeutic window toward lower doses (Goldberg, 1980).

Possible explanations for the therapeutic window include: a) greater induction at higher tryptophan doses of the liver enzyme tryptophan pyrrolase, which catabolizes tryptophan; b) competition of tryptophan with tyrosine for uptake into brain, so that excessive doses would lower brain NE synthesis; c) increased formation at high doses of other active amines, such as tryptamine, which may adversely affect normal 5-HT function (Young et al., in press).

It is interesting that several more recent studies failed to find an antidepressant effect of tryptophan (Cooper & Datta, 1980; Wålinder, Carlsson, Persson, & Wallin, 1980). In each, the dosages were above the therapeutic window determined by Chouinard (1979).

3) Heterogeneity of patients—As noted above, there is evidence that bipolar and unipolar patients may respond differently to tryptophan. In addition, as was the case with 5-HTP, it is conceivable that only those patients whose depression is characterized by low 5-HT activity will respond selectively to tryptophan treatment.

Another source of interpatient variability concerns plasma levels of amino acids. Brain tryptophan concentrations is determined, in part, by the ratio of plasma tryptophan to the plasma concentrations of competing LNAA (see page 10). Consistent with this observation, Møller and colleagues have reported that patients with the lowest tryptophan/LNAA ratio achieved a remission frequency of 80% by Day 14 of tryptophan therapy, while patients at the higher end of the spectrum did not benefit from tryptophan more than from placebo (Møller, Kirk, & Honore, 1980). Therapeutic efficacy has also been related to increases in fasting plasma tryptophan during tryptophan treatment: the larger the increase, the greater the improvement in score on a standard depression rating scale (Chouinard et al., 1979).

4) Interaction with other antidepressants—Until more is known about the effects of administering tryptophan alone, it may be difficult to puzzle out the effectiveness of tryptophan as an adjunct to antidepressant drug therapy. For example, Wålinder and associates (1976) found that tryptophan hastened the onset of therapeutic action of clomipramine, a particularly potent inhibitor of 5-HT uptake (although one whose active metabolite also blocks NE uptake). By contrast, however, Wålinder and his colleagues were unable to find any advantage of combining tryptophan with zimelidine, an even more potent inhibitor of 5-HT uptake Wålinder, Carlsson, & Persson, 1981).

Conclusion

Although none of the amino acid precursors can do for depression what penicillin does for pneumococcal pneumonia, there is every reason to continue clinical trials with tyrosine, tryptophan, and 5-HTP. Unfortunately, the lack of pharmaceutical industry support to fund studies on these substances, coupled with the easy availability of the amino acid tryptophan, has resulted in widespread use of this substance and many publications but, at least until recently, little in the way of conclusive data.

Aside from attending to generally accepted methods of clinical research in depression—including adequate numbers, adequate trial periods, and careful distinction among phenomenologic subtypes—future studies on these substances would do well to incorporate important biochemical markers such as plasma amino acid levels, urine, and possibly CSF amine metabolites, careful control of diet, and attention to optimal levels of drug dosages.

It is possible that a subtype of depressed patient may respond to one or several of these precursors. Possibly, for some patients a combination of a 5-HT and an NE precursor may be optimal therapy. If so, it is conceivable that these agents, alone or in combination with antidepressant drugs, may enhance therapy for depression. In any case, studies designed to test out these hypotheses will clearly shed new light on the biochemistry and the pharmacotherapy of depression and of brain function in general.

Acknowledgment: The author would like to thank Mrs. Emily N. Prins for typing and proofing the manuscript.

References

Angst, J., Woggon, B., and Schoepf, J. The treatment of depressions with L-5-hydroxytryptophan versus imipramine. *Arch. Psychiatr. Nervenkr.*, 24:175-186, 1977.

Åsberg, M., Thorén, P., and Träskman, L. 'Serotonin depression': A biochemical subgroup within the affective disorders? *Science*, 191:478-480, 1976.

Axelrod, J. Dopamine-beta-hydroxylase: Regulation of its synthesis and release from nerve terminas. *Pharmacol. Rev.*, 24:233-243, 1972.

Beckmann, H., and Goodwin, F.K. Antidepressant response to tricyclics and urinary MHPG in unipolar patients—clinical response to imipramine or amitriptyline. *Arch. Gen. Psychiatry*, 32:17-21, 1975.

Beckmann, H., and Goodwin, F.K. Urinary MHPG in subgroups of depressed patients and normal controls. *Neuropsychobiology*, 6:91-100, 1980.

Benkert, O., Renz, A., Marano, C., and Matussek, N. Daytime plasma levels in endogenous depressive patients. *Arch. Gen. Psychiatry*, 25:359-363, 1971.

Birkmayer, W., and Riederer, P. Biochemical post-mortem findings in depressed patients. *J. Neural Transm.*, 37:95-109, 1975.

Blombery, P.A., Kopin, I.J., Gordon, E.K., et al. Conversion of MHPG to vanillylmandelic acid; Implications for the importance of urinary MHPG. *Arch. Gen. Psychiatry*, 37:1095-1098, 1980.

Bopp, B., and Biel, J.H. Antidepressant drugs. *Life Sci.*, 14:415-423, 1974.

Bourne, H.R., Bunney, W.E., Colburn, R.W., et al. Noradrenaline, 5-hydroxytryptamine, and 5-hydroxyindoleacetic acid in hindbrains of suicidal patients. *Lancet*, 2:805-808, 1968.

Bridges, P.K., Bartlett, J.R., and Sepping, P. Precursors and metabolites of 5-hydroxytryptamine and dopamine in the ventricular cerebrospinal fluid of psychiatric patients. *Psychol. Med.*, 6:399-405, 1976.

Brodie, H.K.H., Sack, R., and Siever, L. Clinical studies of L-5-hydroxytryptophan in depression. In: Barchas, J., and Usdin, E. (eds.), *Serotonin and Behavior*. New York: Academic Press, 1973, pp. 549-559.

Bunney, W.E., Brodie, H.K.H., Murphy, D.L., and Goodwin, F.K. Studies of alpha-methyl-para-tyrosine, L-DOPA, and L-tryptophan in depression and mania. *Am. J. Psychiatry*, 127:872-881, 1971.

Carlsson, A., and Lindqvist, M. Dependence of 5-HT and catecholamine synthesis of concentrations of precursor amino acids in rat brain. *Naunyn Schmiedesbergs Arch. Pharmacol.*, 303:157-164, 1978.

Carroll, B.J. Monoamine precursors in the treatment of depression. *Clin. Pharmacol. Ther.*, 12:743-761, 1972.

Chouinard, G., Young, S.N., Annable, L., and Sourkes, T.L. Tryptophan nicotinamide, imipramine, and their combination in depression. *Acta Psychiatr. Scand.*, 59:395-414, 1979.

Cole, J.O., Hartmann, E., and Brigham, P. L-tryptophan: Clinical studies. *McLean Hosp. J.*, 5:37-71, 1980.

Cooper, A.J. Tryptophan antidepressant: Physiological sedative, fact or fancy? *Psychopharmacology (Berlin)*, 61:97-102, 1979.

Cooper A.J., and Datta, S.R. A placebo-controlled evaluation of L-tryptophan in depression in the elderly. *Can. J. Psychiatry*, 25:386-390, 1980.

Cymerman, A., and Francesconi, R.F. Alteration of circadian rhythmicities of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) and vanillylmandelic acid (VMA) in man during cold exposure. *Life Sci.*, 16:225-236, 1975.

deMet, E.M., and Halaris, A.E. Origin and distribution of 3-methoxy-4-hydroxyphenylglycol in body fluids. *Biochem. Pharmacol.*, 28:3043-3050, 1979.

Dunner, D.L., and Fieve, R.R. Affective disorder: Studies with amine precursors. *Am. J. Psychiatry*, 132:180-183, 1975.

Ebert, M.H., Post, R.M., and Goodwin, F.K. Effect of physical activity on urinary MHPG excretion in depressed patients. *Lancet*, 2:766, 1972.

Everett, G.M., and Borcherding, J.W. L-DOPA: Effect on concentrations of dopamine, norepinephrine, and serotonin in brain of mice. *Science*, 168:849-850, 1970.

Fawcett, J., Maas, J.W., and Dekirmenjian, H. Depression and MHPG excretion: Response to dextroamphetamine and tricyclic antidepressants. *Arch. Gen. Psychiatry*, 26:246-251, 1972.

Fernstrom, J.D., and Wurtman, R.J. Brain serotonin content: Physiological dependence of plasma tryptophan levels. *Science*, 173:149-152, 1971.

Fernstrom, J.D., and Wurtman, R.J. Brain serotonin content: Physiological regulation by plasma neutral amino acids. *Science*, 178:414-416, 1972.

Friedman, P.A., Kappelman, A.H., and Kaufman, S. Partial purification and characterization of tryptophan hydroxylase from rabbit hindbrain. *J. Biol. Chem.*, 247:4165-4173, 1972.

Gaillard, J.M., and Tissot, R. Blood-brain movements of tryptophan and tyrosine in manic-depressive illness and schizophrenia. *J. Neural Transm. (Suppl.)*, 15:189-196, 1979.

Garver, D.L., and Davis, J.M. Biogenic amine hypotheses of affective disorders. *Life Sci.*, 24:383-394, 1979.

Gelenberg, A.J. How do antidepressants work? *MGH Biol. Ther. Psychiatry Newsl.*, 3:33, 1980.

Gelenberg, A.J., Wojcik, J.D., Growdon, J.H., et al. Tyrosine for the treatment of depression. *Am. J. Psychiatry*, 137:622-623, 1980.

Gibson, C.J., and Wurtman, R.J. Physiological control of brain catechol synthesis by brain tyrosine concentration. *Biochem. Pharmacol.*, 26:1137-1142, 1977.

Gibson, C.J., and Wurtman, R.J. Physiological control of brain norepinephrine synthesis by brain tyrosine concentration. *Life Sci.*, 22:1399-1406, 1978.

Glaeser, B.S., Melamed, E., Growdon, J.H., and Wurtman, R.J. Elevation of plasma tyrosine after a single oral dose of L-tyrosine. *Life Sci.*, 25:265-272, 1979.

Goldberg, I.K. L-tyrosine in depression. *Lancet*, 2:364, 1980.

Goodwin, F.K., Murphy, D.L., Brodie, H.K.H., and Bunney, W.E. Levo-DOPA: Alterations in behavior. *Clin. Pharmacol. Ther.*, 13:383-396, 1971.

Goodwin, F.K., Post, R.M., Dunner, D.L., and Gordon, E.K. Cerebrospinal fluid amine metabolites in affective illness: The probenecid technique. *Am. J. Psychiatry*, 130:73-79, 1973.

Gordon, E.K., and Oliver, J. 3-Methoxy-4-hydroxyphenylethyleneglycol in human cerebrospinal fluid. *Clin. Chim. Acta*, 35:145-150, 1971.

Growdon, J.H. Neurotransmitter precursors in the diet: Their use in the treatment of brain diseases. In: Wurtman, R.J., and Wurtman, J.J. (eds.), *Nutrition and the Brain*. Vol. 3: *Disorders of Eating and Nutrients in Treatment of Brain Diseases*. New York:Raven Press, 1979, pp. 117-181.

Hollister, L.E., Davis, K.L., Overall, J.E., and Anderson, T. Excretion of MHPG in normal subjects: Implications for biological classification of affective disorders. *Arch. Gen. Psychiatry*, 35:1410-1415, 1978.

Hollister, L.E., Prusmack, J.J., Knopes, K., and Kanaske, K. Asthma and alcohol withdrawal as sources of artifact in urinary excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG). *Commun. Psychopharmacol.*, 4:135-140,1980.

Hollister, L.E., Davis, K.L., and Berger, P.A. Subtypes of depression based on excretion of MHPG and response to nortriptyline. *Arch. Gen. Psychiatry*, 37:1107-1110, 1980.

Izzo, J.L., Horwitz, D., and Keiser, H.R. Reduction in human urinary MHPG excretion by guanethidine: Urinary MHPG as an index of sympathetic nervous activity. *Life Sci.*, 24:1403-1406, 1979.

Jones, F.D., Maas, J.W., Dekirmenjian, H., and Fawcett, J.A. Urinary catecholamine metabolites during behavioral changes in a patient with manic-depressive cycles. *Science*, 179:300-302, 1973.

Jones, F.D., Maas, J.W., Dekirmenjian, H., and Sanchez, J. Diagnostic subgroups of affective disorders and the urinary excretion of catecholamine metabolites. *Am. J. Psychiatry*, 132:1141-1148, 1975.

Karobath, M., Diaz, J.L., and Huttunen, M.O. The effect of L-DOPA on the concentrations of tryptophan, tyrosine, and serotonin in the rat brain. *Eur. J. Pharmacol.*, 14:393-396, 1971.

Kishimoto, H., and Hama, Y. The level and diurnal rhythm of plasma tryptophan and tyrosine in manic-depressive patients. *Yokohama Med. Bull.*, 27:89-97, 1976.

Klerman, G.L., Schildkraut, J.J., Hasenbush, L.L., et al. Clinical experience with dihydroxyphenylalanine (DOPA) in depression. *J. Psychiatr. Res.*, 1:289-297, 1963.

Langrall, H.M., and Joseph, C. Status of the clinical evaluation of L-DOPA in the treatment of Parkinson's disease and syndrome. *Clin. Pharmacol. Ther.*, 12:323-331, 1972.

Lecrubier, Y., Puech, A.J., Frances, H., et al. Beta-adrenergic stimulation and antidepressant activity. *Acta Psychiatr. Scand.*, (Suppl.) 63:290, 1981.

Lichtensteiger, W., Mutzner, U., and Langemann, H. Uptake of 5-hydroxytryptamine and 5-hydroxytryptophan by neurons of the central nervous system normally containing catecholamines. *J. Neurochem.*, 14:489-497, 1967.

Lloyd, K.J., Farley, I.J., and Deck, J.H.N. Serotonin and 5-hydroxyindoleacetic acid in discrete areas of the brainstem of suicide victims and control patients. *Adv. Biochem. Psychopharmacol.*, 11:387-397, 1974.

Lovenberg, W., Weissbach, H., and Udenfriend, S. Aromatic L-amino acid decarboxylase. *J. Biol. Chem.*, 237:89-93, 1962.

Maas, J.W. Biogenic amines and depression. *Arch. Gen. Psychiatry*, 32:1357-1361, 1975.

Maas, J.W. Neurotransmitters in depression. *Trends Neurosci.*, 2:306-308, 1979.

Maas, J.W., Hattox, S.E., and Greene, N.M. 3-Methoxy-4-hydroxyphenylglycol (MHPG) production by human brain in vivo. *Science*, 205:1025-1027, 1979.

Melamed, E., Hefti, F., and Wurtman, R.J. Tyrosine administration increases striatal dopamine synthesis in haloperidol-treated rats. *J. Neural Transm.*, 41:1-6, 1977.

Mendels, J., Stinnett, J.L., Burns, D., and Frazer, A. Amine precursors and depression. *Arch. Gen. Psychiatry*, 32:22-30, 1975.

Meyers, J.S., Welch, K.M.A., Deshmukh, V.D., et al. Neurotransmitter precursor amino acids in the treatment of multi-infarct dementia and Alzheimer's disease. *J. Am. Geriatr. Soc.*, 25:289-298, 1977.

Móller, S.E., Kirk, L., and Honore, P. Relationship between plasma ratio of tryptophan to competing amino acids and the response to L-tryptophan treatment in endogenously depressed patients. *J. Affect. Disord.*, 2:47-59, 1980.

Murphy, D.L., Goodwin, F.K., Brodie, H.K.H., and Bunney, W.E. L-DOPA, dopamine, and hypomania. *Am. J. Psychiatry*, 130:79-82, 1973.

Muscettola, G., Wehr, T., and Goodwin, F.K. Effect of diet on urinary MHPG excretion in depressed patients and normal control subjects. *Am. J. Psychiatry*, 134:914-916, 1977.

Nagatsu, T., Levitt, M., and Udenfriend, S. Tyrosine hydroxylase: The initial step in norepinephrine biosynthesis. *J. Biol. Chem.*, 239:2910-2917, 1964.

Ng, K.Y., Chase, T.N., Colburn, R.W., and Kopin, I.J. L-DOPA induced release of cerebral monoamines. *Science*, 170:76-77, 1970.

Nomra, M., Colmenares, J., and Wurtman, R.J. Effect of dietary protein on urinary 5-hydroxyindoleacetic acid levels. *J. Neurochem.*, 29:267-271, 1977.

Papeschi, R., and McClure, D.J. Homovanillic and 5-hydroxyindoleacetic acid in cerebrospinal fluid of depressed patients. *Arch. Gen. Psychiatry*, 25:354-358, 1971.

Persson, T., and Wålinder, J. L-DOPA in the treatment of depressive symptoms. *Br. J. Psychiatry*, 119:277-278, 1971.

Post, R.M., Lake, C.R., Jimerson, D.C., et al. Cerebrospinal fluid norepinephrine in affective illness. *Am. J. Psychiatry*, 135:907-912, 1978,

Ridges, A.P., Bishop, F.M., and Goldberg, I.J.L. Urinary amine metabolites in depression: A combined biochemical and general practice study. II. Biochemical aspects. *J. Int. Med. Res.*, 9(S-3):37-44, 1980.

Rieder, E.R. L-DOPA competes with tyrosine and tryptophan for human brain uptake. *Nutr. Metab.*, 24:417-423, 1980.

Riederer, P., Birkmayer, W., Seeman, D., and Wuketich, S. 4-Hydroxy-3-methoxyphenylglycol as an index of brain noradrenile turnover in endogenous depression. *Acta Psychiatr. Scand.*, (Suppl. 280), 61:251-257, 1980.

Scally, M.D., Ulus, I.H., and Wurtman, R.J. Brain tyrosine levels controls striatal dopamine synthesis in haloperidol-treated rats. *J. Neural Transm.*, 41:1-6, 1977.

Schildkraut, J.J. The catecholamine hypothesis of affective disorders: A review of supporting evidence. *Am. J. Psychiatry*, 122:509-522, 1965.

Schildkraut, J.J., and Kety, S.S. Biogenic amines and emotion. *Science*, 156:21-30, 1967.

Schildkraut, J.J., Orsulak, P.J., Schatzberg, A.F., et al. Toward a biochemical classification of depressive disorders: Part I. *Arch. Gen. Psychiatry*, 35:1427-1433, 1978(a).

Schildkraut, J.J., Orsulak, P.J., LaBrie, R.A., et al. Toward a biochemical classification of depressive disorders: Part II. *Arch. Gen. Psychiatry*, 35:1436-1439, 1978(b).

Shopsin, B., Wilk, S., Gershon, S., et al. Collaborative psychopharmacologic studies exploring catecholamine metabolism in psychiatric disorders. In: Usdin, E., Kopin, I.J., and Barchas, J. (eds.), *Frontiers in Catecholamine Research*. New York: Pergamon Press, 1973, pp. 1173-1179.

Sulser, F., Vetulani, J., and Mobley, P.L. Mode of action of an antidepressant drug. *Biochem. Pharmacol.*, 27:257-261, 1978.

Sved, F.F., Fernstrom, J.D., and Wurtman, R.J. Tyrosine administration reduces blood pressure and enhances brain norepinephrine release in spontaneously-hypertensive rats. *Proc. Natl. Acad. Sci. USA*, 76:3511-3514, 1979.

Sweeney, D.R., Maas, J.W., and Heninger, G.R. State anxiety, physical activity, and urinary 3-methoxy-4-hydroxyphenethyleneglycol excretion. *Arch. Gen. Psychiatry*, 35:1418-1423, 1978.

Takahashi, S., Takahashi, R., and Masamura, I. Measurement of 5-hydroxyindole compounds during 5-HTP treatment in depressed patients. *Folia Psychiatr. Neurol. Jap.*, 30:463-474, 1976.

van Hiele, L.J. L-5-hydroxytryptophan in depression: The first substitution therapy in psychiatry? *Neuropsychobiology*, 6:230-240, 1980.

van Praag, H.M. Significance of biochemical parameters in the diagnosis, treatment, and prevention of depressive disorders. *Biol. Psychol.*, 12:101-131, 1977.

van Praag, H.M., and deHaan, S. Central serotonin metabolism and frequency of depression. *Psychiatr. Res.*, 1:219-224, 1979.

van Praag, H.M. Central monoamine metabolism in depression. I. Serotonin and related compounds. *Compr. Psychiatry*, 21:30-43, 1980(a).

van Praag, H.M. Central monomine metabolism in depression. II. Catecholamines and related compounds. *Compr. Psychiatry*, 21:44-54, 1980(b).

van Praag, H.M., and deHaan, S. Depression vulnerability and 5-hydroxytryptophan prophylaxis. *Psychiatry Res.*, 3: 75-83, 1980.

van Praag, H.M., and deHaan, S. Chemoprophylaxis of depressions: An attempt to compare lithium with 5-hydroxy-tryptophan. *Acta Psychiatr. Scand.*, 63:191-201, 1981.

Wålinder, J., Skott, A., Carlsson, A., et al. Potentiation of the antidepressant action of clomipramine by tryptophan. *Arch. Gen. Psychiatry*, 33:1384-1389, 1976.

Wålinder, J. Carlsson, A., Persson, R., and Wallin, L. Potentiation of the effect of antidepressant drugs by tryptophan. *Acta Psychiatr. Scand.*, 61(S-280):243-249, 1980.

Wålinder, J., Carlsson, A., and Persson, R. 5-HT reuptake inhibitors plus tryptophan in endogenous depression. *Acta Psychiatr. Scand.*, 63(S-290):179-180, 1981.

Wirz-Justice, A. Theoretical and therapeutical potential of indoleamine precursors in affective disorders. *Neuropsychobiology*, 3:199-233, 1977.

Wurtman, R.J., Larin, F., Mostafapour, S., and Fernstrom, J.D. Brain catechol synthesis: Control by brain tyrosine concentration. *Science*, 185:183-184, 1974.

Wurtman, R.J. Control of the synthesis of neurotransmitters by their circulating precursors. In: Usdin, E., Kvetzansky, R., and Kopin, I.J. (eds.), *Catecholamines and Stress: Recent Advances*. Amsterdam:Elsevier/North Holland Biomedical Co., Inc. 1980, pp. 383-391.

Young, S.N. and Sourkes, T.L. Tryptophan in the central nervous system: Regulation and significance. *Adv. Neurochem.*, 2:133-191, 1977.

Young, S.N., Gibson, C.J., and Gauthier, S. Possible explanation for the therapeutic window in antidepressant action of tryptophan. In: Grof, P., and Saxena, B. (eds.), *Advances in Canadian Neuropsychopharmacology*. London: S. Karger Co. (In press)

Dosage and Treatment Strategies in Schizophrenia and Affective Disorders

Chair: Samuel Gershon, M.D.
Department of Psychiatry
Wayne State University
Detroit, Michigan

and

Nina R. Schooler, Ph.D.
Pharmacologic and Somatic Treatments Research Branch
National Institute of Mental Health
Rockville, Maryland

Low-Dose Neuroleptics in Outpatient Schizophrenics
John Kane, Arthur Rifkin, Margaret Woerner, and Gerard Reardon
Long Island Jewish-Hillside Medical Center and Mt. Sinai Medical Center, New York, NY

Early Intervention vs Continuous Pharmacotherapy of Schizophrenia
William T. Carpenter, Jr.
Maryland Psychiatric Research Center and University of Maryland School of Medicine, Baltimore, MD

*A Strategy for Maximal Therapeutic Delivery of Antidepressants in the Context of Experimental Clinical Trials
Jan Fawcett
Rush Presbyterian-St. Luke's Medical Center, Chicago, IL

*Maintenance Drug Therapy in Depression: Current Status and Strategies
Robert F. Prien
National Institute of Mental Health, Rockville, MD

Routine Use of Psychotropic Plasma Levels in Medically Ill Psychiatric Patients
Richard Dorsey
Epp Memorial Hospital, Cincinnati, OH

---

*Denotes paper was presented at NCDEU meeting but not received before going to press.

Low-Dose Neuroleptics in Outpatient Schizophrenics

John M. Kane, M.D.,[2] Arthur Rifkin, M.D.,[3] Margaret Woerner, Ph.D.[2] and Gerard Reardon, M.A.[3]

Introduction

The value of maintenance neuroleptics in preventing psychotic relapse among schizophrenic outpatients has been well established. Increasing attention, however, must be given towards improving the benefit-to-risk ratio of long-term treatment. Side effects, particularly tardive dyskinesia, remain an important problem, and attempts to reduce toxicity by establishing minimum dosage requirements are necessary. No systematic dose response studies of maintenance medication is schizophrenic outpatients have been reported. In addition, there is a need for more information as to the impact of maintenance medication on patients' social and vocational adjustment and their interactions with significant others.

The present investigation was preceded by a pilot study (Kane, Rifkin, Quitkin, et al., 1979) in which the authors openly treated 57 stable or remitted patients meeting Research Diagnostic Criteria (RDC) for schizophrenia with dosages of fluphenazine decanoate (FD) ranging from 1.25 mg to 5.0 mg, administered intramuscularly (i.m.) every 2 weeks. Though relapse rates were higher than those expected with standard doses, the majority of patients were able to maintain good remission for 6 months. A subgroup of the patients who had completed 6 months of low-dose treatment were randomly assigned, double-blind, to continue on low-dose treatment or be switched to placebo. Seven of eight placebo-treated patients relapsed as compared to one of eight patients continuing on active medication ($p = .02$).

Method

This report presents preliminary results from an ongoing double-blind comparison of low dose (1.25-5.0 mg) and standard dose (12.5-50.0 mg/2 weeks) FD, conducted at three separate sites. Subjects are remitted or partially remitted RDC schizophrenics. Criteria for remission and relapse are defined in terms of Brief Psychiatric Rating Scale (BPRS) and Global Adjustment Scale (GAS) ratings. Relapsed patients are treated openly with standard doses of FD as needed (in addition to experimental medication). Following recovery from relapse, patients are continued in the study on experimental medication only. The length of the study is 1 year. Assessment measures included the BPRS every 4 weeks, the Clinical Global Improvement (CGI) every 2 weeks, and the GAS every 12 weeks. Extrapyramidal side effects and abnormal involuntary movements are assessed every 12 weeks utilizing the Simpson Angus Scale and the Simpson Dyskinesia Scale. The Premorbid Asocial Adjustment Scale is completed by the research assistant at baseline, and a modifed version of the Social Adjustment Scale is administered to the patient and a family member at baseline, Week 26, termination, and (in the case of the family assessment) at any point of relapse. The patient completes the Symptom Checklist-90 every 12 weeks. Laboratory measures include drug-free prolactin levels at baseline followed by a 2-hour prolactin response to an intramuscular injection of haloperidol. Subsequent prolactin and fluphenazine blood levels are obtained at eight additional time points during the year. The present report will not include any laboratory data.

To date, 126 patients have entered the study. Their mean age is 29 (*SD* 7.1). The mean age at first hospitalization is 23 (*SD* 5.2), and the average number of previous hospitalizations is 3.2 (*SD* 1.9). The mean number of weeks since hospital discharge is 64 (*SD* 78.5)

Results

Twenty-six of the 62 patients assigned to low-dose treatment have relapsed a total of 31 times (5 relapsed twice). Seven of these required rehospitalization. Among the 64 patients receiving

---

[1] This study was supported by NIMH Grants MH-31776 and MH-33814.

[2] Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 11004.

[3] Mount Sinai Medical Center, New York, NY 10029.

standard doses, three patients relapsed a total of four times, none requiring rehospitalization. Eighty percent of those patients relapsing on low dose did so within the first 6 months. The median length of time required to restabilize patients relapsing on low dose was 6 weeks; the mean was 11 weeks.

The results of a life-table analysis indicate that the cumulative proportion relapsing on low-dose treatment is 56%. For those patients receiving standard dose, the cumulative proportion relapsing is 7% ($p<.001$). Using the measure of relapse, the low-dose preparation is clearly not as effective as standard doses. However, there are other issues involved in assessing the risk benefit ratio. To date, four patients on standard dose and two patients on low dose have developed presumptive tardive dyskinesia. In a subgroup of 51 patients at Long Island Jewish-Hillside Hospital who completed at least 24 weeks in the study, an analysis of covariance involving the end-point Simpson Dyskinesia Scale scores revealed a significant advantage for low-dose treatment. Our preliminary analyses employing the Simpson Angus Scale for extrapyramidal side effects did not demonstrate a significant difference between the two treatment groups.

Given the relapse rates on low dose, it is important to determine the ultimate cumulative dose administered to these patients. If this proved to be equivalent to standard doses, the original goal would not be met. In a comparison of 9 low-dose patients who relapsed but completed the 1-year study with 20 patients on standard dose who completed 1 year without relapse, the low-dose patients received significantly less medication despite the relapses (16 cc's as compared to 27½ cc's in standard dose equivalents; $t = 2.39$, $p < .05$).

To assess social adjustment and family burden, interviews with the patient and separately with the family were conducted by a trained research assistant. The preliminary results from the social adjustment and family burden measures suggest that despite the increased risk of relapse, the low-dose patients are not significantly worse off than the standard dose patients and, in fact, may be doing significantly better in some areas.

Conclusion

It would appear that low-dose treatment is a viable strategy for a subgroup of remitted or partially remitted outpatient schizophrenics. Further analyses (including the laboratory data) will attempt to identify predictive factors which might help in selecting patients for whom this strategy is most likely to be effective. At present, we are left with a complex interaction of various factors which need to be taken into consideration in planning long-term treatment.

Reference

Kane, J.M., Rifkin, A., Quitkin, F. et al. Low-dose fluphenazine decanoate in maintenance treatment of schizophrenia. *Psychiatr. Res.*, 1:341,1979.

Early Intervention vs. Continuous Pharmacotherapy of Schizophrenia

William T. Carpenter, Jr., M.D.,[1] Joseph H. Stephens, M.D.,[1] Alix C. Rey, M.D.,[1] Thomas E. Hanlon, Ph.D.,[1] and Douglas W. Heinrichs, M.D.[1]

There is an increasing appreciation that long-term use of high-dose neuroleptics does not produce a generalized and continuous therapeutic effect in all schizophrenics. Neuroleptics may impair functioning in areas not affected by the illness *per se*. Also, tardive dyskinesia has become a compelling reason for avoiding indiscriminant use of neuroleptics.

The present study attempts to assess the relative merits and limitations of continuous maintenance pharmacotherapy when compared with the targeted use of neuroleptics in an early intervention strategy, followed by drug discontinuation when the patient is stabilized. The issue is not how no-drug use compares with drug use, but rather how the targeted and time-limited use of drugs compares with continuous use. The targeted alternative is, in fact, already utilized by some clinicians and viewed favorably from the perspective of long-term followup (Bleuler, 1978).

---

[1] Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228.

Conceptual Model for an Early Intervention Strategy

Schizophrenia is conceptualized as a relapsing illness, and the aim of an early pharmacologic intervention is to prevent, or minimize, impending psychotic episodes. Presumably, good candidates for this approach would be robust drug responders with prodromal signs of impending relapse over a sufficient time period to permit identification and intervention. Patients who maintain insight concerning their illnesses during early phases of relapse should be more likely to seek treatment and cooperate with intervention efforts. An ongoing therapeutic relationship is crucial for the tasks of discerning prodromal signs during previous episodes, educating family and patient as to their importance in the intervention strategy, and providing a personal availability at times of impending relapse.

Methods

Patients selected for this study had recently been discharged from hospital care with a diagnosis of schizophrenia. Since one aim of the study was to characterize both good and poor candidates for a targeted drug approach, the selection of patients attempted only to assure the diagnosis of schizophrenia and the probability that patients were suitable candidates for antipsychotic medication. Patients who passed screening and agreed to participate in the treatment program were followed through an initial 4- to 8-week stabilization period in which further baseline psychiatric history, family history, and prognostic data were collected. The patient then entered a 28-day off-drug phase (42 days if withdrawal from long acting depot medication) aimed at identifying covert dyskinesia and which provided baseline assessment of psychopathology, a basis for making a diagnosis using the Research Diagnostic Criteria (RDC) and psychophysiological, neuropsychological, and biochemical data. At the end of 28 days (or sooner, if psychiatric decompensation had already required pharmacologic intervention), patients began a 2-year course of treatment with either continuous or targeted antipsychotic drug use assigned on a random basis. Subsequent interventions (increase of medication in continuous drug patients and initiation of medication in targeted drug patients) were based on a clinical judgment that prodromal symptoms had appeared and that a relapse was imminent. Drug reduction in the continuous, or drug discontinuation in the targeted groups, followed either return to baseline or stabilization of the patient's condition. All patients remained in their treatment group regardless of factors such as decompensation and rehospitalizations. Since treatment failure patients retained their original group assignment, it was possible for a patient on targeted drug treatment to remain on medication during most of the 2-year treatment course. Key points of assessment were at baseline, surrounding each decompensation, and at 6, 12, 18, and 24 months following the beginning of the experimental treatment phase. A variety of assessment techniques aimed at deficit symptoms, quality of life, role performance, and symptom course were utilized. Evaluations were made by an independent assessor free of all responsibility for clinical care.

Results

Two issues will be examined with the preliminary data from a cohort of 57 patients: consequences of drug cessation in 55 patients, and consequences of treatment assignment in the 41 patients already completing 6 months. Two of the 57 patients are excluded from the drug cessation observation. One patient was not on drugs when admitted to our clinic and one patient agreed to discontinue drugs only if returned to medication 2 weeks later. Thirty-eight of 55 patients (69%) completed 28 days off drugs without decompensation. The remaining 17 patients showed signs of relapsing and return to drugs was initiated. Four of the 17 patients required hospitalization as a result of their decompensation while off drugs. One hospitalized patient was rediagnosed manic depressive and did not return to the clinic. For the other three patients, the average hospital stay was 23 days.

The course of decompensation was charted in the 16 cases available for followup. Factor I of the Brief Psychiatric Rating Scale (BPRS) and total BPRS scores indicated that 8 patients returned to baseline levels within 2 weeks, 12 within 8 weeks, and all 16 within 12 weeks.

During the pilot phase of this project, patients were randomized into one of the following groups: continuous drugs plus psychosocial treatment; continuous drugs without psychosocial treatment; and targeted drug with psychosocial treatment. Four patients refused their assignment to continuous drugs and were dropped from the study. Six-month followups are available on 41 patients thus far. Because there were no significant differences on primary outcome measures between the two continuous drug groups, they are combined in the Table. This Table reveals no differences between continuous and targeted drug use on several outcome measures in spite of the significantly lower exposure to drugs in the targeted group. Patients in the targeted group averaged 34% of time on drugs compared with 97% for the continuous group. Three of the 14 targeted drug patients were conspicuous failures (i.e., remained on moderate to high dose for the entire 6-month period). They were also poor outcome patients in spite of the continuous use of medication. The remaining 11 targeted drug patients averaged only 17% of time on drugs. Although the targeted group required more hospitalizations, the number is small and the difference was not statistically significant. The 14 patients in the targeted group were similar to the 27 patients on continuous drugs at 6-month followup (preliminary data at 12 months support this conclusion). Neither our clinicians' observations nor research data revealed evidence at 6-month followup that patients not receiving continuous antipsychotic drugs experienced more severe clinical or social consequences.

Conclusion

It is hoped that a 2-year treatment and observation period in a large number of cases will produce further data relevant to feasibility, prediction of response, and the impact of long-term medication on deficit symptomatology and interpersonal functioning. Present pilot data support the feasibility of the targeted drug treatment of schizophrenia and encourage an optimistic view of the potential applicability of targeted drug intervention in a sizable portion of schizophrenic patients.

Table

Outcome Variables at 6 Months in Two Drug Treatment Conditions

	Targeted Drug ($N = 14$)	Continuous Drug ($N = 27$)	P-values*
Strauss-Carpenter Outcome Score	21.5	22.9	N.S.
Global Assessment Score	52.0	54.8	N.S.
BPRS Total Score	1.93	1.75	N.S.
Number of Hospitalizations	4	2	N.S.
Days in Hospital	35	32	N.S.
Numbers of Weeks on Drugs	8.8	25.2	<.001
Total Drug Dose per Patient in CPZ Equivalents over 6 Months	28,095	69,210	<.001

* P-values based on non-paired t-tests.

Scores above are means except for number of hospitalizations.

Acknowledgment: The authors wish to thank Sue Parks who assisted in data processing and analysis.

Reference

Bleuler, M. *The Schizophrenic Disorders: Long-Term Patients and Family Studies.* New Haven: Yale University Press, 1978.

Routine Use of Psychotropic Plasma Levels in Medically Ill Psychiatric Patients

Richard Dorsey, M.D.,[1] and Ann Bahrani, M.D.[1]

This preliminary report covers experience gained in the routine use of psychotropic plasma level measures in medically ill psychiatric patients during calendar year 1980. All patients were hospitalized and treated on a private basis by a team com-

---

[1] Epp Memorial Hospital, Cincinnati, OH 45243.

prised of psychiatrists and internists. The program was conducted in an open medical setting, with major emphasis on psychopharmacology.

Our group had primary or sole responsibility for providing psychiatric services at three hospitals during the year reported. Our total admissions were 1,023, with principal psychiatric diagnoses being effective psychoses, schizophrenic disdisorders, drug/alcohol dependence, and organic brain syndrome. Patients aged 65 and over comprised about 20% of admissions and accounted for about 40% of hospital days. Ninety-five percent of geriatric patients had one or more significant medical diagnoses (e.g., arteriosclerotic heart disease, diabetes mellitus, malnutrition). Approximately 70% of nongeriatric patients had one or more significant medical diagnosis (e.g., gastrointestinal/hepatic disorders, diabetes, or arteriosclerotic heart disease).

Method

Plasma Level Measures

All specimens from our two Cincinnati hospitals were sent to National Psychopharmacology Laboratories in Knoxville, Tennessee, with our system providing 36-hour turn-around time. Our third hospital, in Columbus, Ohio, used a local reference laboratory affiliated with Ohio State University and provided 24-hour turn-around time.

Our primary Cincinnati hospital service had 619 admissions, of which 15% were geriatrics; 1215 assays were done, for an average of 1.96 assays per patient admission. Our smaller Cincinnati hospital service accounted for 162 admissions, with 65% geriatrics; assays there were 511, or 5.16 per admission. Our Columbus service, which opened in October, accounted for 242 admissions (October to December) with geriatrics comprising less than 5%. Total assays were 246, or 1.01 per patient.

Therapeutic ranges were those reported by the National Psychopharmacology Laboratory (see Table) based on published literature. Limitations of underlying evidence for some drugs were acknowledged, and ranges were regarded as useful for clinical guidance rather than as a definitive basis for dosage determination.

Table 1

Plasma and Whole Blood Assays of Psychoactive Drugs

Tricyclic Antidepressants	Therapeutic Plasma Range ng/ml	Sensitivity of the Method* ng/ml	Fee
Amitriptyline (Elavil) + Nortriptyline	125-250	5	$30
Clomipramine (Anafranil)	70-200	5	$30
Desmethylclomipramine	150-300	5	$30
Desipramine (Norpramin, Pertofrane)	40-150	5	$30
Doxepin (Sinequan) + Desmethyldoxepin	75-200	5	$30
Imipramine (Tofranil) + Desipramine (Norpramin, Petrofrane)	150-300	5	$30
Nortriptyline (Aventyl, Pamelor)	50-150	5	$30
Protriptyline (Vivactil)	50-150	5	$30

A minimum of 2 ml of plasma is required per assay for tricyclic antidepressants.

National Psychopharmacology Laboratory automatically assays the secondary amines for the tertiary tricyclics at no added cost, since interpretation without the secondary amines is not possible.

*Reporting low plasma levels is essential in distinguishing between the rapid metabolism and/or elimination versus noncompliance.

Benzodiazepines	Therapeutic Plasma Range ng/ml	Sensitivity of the Method ng/ml	Fee
Chlordiazepoxide (Librium)	400-1000	20	$22.50
Clorazepate (Tranxene) as Desmethyldiazepam	200-500	20	$22.50
Diazepam (Valium) and	200-400	10	$22.50
Desmethyldiazepam	200-500	20	—
Flurazepam (Dalmane)	70-120	—	—
Lorazepam (Ativan)	Bio-availability data only	10	$22.50
Oxazepam (Serax)	200-500	20	$22.50
Prazepam (Verstran) as Desmethyldiazepam	200-500	20	$22.50

Urinary MHPG	MHPG Normal Controls		
3-methoxy-4-hydroxy phenethyleneglycol (24-hour urinary collection)	Males $N = 27$ 1690μg/24 hr ± 526 *(SD)*	Females $N = 28$ 1337μg/24 hr ± 310 *(SD)*	$45

Where the therapeutic response ranges are not given, they will be furnished in our reports.

Antipsychotics	Therapeutic Plasma Range ng/ml	Sensitivity of the Method ng/ml	Fee
*Acetophenazine (Tindal)	Bio-availability data only	0.5	$30
Butaperazine (Repoise)	100-200	2	$30
Chlorpromazine (Thorazine)	50-500	5	$30
Chlorprothixene (Taractan)	Bio-availability data only	5	$30
*Fluphenazine (Prolixin)	0.2-4	0.2	$30
*Haloperidol (Haldol)	3-15	1.0	$30
Loxapine (Loxitane)	Bio-availability data only	5	$30
Mesoridazine (Serentil)	150-1000	5	$30
*Perphenazine (Trilafon)	1-6	0.2	$30
*Piperacetazine (Quide)	Bio-availability data only	0.5	$30
Thioridazine (Mellaril)	250-1250	5	$30
*Thiothixene (Navane)	0.4-4	0.2	$30
*Trifluoperazine (Stelazine)	>4	0.2	$30

*A minimum of 5 ml of plasma is required for these antipsychotic drugs. Given sensitivities based on 5 ml of plasma.

Lithium	
Plasma Lithium	$7
RBC and Plasma Lithium and calculated RBC/Plasma Ratio	$15

Other
Whole blood or RBC levels are assayed for the same price.

Drug levels were usually measured for psychotropic medications that patients had reportedly been taking just prior to admission. Levels for medications given in hospital were measured at about Days 5-7, and about every 5-7 days thereafter.

Clinical Utility

Our strategy for the use of psychotropic plasma levels in patient management was developed on the basis of clinical impression, without detailed data analysis. Most of our time was devoted to the patient care and administrative demands associated with establishing and running these services.

Patients found to have low psychotropic drug levels on admission were considered likely to be underdosed and/or noncompliant. Generally, the pre-admission drug was continued at a higher dose as initial treatment.

For those whose pre-admission medication produced a plasma level within the therapeutic range, we inferred that the patient was probably receiving the wrong drug. Accordingly, a different drug or class was used for initial treatment in the hospital.

High admission plasma levels suggested toxicity and/or the wrong drug (with the possible exception of a few "therapeutic window" drugs). Management in these cases consisted of initial benzodiazepine washout, followed by clinical reassessment.

After initiation of drug therapy in the hospital, plasma level guidance to dosing was used in the following way. Low plasma levels associated with poor therapeutic response justified increasing dosage on the basis of prospective benefit with minimal additional risk. Both factors were important considerations in the medically ill patient population with which we dealt.

Patients showing satisfactory therapeutic response were continued on the same medication even if the plasma levels were low, and were considered ready for discharge. Intolerance of side effects associated with low plasma level generally led us to discontinue medication.

Nongeriatric patients whose drug levels were within the appropriate range and who showed a satisfactory response were generally discharged. Geriatric patients generally were kept somewhat longer and rechecked for possible drug accumulation before being released.

A correct plasma level associated with poor therapeutic response led us to change drugs. Faced with a therapeutic level and poor side-effect tolerance, we generally tried lowering the dose, and/or blocking the most troublesome side effects. In some cases, a change of medication proved necessary.

High plasma levels associated with good therapeutic response led us to reduce the dose but continue the same medication. Generally, fewer side effects resulted, with no loss of therapeutic benefit.

High plasma level with poor therapeutic response also led us to reduce dosage. In some cases, the decrease in side effects when dosage was reduced gave us an opportunity to observe the beneficial effects of the drugs which had been masked by the side effects. In others, reduced dosage led to lowered plasma levels which had been above the therapeutic window but now fell in this range and may have contributed to a better response. Similarly, multiple side effects associated with high plasma levels were dealt with initially by reduction of dose of the same medication.

Conclusions

We found a high correlation between published therapeutic ranges and our clinical experience with patient response. Our focus was on plasma level categories of "too high," "about right," or "too low." The best correlation between plasma level and therapeutic response occurred in the sickest patients, where laboratory guidance to supplement clinical decision-making was especially desired.

In addition, we found enhanced patient satisfaction through use of laboratory testing to help establish proper treatment (an approach consistent with patient expectations from treatment in other areas of medicine). Other physicians were much more inclined to accept recommendations for high-dose psychotropic medications in medically ill patients if plasma level measurements offered reassurance concerning potential toxicity. Similarly, family physicians or outpatient psychiatrists, to whom many of our patients were referred for followup treatment, were more likely to continue therapeutic regimens with unusually high or low doses of medication when supporting plasma level data were provided. Finally, utilization review staff were impressed with the systematic approach to trying psychotropic drugs in sequence guided by plasma level measures, and would accept longer hospitalizations than otherwise would have been the case.

Overall, we believe psychotropic plasma levels constitute an extremely valuable guide to the clinician caring for the kind of patient population described. We acknowledge limitations in scientific data about the exact therapeutic range for each drug, but believe that even crude laboratory guidance is far superior to none at all. Based on our experience to date, we believe routine use of psychotropic plasma levels helps to maximize therapeutic benefit while minimizing risk and side effects for the medically ill psychiatric patient.

Assessing the Effects of Electroconvulsive Therapy (ECT)

Chair: **Richard D. Weiner, M.D.**
Department of Psychiatry
VA Hospital
Durham, North Carolina

and

Jack D. Blaine, M.D.
Pharmacologic and Somatic Treatments Research Branch
National Institute of Mental Health
Rockville, Maryland

Critical Research Issues in Assessing the Effects of ECT
Jack Blaine
National Institute of Mental Health, Rockville, MD
Evaluation of the Central Nervous System Risks of ECT
Richard D. Weiner, Helen Rogers, and Jonathan Davidson
Duke University Medical Center and VA Hospital, Durham, NC
Efficacy of ECT in the Treatment of Depression: Wave Form and Electrode Placement Considerations
Charles A. Welch, Douglas Weir, Jane F. Cahill, and Michel R. Mandel
Massachusetts General Hospital and Harvard Medical School, Boston, MA
ECT Combined with Neuroleptics in the Treatment of Schizophrenia
Joyce G. Small, Victor Milstein, Marietta H. Klapper, Jeffrey J. Kellams, and Iver S. Small
Larue D. Carter Memorial Hospital and Indiana University School of Medicine, Indianapolis, IN

Critical Research Issues

Jack D. Blaine, M.D.[1]

The inclusion of a session on ECT in the New Clinical Drug Evaluation Unit (NCDEU) meeting program reflects the new responsibility for research on somatic treatments, including ECT, given the Pharmacologic and Somatic Treatments Research Branch as a result of the Fall 1980 reorganization of the Division of Extramural Research Programs of the National Institute of Mental Health. Therefore, the Branch intends to develop a program of research support of ECT projects assessing the effects and role of ECT in the treatment of the mentally ill. In this session, the panel will discuss some of the critical research issues in the ECT field and report data from several of the ongoing clinical ECT research studies.

ECT was first introduced into clinical psychiatry over 45 years ago. Seizures modified by anesthesia and muscle paralysis have been commonly used for over 30 years. Despite this extensive clinical experience, ECT remains a controversial treatment among both mental health professionals and the general public. Much of this controversy arises from emotionally laden concerns including those about irreparable brain damage and abuses of patients' rights. These fears and concerns are elicited by the images of ECT treatment itself in contrast to more graphically benign psychotherapy or pharmacotherapy.

---

[1] National Institute of Mental Health, Rockville, MD 20857.

The controversy also exists in part because of a paucity of studies meeting contemporary scientific standards. ECT was developed and accepted as an effective treatment prior to the psychopharmacologic agents, and prior to the advent of the controlled clinical trial methodologies devised to assess the safety and efficacy of drugs. In addition, the complexity of the ECT treatment procedures and processes, in contrast to swallowing a pill, complicates the feasibility of carrying out well-controlled clinical ECT trials. For example, the inclusion of a "placebo" or simulated sham ECT control group raises ethical concerns. This design exposes severely ill patients to the potential risks of general anesthesia and muscle paralysis without probable therapeutic benefits. Because most patients referred for ECT are severely ill and often are not responsive to ongoing pharmacotherapy and psychotherapy, avoiding subject selection bias poses significant additional difficulties for the design of ECT studies, especially those comparing ECT to other therapies. Also, the side effects of confusion and memory loss potentially disrupt the blind status of the subjects, treatment staff, and raters. These are but a few of the critical design issues which need to be addressed and solved.

Fortunately, interest in ECT research has increased in recent years. As a result, increasing numbers of studies are being done using contemporary scientific designs and methodologies. The findings from several recent sham-controlled studies done in England demonstrate the effectiveness and safety of ECT as a treatment of endogenous depression (Freeman et al., 1978; Johnstone et al., 1980; West, 1981). Together with Ottosson's sophisticated series of studies in Sweden in the late 1950s, they demonstrate that the occurrence of a generalized central nervous system seizure is the essential therapeutic component. Further, the intensity of the electrical current inducing the seizure appears not to be related to therapeutic effect, but seems directly related to the primary side effects of ECT, post-ECT confusion, and memory impairment (Ottosson, 1960).

Therefore, research effort is being directed at more sophisticated issues than primary efficacy and safety. Considerable research effort is focusing on the nature, extent, and duration of the ECT-induced impairment in memory and other cognitive functions. The differential outcome of ECT techniques utilizing various electrical stimuli (brief pulse vs sine wave current) and electrode placements (unilateral nondominant vs bilateral position) is being assessed in terms of the side effects of memory and other cognitive function impairments as well as the therapeutic effect on depressive affect.

The following two papers by R. Weiner and C. Welch and their colleagues will focus on these issues. The final paper, by J. Small, will address aspects of two other critical issues in the efficacy area. The first issue is clinical indications for ECT. The second issue is the safety and efficacy of ECT compared to and combined with drugs. Dr. Small's presentation will present data on the combined use of ECT and neuroleptics in the treatment of schizophrenia. However, the question of safety and efficacy of ECT compared to and combined with optimal antidepressant therapy in the treatment of acute depression remains to be definitively answered.

While most endogenously depressed patients respond to pharmacotherapy, significant numbers of nonresponders are successfully treated with subsequent ECT (Paul et al., 1981). Clinical reviews also indicate the superior effectiveness of ECT for patients unable to take adequate doses of antidepressants for medical reasons (e.g., the elderly or patients with cardiac disease), and superior effectiveness for delusional or catatonic patients, and for severely ill suicidal or cachetic patients requiring a rapid response (APA, 1978; Fink, 1979). Thus, a critical area requiring investigation appears to be delineation and the definitive testing of clinical predictors or historical indicators for selecting ECT vs antidepressant medication as a first-line treatment for endogenous depression.

Finally, recent studies have shown that many patients who recover from an acute episode of major depression, whether treated with ECT or tricyclic antidepressants, have chronic course or become symptomatic again (Prien, 1981). Thus, the effectiveness of ECT, compared to and combined with antidepressants in preventing relapse or recurrences of new depressive episodes, requires investigation. Hopefully, the recent availability of potential biological markers of endogenous depression (e.g., dexamethasone suppression test, sleep electroencephalography (EEG) abnormalities) and techniques reassessing the adequacy of therapy (e.g., tricyclic antidepressant plasma levels, seizure time, and EEG changes with ECT) will facilitate the performance of definitive studies in these important areas.

References

American Psychiatric Association Task Force on Electroconvulsive Therapy, *Electroconvulsive Therapy.* Washington, D.C., American Psychiatric Association, 1978.

Fink, M. *Convulsive Therapy: Theory and Practice.* New York: Raven Press, 1979.

Freeman, C.P.L., Basson, J.V., and Crighton, A. Double-blind controlled trial of electroconvulsive therapy (ECT) and simulated ECT in depressive illness. *Lancet,* 1:738-740, 1978.

Johnstone, E.C., Deakin, J.F.W., Lawler, P., et al. The Northwick Park electroconvulsive therapy trial. *Lancet,* 2:1317-1320, 1980.

Ottosson, J.O. Experimental studies in the mode of action of electroconvulsive therapy. *Acta Psychiatr. Scand. (Suppl.),* 145:1-141, 1960.

Paul, S.M., Extein, I., Calil, H.M., et al. Use of ECT with treatment-resistant depressed patients at the National Institute of Mental Health. *Am. J. Psychiatry,* 138(4):486-489, 1981.

Prien, R. Maintenance drug therapy in depression: Current status and strategies. Paper read at the Annual Meeting, New Clinical Drug Evaluation Unit, Key Biscayne, Florida, May 26, 1981.

West, E.D. Electric convulsion in depression: A double-blind controlled trial. *Br. Med. J.,* 282:355-357, 1981.

Evaluation of the Central Nervous System Risks of ECT

Richard D. Weiner, M.D., Ph.D., [1,2] **Helen J. Rogers, Ph.D.,** [2] **Jonathan Davidson, M.B., M.R.C. Psych.,** [2,3] **and Robert D. Miller, M.D., Ph.D.** [2,3]

Introduction

Electroconvulsive therapy (ECT) is currently used as a treatment modality for severely ill psychiatric patients, particularly for major depressive disorders (Weiner, 1979). There continues to be controversy, however, with respect to ECT's risk/benefit considerations, a situation which is confounded by the widely varying types of ECT in use today, particularly in terms of electrode placement and stimulus waveform.

To help resolve this matter, a controlled prospective clinical study has been set up to investigate the acute and long-term effects of ECT upon memory, the electroencephalogram (EEG), and clinical status. In particular, this study considers the differential effects of stimulus electrode placement and stimulus waveform. As this is an ongoing study now in its third year, data collection and analysis have not been completed and only salient features of the data regarding the acute effects of ECT upon certain memory and EEG parameters will be presented here. Preliminary data regarding therapeutic response are reported elsewhere (Welch, Weiner, Weir, Cahill, Rogers, Davidson, Miller, & Mandel, 1981).

Methods

Experimental subjects have been referred for voluntary ECT treatment by their psychiatrists. All of those who meet Research Diagnostic Criteria (Spitzer, Endicott, & Robins, 1978) for major depressive disorder and have no evidence of preexisting central nervous system (CNS) impairment are subjected to a full series of test measures (memory, EEG, and clinical). ECT subjects who do not meet these criteria are tested only in terms of EEG. Control subjects meet all study criteria except for not being referred for ECT. Memory data will be presented on 33 experimental and 8 control subjects, while EEG data is presented on 40 experimental and 4 control subjects.

All experimental (ECT) subjects are randomly assigned to either unilateral nondominant or bilateral electrode placement and either sine wave or bipolar pulse stimuli. Standard modified ECT procedures are otherwise carried out, with the addition of EEG and stimulus energy monitoring.

---

[1] Psychiatry Service, Durham VA Medical Center, Durham, NC 27705.

[2] Department of Psychiatry, Duke University Medical Center, Durham, NC 27710.

[3] John Umstead State Hospital, Butner, NC 27059.

The number of ECT treatments is determined by the subject's psychiatrist on a clinical basis. No significant difference in age, sex, education, I.Q., or socioeconomic status among the various treatment groups was noted.

All testing is done prior to ECT, 2-3 days post completion of the treatments, and 6 months later (only the acute data will be presented here). Clinical measures have been discussed in part elsewhere (Welch et al., 1981). Memory measures include a variety of tests of anterograde and retrograde memory performance (for both dominant and nondominant hemispheric function). The personal, or autobiographic memory questionnaire focuses upon specific events relating to the subject's own life, particularly over the past year. A time frame which appears to be especially sensitive (Squire, Slater, & Miller, 1981) will serve as the memory measure presented below. In terms of physiologic abnormalities (Small, Small, & Milstein, 1978), both visual rating of EEG slowing and computer spectral analysis are utilized, with data from the latter being presented here. Testing is done blind with respect to subject group assignment, as indicated.

Results

The fraction of baseline personal memory items not remembered at the second testing session (2-3 days post completion for ECT experimental subjects) is shown in Figure 1. Analysis of variance shows control subjects to be *less* amnestic than ECT subjects ($p \leq .001$), and unilaterally treated subjects to be *less* amnestic than those receiving bilateral treatment ($p \leq .01$). A small trend for sine wave-treated subjects to be more impaired than those treated with pulse stimuli did not reach clinical significance ($p \leq .08$). Further statistical investigations revealed that the degree of apparent amnesia was *not* correlated with mean seizure length or total seizure duration, but *was* positively correlated with number of treatments ($p \leq .03$).

The difference in EEG slowing between the second testing session (2-3 days post completion of ECT for the experimental subjects) and the baseline measurements is shown in Figure 2. Analysis of variance shows control subjects to exhibit *less* slowing than ECT subjects ($p \leq .05$). Also, unilaterally treated subjects show *less* slowing than bilaterally treated subjects ($p \leq .02$). An additional finding, different from the memory results, is that subjects receiving pulse ECT show significantly *less* slowing than subjects receiving sine wave administration ($p \leq .01$).

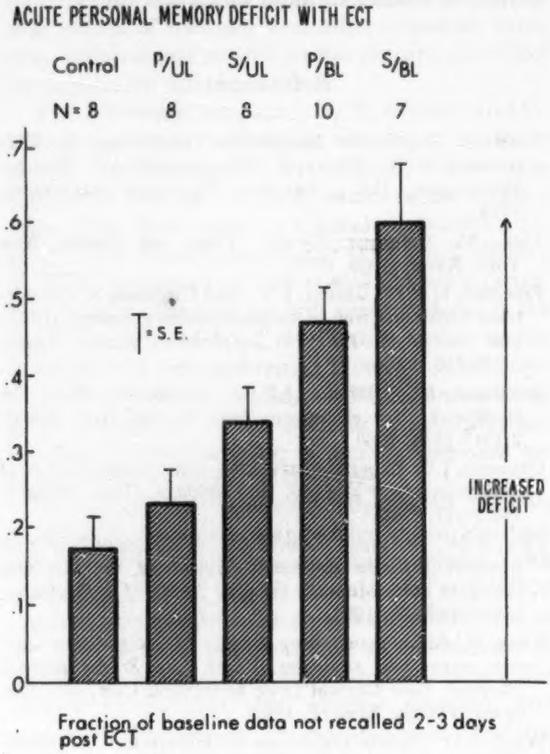


FIGURE 1

Discussion and Conclusion

The above findings indicate that the use of personal memory questionnaires and computerized EEG spectral analytic techniques can be used to extend the sensitivity of the assessment of CNS impairment following ECT. Acute personal memory impairment is less with unilateral nondominant electrode placement, as reported by

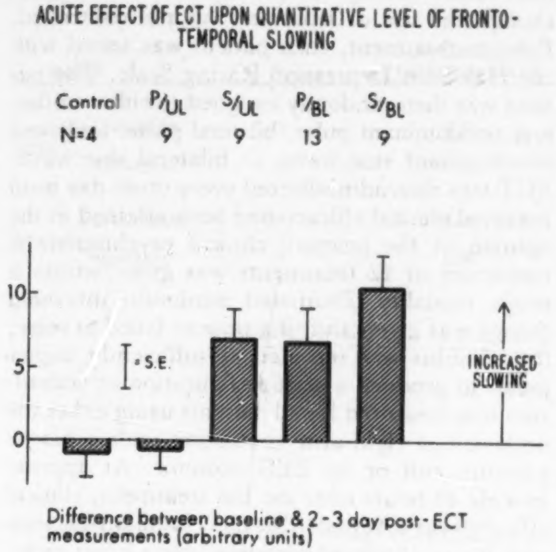


FIGURE 2

many others (e.g., Squire, 1977). No clear effect of stimulus waveform upon acute memory deficits is apparent, though a possible mild dysmnestic effect of sine wave stimuli requires further evaluation. In addition, the number of treatments, but not seizure duration, was found to exert a cumulative effect upon acute memory impairment, suggesting that, in general, brief electrically induced seizures appear to exert discrete effects upon memory performance.

In terms of acute EEG changes, unilateral nondominant ECT results in less slowing than bilateral ECT, while pulse ECT results in less slowing than sine wave ECT. This indicates that EEG slowing, which appears more sensitive to stimulus waveform than does amnesia, may represent a somewhat different phenomenon than amnesia, with the former being a nonspecific encephalopathic change, perhaps related to confusion, and the latter being a more specific effect of ECT, perhaps mediated through temporal lobe mechanisms.

References

Small, J.G., Small, I.F., and Milstein, V. Electrophysiology of EST. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress*. New York:Raven Press, 1978, pp. 759-769.

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry*, 35(6):773-782, 1978.

Squire, L.R. Electroconvulsive therapy and memory loss. *Am. J. Psychiatry*, 134(9):997-1001, 1977.

Squire, L.R., Slater, P.C., and Miller, P.L. Retrograde amnesia and bilateral electroconvulsive therapy: Long-term follow-up. *Arch. Gen. Psychiatry*, 38(1):89-95, 1981.

Weiner, R.D. The psychiatric use of electrically induced seizures. *Am. J. Psychiatry*, 136(12):1507-1517, 1977.

Welch, C.A., Weiner, R.D., Weir, D., et al. Efficacy of ECT in the treatment of depression: Waveform and electrode placement considerations. *Psychopharmacol. Bull.* 18(1):31-34, 1982.

Efficacy of ECT in the Treatment of Depression: Wave Form and Electrode Placement Considerations

Charles A. Welch, M.D.,[1] Richard D. Weiner, M.D.[2,3] Douglas Weir, M.D.,[1] Jane F. Cahill, R.N.M.S.,[1] Helen J. Rogers, Ph.D.,[2] Jonathan Davidson, M.B., M.R.C. Psych.[4] Robert D. Miller, M.D., Ph.D.,[2] and Michel R. Mandel, M.D.[4]

There is wide variation in electroconvulsive therapy (ECT) technique and little data to indicate which technique, if any, is must efficacious. The two most important variables are the position of the treatment electrodes on the head, and the shape of the electrical wave form. Many clinicians have strong opinions about the effect of these variables on efficacy, but studies to date have been inconclusive.

Bilateral fronto-temporal electrode placement is still the standard technique in this country, in spite of an increasing body of evidence that unilateral nondominant placement has less side effects (d'Elia, 1970; Squire, 1977) and that it may be equally efficacious (d'Elia & Raotma, 1975). Although existing studies vary widely in methodology, more rigorously designed studies tend to show equal efficacy, while those lacking control groups, blind raters, objective treatment criteria, or other important design features tend to show a differential in efficacy favoring bilateral.

---

[1] Somatic Therapies Consultation Service, Massachusetts General Hospital, Boston, MA 02124.

[2] Department of Psychiatry, Duke University Medical Center, Durham, NC 27705.

[3] Durham VA Medical Center, Durham, NC 27705.

[4] Umstead State Hospital, Butner, NC 27059.

Stimulus wave form has also been studied with respect to efficacy. Again, wide variations in methodology make it difficult to draw firm conclusions from the published studies. In the seven comparisons between sine wave and brief pulse performed since 1944, methodology varied widely, but several trends do emerge from this data (Weaver, Ives, Williams, & Nies, 1977; Weiner, 1980). In all but one study, sinusoidal and pulse wave forms were found to be equal in their ability to produce satisfactory seizures. Furthermore, pulse stimulation required less total energy to trigger a seizure, generally 50% or less than the energy required for sine wave stimulation. Clinical efficacy was found to be equal in all but one study, in which sine wave was found to be slightly more effective.

Unfortunately, a variety of different stimulus doses and electrode placements were used in these studies, and a clear comparison of wave forms, free of other variables, cannot be made. Furthermore, there has been no therapeutic comparison of wave forms using the vertex-temporal placement technique as described by d'Elia (1970). This placement requires less energy than the bilateral or other unilateral placements (Erman, Welch, & Mandel, 1979), appears to be equally efficacious, and is therefore clearly deserving of further study.

Because of the foregoing methodological problems, the present study was initiated with the intent to control simultaneously for variables of wave form and electrode placement. The objectives are to assess the previous findings: That unilateral ECT may be as effective clinically as bilateral ECT, and that brief pulse stimulus is as effective as sine wave stimulus.

Method

Patients in the study were referred for ECT on the basis of clinical indications, and most were resistant or intolerant to antidepressant medications. They were required to fit the Diagnostic Statistical Manual-III (DSM-III) criteria for major depressive episode with melancholia, and to have no evidence of preexisting cognitive impairment other than that consistent with depressive illness. All patients were free of antidepressant medication during the course of treatment, although the use of sedatives was not controlled. Prior to treatment, each patient was tested with the Hamilton Depression Rating Scale. The patient was then randomly assigned to either unilateral nondominant pulse, bilateral pulse, unilateral nondominant sine wave, or bilateral sine wave. ECT was then administered every other day until maximal clinical efficacy had been attained in the opinion of the primary clinical psychiatrist. A maximum of 12 treatments was given within a single modality. Estimated minimum threshold dosage was given and, if a patient failed to seize, the stimulus was repeated at sufficiently higher joules to produce a seizure. Duration of convulsion was measured for all patients using either the occlusion of right-arm circulation with a blood-pressure cuff or an EEG monitor. At approximately 48 hours after the last treatment, clinical efficacy was assessed with the Hamilton Depression Rating Scale administered by a blind rater. Efficacy was measured as reduction in raw Hamilton score from pretreatment testing to the score at 48 hours after the last treatment.

Results

Figure 1 compares the degree of improvement for each cell, and Figures 2 and 3 compare patients by electrode placement and wave form, respectively. Figure 1 indicates that the two unilateral cells had greatest mean improvement. Figure 2 shows a superiority of unilateral ECT over bilateral ECT that is statistically significant at the $\leq .05$ level. When the two centers are analyzed separately, the Duke data continue to show a statistically significant difference, while the Massachusetts General Hospital data show a trend in the same direction, although it is not statistically significant. Figure 3 indicates no significant difference in efficacy between the two wave forms.

FOUR CELL COMPARISON

DUKE AND MGH COMBINED

GROUP		N	MEAN REDUCTION IN HAMILTON SCORE
PULSE	UNILATERAL	12	33.50
	BILATERAL	18	25.28
SINE	UNILATERAL	17	36.35
	BILATERAL	12	25.00

Figure 1

COMPARISON OF ELECTRODE PLACEMENT

DUKE AND MGH COMBINED

GROUP	N	MEAN REDUCTION IN HAMILTON SCORE
UNILATERAL	29	35.17
BILATERAL	30	25.17

Figure 2

COMPARISON OF WAVE FORM

DUKE AND MGH COMBINED

GROUP	N	MEAN REDUCTION IN HAMILTON SCORE
PULSE	30	28.57
SINE	29	31.66

Figure 3

Discussion

The finding that sine wave and brief pulse stimulus appear equally efficacious is not surprising in the light of previous research. Ottosson's (1960) milestone work indicated that a generalized grand mal seizure is the essential component of the treatment and that other variables such as mode of stimulus and severity of side effects were unrelated to ultimate efficacy. Subsequent clinical comparisons of wave form have continued to support the contention that how you trigger a seizure is unrelated to efficacy, but whether or not you trigger a seizure is related to efficacy.

The findings on electrode placement are somewhat more surprising. Although a number of investigators have found unilateral electrode placement to be just as efficacious as bilateral, this is the first randomly assigned prospective trial to find a greater efficacy associated with unilateral placement. The investigators' interpretation of these findings is that the bilateral group appeared less improved because of the greater cognitive side effects associated with that treatment at the time of measurement. It is possible that these placements are equally efficacious when the artifact of cognitive side effect is removed and this view, again, would be consistent with the work of Ottosson (1960) regarding the importance of the seizure itself.

While the investigators feel that it is premature to draw firm conclusions from their data until the study is completed, they also feel that the trends from this preliminary analysis are unlikely to change significantly as the study proceeds. The clinical importance of these findings is that there is probably at least equal efficacy with unilateral and pulse techniques in addition to markedly reduced side effects, compared with bilateral sine wave treatment.

References

d'Elia, G. Unilateral electroconvulsive therapy. *Acta Psychiatr. Scand. (Suppl.)*, 215, 1970.

d'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? *Br. J. Psychiatry*, 126:83-89, 1975.

Erman, M.K., Welch, C.A., and Mandel, M.R. A comparison of two unilateral ECT electrode placements: Efficacy and electrical energy consideration. *Am. J. Psychiatry*, 136

(10):1317-1319, 1979.

Ottosson, J.O. Experimental studies in the mode of action of electroconvulsive therapy. *Acta Psychiatr. Scand. (Suppl.)*, 145:1-141, 1960.

Squire, L.R. ECT and memory loss. *Am. J. Psychiatry*, 134: 997-1001, 1977

Weaver, L.A., Ives, J.O., Williams, R. and Nies, A. A comparison of standard alternating current and low energy brief pulse electrotherapy. *Biol. Psychiatry*, 12(4):525-543, 1977.

Weiner, R.D. ECT and seizure threshold: Effects of stimulus wave form and electrode placement. *Biol. Psychiatry*, 15(2): 225-241, 1980.

ECT Combined with Neuroleptics in the Treatment of Schizophrenia[1]

Joyce G. Small, M.D.,[2] Victor Milstein, Ph.D.,[2] Marietta Klapper, M.S.,[2] Jeffrey J. Kellams, M.D.,[2] and Iver F. Small, M.D.[2]

The purpose of the present study was to assess the relative efficacy of neuroleptics combined with electroconvulsive therapy (ECT) compared with neuroleptics alone in the treatment of schizophrenia. Study patients met criteria (Feighner, Robins, Guze, & Woodruff, 1972) for schizophrenia. The design included randomization of treatment, placebo controls, a modified double-blind design, and short- and long-term followup. The majority of patients were assigned to treatment either with thiothixene hydrochloride or thiothixene combined with ECT. Fewer patients were assigned to placebo combined with ECT and still fewer to placebo alone. Nondominant unilateral ECT was employed with electroencephalographic monitoring to assure that major generalized seizures were induced. A standard rating scale battery (Levine, 1979) plus the Emotional Blunting Scale (EBS) (Abrams & Taylor, 1978) were employed. The Halstead-Reitan-Wepman Neuropsychological test battery (Reitan, 1966) was utilized for evaluation of cognitive impairment. Dosage of drugs and number of ECT were individualized, but a lower limit of 12 treatments for an ECT regimen was imposed. Video-taped samples of interview behavior were obtained for time-blind psychiatric ratings (Renfordt & Busch, 1976). Patients were assessed biweekly for the first 2 weeks and weekly thereafter for 6 weeks with followup at 6 and 12 months. Patients were maintained in the initially assigned treatment groups for as long as possible but were dropped because of patient refusal to continue, clinical deterioration, uncontrollable side effects, or insufficient therapeutic response. Treatment related dropouts were not replaced and were included in the statistical analyses by substitution of last active scores for missed evaluation points.

Seventy-five patients were enrolled in the study and randomly assigned to treatment. There were no differences between the treatment groups in terms of age, sex, education, duration of illness, nor in the pretreatment assessments of psychopathology.

Survival time on the study was one of the dependent variables examined. Patients on placebo, and placebo combined with ECT were dropped from the study significantly sooner than the others on an average of 11 and 19 days, respectively. Mean survival time was 46 days for thiothixene-ECT and 60 days for thiothixene. The difference between the latter two was not statistically significant. Reasons for study termination were similar in the four treatment groups. The only difference was that compliance with taking medications was better in the ECT-treated patients.

There were no significant differences in doses of neuroleptics or corresponding amounts of placebo in the three active treatment groups. More anticholinergic agents were used in the patients treated with thiothixene alone. The two ECT groups received a series of 15 treatments on the average. The seizures were shorter in the thiothixene-ECT combined group than in the patients on placebo with ECT, 37 seconds compared to 43 seconds.

Neuropsychological test data revealed no group differences before treatment. Afterwards there were indications of greater impairment of performance in the thiothixene – ECT group in comparison with performance of patients receiving

---

[1] This study was supported by USPHS Grant No. 27519 from the National Institutes of Health.

[2] Indiana University School of Medicine, Larue D. Carter Memorial Hospital, Indianapolis, IN 46202.

placebo—ECT. This was true for tests involving right, left, or both hemispheres. Dosage of neuroleptic or anticholinergic medication was not associated with impaired test performance.

Two-way analysis of variance for repeated measures of the four treatment groups over the nine assessment periods yielded significant treatment group and time effects with no significant interactions. On the Clinical Global Impression Scale the majority of significant differences favored the thiothixene-ECT combined group in comparison to the placebo-ECT and placebo reference conditions. There were no statistically significant differences between the two groups receiving active drug. The Brief Psychiatric Rating Scale (BPRS) discriminated between the thiothixene patients and those treated with placebo-ECT or placebo, favoring the former on factors of thinking disturbance and anxiety-depression. The drug-ECT combination group did best in areas assessed by the EBS. The Abnormal Involuntary Movement Scale (AIMS) indicated that patients given neuroleptics alone had more orofacial movements than the other treatment groups.

The overall conclusion was that thiothixene alone and thiothixene combined with ECT are both effective treatments of exacerbations of schizophrenia as compared to the reference groups which received placebo and unlateral ECT or placebo alone. The course of treatment with thiothixene-ECT was smoother, with fewer problems with drug compliance, less apathy, withdrawal and indifference, fewer movement disorders, and other side effects as well as overall better global improvement and therapeutic efficacy. There were no differences in survival time on the study, duration of hospitalization, or disposition on discharge, but family adjustment in those patients living at home was significantly better in the ECT-combined group than for those who received neuroleptics alone. There was more impairment in neuropsychological test performance with drug-ECT combined than with ECT without active drugs, and seizures were shorter, although these differences may not by clinically important. Neuroleptics alone were more effective in controlling signs and symptoms assessed by BPRS factors of thinking disturbance and anxiety and depression.

The conclusion is that neuroleptics combined with ECT and neuroleptics alone are useful therapeutic interventions in schizophrenia, each with a somewhat different symptomatic profile. Projected followup investigations may determine whether or not there are long-range advantages to either form of treatment.

References

Levine, J. (ed.) *Coordinating Clinical Trials in Psychopharmacology: Planning, Documentation, and Analysis.* Washington, D.C.:DHEW Publ. No. (ADM) 79-803, 1973.

Feighner, J.R., Robins, E., Guze, S.B., et al. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry*, 26:57-63, 1972.

Abrams, R., and Taylor, M.A. A rating scale for emotional blunting. *Am. J. Psychiatry*, 135:226-229, 1978.

Reitan, R.M. Problems and prospects in studying the psychological correlates of brain lesions. *Cortex*, 2:127-154, 1966.

Renfordt, E., and Busch, H. Time-blind analysis of TV-stored interviews: An objective method to study antidepressive drug-effects. *Int. Pharmacopsychiatry*, 11:129-134, 1976.

Current Issues in the Treatment of Anxiety States and Disorders

Chair: Karl Rickels, M.D.
Department of Psychiatry
University of Pennsylvania
Philadelphia, Pennsylvania

and

Allen Raskin, Ph.D.
National Institute of Mental Health
Rockville, Maryland

*Imipramine Treatment for Primarily Anxious Outpatients
Ronald S. Lipman
National Institute of Mental Health
Rockville, MD

Predictability of Treatment Reponse of Diazepam at Several Points During the Course of a 6-Week Drug Trial
Robert W. Downing
University of Pennsylvania, Philadelphia, PA

Issues in Long-Term Treatment with Diazepam
Karl Rickels
University of Pennsylvania, Philadelphia, PA

*Pharmacological Dissection of Anxiety
Donald F. Klein
New York State Psychiatric Institute and Columbia University, New York, NY

*Agoraphobics' Response to Imipramine and Chlordiazepoxide
Douglas M. McNair
Boston University, Boston, MA

Behavioral Assessment of Drug Effects in Obsessive-Compulsive Disorder
Samuel M. Turner
Western Psychiatric Institute and Clinic, Pittsburgh, PA

---

*Denotes paper was presented at NCDEU meeting but not received before going to press.

Predictability of Treatment to Response to Diazepam at Several Points During the Course of a 6-Week Drug Trial[1]

Robert W. Downing, Ph.D.,[2] and Karl Rickels, M.D.[2]

Among the aims of a recently completed large-scale study of diazepam treatment in patients suffering from chronic anxiety is the determination of predictors of response to both an acute (6 weeks) and a maintenance (6 months) treatment phase of the trial. The present report deals with a preliminary investigation of the predictability of treatment response at several points during the course of the acute phase of the study (after a 1-week placebo washout period, and after 2, 4, and 6 weeks of treatment with diazepam). It is also concerned with the contributions to predictability made at each of these points by each member of a small set of predictors, selected either on the basis of the predictive role they have played in previous studies (age, social class, presence or absence of previous treatment, and the severity of initial anxiety and initial depression), or because of theoretical considerations (Eysenck Neuroticism and Precipitating Stress).

Of the 133 primarily anxious, nonpsychotic outpatients included in the present investigation, 59% were female, 81% white, and 62% married. Mean age was 42.7 ± 12.6 years. Class IV formed the modal socioeconomic level (47%), but the remaining classes were well represented (I-II, 12%; III, 23%; V, 18%). In terms of illness-related factors, 38% of the group had been ill for 3 or more years; 62%, for 1 or more years. Seventy percent of the sample had received previous treatment for emotional problems. Mean score on the Covi Anxiety Screen was 10.4 ± 1.7, and on the Raskin Depression Screen, 6.8 ± 1.83. Precipitating stress was reported for 50% of the group.

The seven independent variables listed in the Table were employed as regressors in a standard multiple regression procedure to assess the predictability of 7-point scale physician ratings of Global Improvement (1 = very much better, 7 = very much worse) after the 1-week placebo washout period and after 2, 4, and 6 weeks of treatment with diazepam (20-40 mg/d). In addition to the multiple R's and R^2's obtained at each time period, the Table includes the partial *r* of each regressor with improvement. The signs of each partial *r* have been adjusted so that the indicated class (e.g.; Previous Treatment: Yes) or dimensional extreme (e.g.; Eysenck Neuroticism: High) are associated with greater improvement when *r* is positive and with lesser improvement when *r* is negative for that variable.

Table

Predictors of Physician Rated Global Improvement After a 1-Week Placebo Washout and After 2, 4, and 6 Weeks of Treatment With Diazepam for 113 Anxious Patients

			Diazepam	
	Placebo	Week 2	Week 4	Week 6
	r_p	r_p	r_p	r_p
Age: Old	00	13	02	06
Previous Treatment: Yes	-16†	-18*	-21*	-30§
Neuroticism: High	-15†	-18*	-14	-19*
Social Class: High	03	21*	22**	11
Precipitating Stress: Yes	16†	06	22**	20*
Covi Anxiety: High	26**	-04	06	02
Raskin Depression: High	-06	-04	-24**	-12
R	.38	.35	.43	.41
R^2	.141	.122	.188	.167
P	.007	.02	.0005	.004

* *p* .05
** *p* .01
† *p* .10
§ *p* .001

The percentage of predicted variance ranges from 12.2% at 2 weeks to 18.8% at 4 weeks. An examination of the R's and R^2's across the four points at which they are assessed provides no evidence of a reliable shift in predictability between the first and seventh weeks of treatment. Predictability after 6 weeks of diazepam treatment is at least as high as it is at any of the previous assessment points. The temporal configuration of the contributions made to predictability, however, varies widely across the set of independent variables employed. Patient age, despite its implications for the kinetics of benzodiazepine metabolism and its putative role as at least a rough indicator of physical, psychological, and social functioning remains uniformly unrelated to treatment response. In contrast, the contribution made by the presence/absence of previous treatment for emotional problems shows a monotonic increase across assessment periods with those patients who have sought previous treatment manifesting the least improvement. The presence of a condition requiring further treatment after previous treatment was obtained would appear to impose tangible limits upon the capacity for treatment response; this factor accounts for 9% of treatment response after 6 weeks of diazepam treatment.

---

[1] This work was supported by USPHS Research Grants MH-08957 and MH-31366.

[2] Psychopharmacology Research and Treatment Unit and the Private Practice Research Group, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104.

Higher scores on the Eysenck Neuroticism scale manifest a modest, but consistently negative impact upon treatment response across all assessment periods. This purported measure of potential for neurotic functioning emerges as sufficiently independent of the predictive impact of presently anxious and depressive symptomatology to make a significant contribution ($p < .05$) after 2 and after 6 weeks of diazepam treatment. Higher socioeconomic class affiliation has a positive implication for response to active drug but not to placebo, while the occurrence of precipitating stress implies more adequate response to both placebo ($p < .10$) and to active drug. More severe presenting anxiety (Covi Screen) is associated with greater response during the placebo washout period but is unrelated to subsequent drug response. More severe presenting depression (Raskin Screen) has negative implications for drug response which are statistically significant at only the 4-week point. Generally, it may be concluded that more adequate treatment response is experienced by those individuals with greater material, personal and social resources supportive of adequate functioning.

Issues in Long-Term Treatment with Diazepam[1]

Karl Rickels, M.D.,[2] W. George Case, M.D.,[2] and Robert W. Downing, Ph.D.[2]

A diazepam maintenance drug trial, initiated several years ago, is presently in its last study phase and all patients have been entered into the trial. This report is based on completed patient data available as of April 1981.

The acute single-blind study phase called for a 1-week placebo washout period and a 6-week active drug treatment period where diazepam was prescribed in daily dosages ranging from 20-40 mg with an average dose of 25 mg/day. Improved patients or patients hoping to derive more benefit through longer diazepam treatment then entered an 18-week double-blind maintenance phase.

One-third of all patients entering the maintenance phase were switched to placebo at the onset, one-third after 8 weeks in the maintenance phase, i.e., after a total diazepam period of 14 weeks, and one-third of patients after 16 weeks in the maintenance phase or a total number of 22 weeks on diazepam. For all patients completing 22 weeks of diazepam treatment, two additional placebo weeks with weekly visits were added. Followups were conducted 3 and 12 months after the patient completed the maintenance phase.

Only chronically anxious, nonpsychotic patients of both sexes between 18 and 65 years of age who were anxious for at least 3 months, and whose mean chronicity was more than 1 year, were initiated into the study. Their initial Covi Anxiety score was at least 8 and their Hamilton Anxiety score at least 18. Of more than 350 anxious patients entering the placebo washout period, 158 patients so far have completed the maintenance phase, either by completing all 24 weeks of the program or by dropping out earlier for various reasons (e.g., return of symptoms or withdrawal reaction).

---

[1] This research was supported by USPHS Research Grant MH-08957.

[2] Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104.

The following preliminary findings have been obtained so far:

1) Clinical improvement observed during the first week of diazepam treatment was a highly significant predictor of a 6-week diazepam treatment response ($p < .001$), with almost 90% of patients reporting "much or very much" improvement after only 1 week of treatment being markedly improved after 6 weeks of treatment. The representative improvement percentage for patients reporting at 1 week only minimal improvement is 45%, and for patients reporting no improvement or getting worse after 1 week is 20%.
2) No tolerance to the diazepam effect developed in improved patients over the total 22 weeks of diazepam treatment.
3) Patients experienced maximal improvement during the initial 6 weeks of treatment, and no additional improvement could be produced in any patient during the entire maintenance phase, even when dosages were increased to a daily maximum of 40 mg/day.
4) Return of symptoms after an abrupt change from diazepam to placebo after 6 weeks of diazepam treatment occurred in 45% of all patients. In those patients who continued 22 weeks on diazepam, the return of symptom rate was reduced to 25%. Thus, about 55% of chronically anxious patients with a mean chronicity of more than 1 year needed only 6 weeks of diazepam treatment to become symptom free and to maintain this freedom for at least several months while on placebo medication.
5) Withdrawal reactions were reported by 20 out of 158 patients (13%). Two withdrawal reactions occurred in patients who were on diazepam for only 6 weeks, ten in patients who were on diazepam for 14 weeks, and eight in patients who were on medication for 22 weeks. Seven of these 20 patients had only very transient reactions that lasted for only a few days and had disappeared 1 week later. Some of these patients reported temporary sleep problems and one patient stated that he felt slightly anxious for 3 days, similar to when he stopped smoking. The withdrawal reaction in the remaining 13 patients were clear withdrawal reactions which occurred within 2-3 days after abrupt diazepam withdrawal and shift to placebo; these symptoms peaked during Days 5 to 7 and disappeared with or without treatment within a few weeks, as was recently reported by Winokur et al. (1). Table 1 summarizes those withdrawal reactions reported by most of the 13 patients.

Table 1

Diazepam Withdrawal Symptoms

Extreme Distress
GI Symptoms (Nausea, Diarrhea, or Constipation)
Diaphorosis
Tremor
Lethargy
Dizziness
Increased Acuity for Sound and Smell
Restlessness
Insomnia
Tinnitus
Feelings of Depersonalization
Difficulties Expressing Thoughts Coherently
Headaches
Irritability
Anxiety
No Convulsions
No Psychotic Reactions

Further examination of our data made it quite clear that withdrawal response could not be looked at only as a function of study medication but had to be viewed in the context of medication taken prior to entering the 1-week placebo washout period. In fact, close inspection of prior drug treatment data indicated that 4 of the 13 patients with clear withdrawal reactions should never have entered our study, since they demonstrated existing clear-cut withdrawal reaction during the placebo washout period. Incidences of withdrawal reactions, irrespective of whether they were mild or severe, are given in Table 2 as a function of total consecutive prior sedative-benzodiazepine intake. Table 2 indicates clearly that chances to develop withdrawal reactions to an abrupt withdrawal of diazepam used in medically acceptable daily dosages of 15-40 mg increases with length of prior sedative treatment. No withdrawal reactions were seen prior to 14 weeks of benzodiazepine treatment; the two withdrawal reactions occurring after 6 weeks of study medication occurred in patients who had been on long-term benzodiazepine use and in fact had already had a withdrawal reaction during the placebo washout period. The three patients who developed clear-cut withdrawal reactions after only 14 weeks of diazepam and without a history of prior sedative drug use were heavy social drinkers, and the question at least should be raised whether this drinking habit may have contributed to the occurrence of withdrawal symptoms.

Table 2

Withdrawal Reactions After Abrupt Discontinuation of Diazepam Treatment as Function of Prior Sedative Drug Use*

	No Withdrawal	Withdrawal
No Prior Sedative	83	6 (7%)
Prior Sedative <8 Months' Duration	38	3 (7%)
Prior Sedative ≥8 Months' Duration	17	11 (39%)

$\chi^2 = 21.83$; $N = 158$

*Patients who terminated on diazepam are counted as "No Withdrawal."

6) Major factors found to contribute to diazepam withdrawal are the following: a) abrupt discontinuation of treatment; b) continuous treatment for at least 4 months' duration in therapeutic dosages; c) the longer the treatment duration with a sedative-benzodiazepine, the higher the chance of withdrawal reactions to occur even in therapeutic dosage; d) however, since many patients with years on benzodiazepine medication did not develop withdrawal reactions in our study, other as yet unknown factors need to be determined.

7) The time course of withdrawal reactions produced by abrupt benzodiazepine discontinuation indicates a swift development of symptoms, peaking after 5 to 7 days and slowly receding over the next 2 to 4 weeks. These symptoms are frequently not only different from the symptom the patient originally had, but also much more disturbing. However, many patients experience only very mild symptoms, lasting only a few days. In contrast, return of symptoms shows a much different time course. Symptoms usually develop over 2 to 4 weeks and once they are fully developed do not disappear without additional treatment. The symptoms also are usually of the same type as the patient's original symptoms and they are generally of less severity and never of more intensity than they were prior to initiating treatment.

8) Based on our experience gained in this maintenance study, we suggest the following guidelines to prevent or treat such symptoms: a) Decrease daily dosage by 2.5 to 5 mg but not more than one-fourth the daily dose every 1-2 weeks. b) Patients with transient reactions, short-lasting symptoms, or patients who do not mind suffering through their withdrawal reactions, may not need any treatment at all, at least when diazepam, a drug with a long half-life, is involved. Convulsions or psychotic reactions were not observed in our study. c) Original symptoms may frequently return. They are never as abrupt, distressing, and different from original symptoms than withdrawal reactions.

9) Finally, 96 patients who completed the maintenance phase were followed by mail interview 12 months after completion of the study. Table 3 gives results from the 1-year followup. These results are most disturbing. Of the 96 patients for whom data are available, 59% were symptomatic at time of followup, this despite the fact that all patients were asymptomatic while on diazepam; and of the 57 symptomatic patients, less than 50% were treated for their symptoms. This treatment involved not only benzodiazepines, but also tricyclic antidepressants (TCA) and neuroleptics. Interestingly, none of these 27 patients had entered psychotherapy or other nondrug treatments. While the use of TCAs is probably appropriate since patients may have become depressed, the use of neuroleptics in seven patients subjects these patients to potentially more dangerous drugs than the benzodiazepines.

10) In summary, more than 50% of chronically anxious patients need at the most only 6

weeks of treatment with diazepam to remain symptom free. Those patients who need continued maintenance treatment do not develop tolerance to their medication, but also do not continue to improve beyond the improvement levels they had reached after 6 weeks of treatment. A return of symptoms is usually indicated by a slow onset and a recurrence of symptoms which are similar to the ones originally present. Withdrawal reactions due to abrupt discontinuation of diazepam range from mild and transient to more severe and very disturbing. They show a rather acute onset, with symptom intensity peaking after 5 to 7 days and with symptoms being much more disturbing than the original symptoms present prior to treatment. These symptoms include many symptoms not present originally. Withdrawal reactions can be prevented in most patients by stepwise reduction of dosage.

Table 3

One-Year Followup
$N = 96$

	Symptoms	
	Present	Absent
Treatment	57 (59 %)	39
Yes	27*	1 (Hypnosis by GP)
No	30	0

*Type of Treatment:

Benzodiazepines (Valium: 12 Other: 4)	16
Neuroleptics	7
T C A	4

References

Winokur, A., Rickels, K., Greenblatt, D.J., et al. Withdrawal reaction from long-term, low-dosage administration of diazepam: A double-blind, placebo-controlled case study. *Arch. Gen. Psychiatry*, 37:101-105, 1980.

Behavioral Assessment of Drug Effects in Obsessive-Compulsive Disorders

Samuel M. Turner, Ph.D.[1]

Research can only advance as far as is permited by our measurement technology. Yet, it is a truism in clinical research that the technology of measurement lags significantly behind research endeavors. The quantity of research appears to exceed what can be justified from the standpoint of measurement quality. Clinical research typically grows out of the existence of interesting and significant clinical problems, and the need to develop some information about pathological behavior in the clinical arena. Thus, there is often little primary attention given to the perplexities of measurement issues.

Clinical studies are often designed to compare treatments with one another, placebo, or no treatment. A typical set of measurements consists of one or more of the following: patient self-report, clinical ratings, and paper and pencil inventories. It is not that there is anything wrong with applying these measures; rather, it is a question of whether or not this represents a completely adequate measurement strategy for the phenomena under consideration. The proper measurement system is essential if treatments (or no treatment) are to be adequately evaluated. A measurement strategy must be developed for a given disorder according to the phenomena under study as well as logical, theoretical, and practical considerations.

In recent years, there has been increased optimism in our thinking concerning the treatment of obsessive-compulsive disorder. Throughout the history of psychiatry, this disorder has been noted for its resistance to most forms of treatment (Grimshaw, 1965; Kringlen, 1965). However, recent studies with pharmacological (Thorén, Åsberg, Cronholm, Jörnestedt, & Träskman, 1980; Thorén, Åsberg, Bertilsson, Mellstrom, Sjöquist, & Träskman, 1980), surgical (Bridges, Goktepe, & Martos, 1973; Mitchell-Heggs, Kel-

---

[1] Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261.

Reprint requests to Samuel M. Turner, Ph.D., Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261.

ly, & Richardson, 1976) and behavioral interventions (Rachman, Cobb, Grey, MacDonald, Mawson, Sartori, & Stern, 1979; Turner, Hersen, Bellack, Andrasik, & Capparell, 1980; Turner, Hersen, Bellack, & Wells, 1979) have produced encouraging results with relatively brief periods of treatment. In most instances, psychosurgery would not be considered an appropriate treatment in this country. Therefore, drug treatment and behavior therapy appear to be the treatments of choice.

Obsessive-compulsive disorder is characterized by recurrent or persistent ideas, images, thoughts, or impulses. These are typically accompanied by an urge to engage in some overt or covert act, usually of a repetitous nature. Along with these subjective symptoms are the well-known behavioral abnormalities which include rituals such as hand washing, checking, and various avoidance behaviors. Rituals often significantly interfere with normal daily functions such as bathing, eating, toileting, and grooming. Moreover, social, economic, vocational, and interpersonal disfunctions may be experienced. In addition, varying degrees of depression and anxiety are an integral part of the syndrome.

Given the complex behavioral and physiological (biochemical) dimensions of the disorder, it is essential that a multifaceted measurement system be employed in research studies. This is rendered even more important if one desires to study the poorly understood relationship of depression and anxiety to obsessive-compulsive disorder. Presently, even the best studies of drugs (e.g., Rachman et al., 1979; Thorén et al., 1980 a,b) employed a set of incomplete outcome measures. Any measurement strategy should involve assessment of self-report, overt behavior, and physiological changes. That results may vary dependent upon the channel of measurement employed is a well-know phenomena. For example, following behavioral treatment, phobics may be able to approach formerly fear-inducing stimuli but still indicate by self-report that they are fearful, while changes in physiological indicators are consistent with their new behavior. This discrepancy among channels of measurement has been labeled desynchrony by Rachman and Hodgson (1974).

Keeping the tripartite measurement system described above in mind, listed below are the elements of an adequate measurement system for employment in obsessive-compulsive research. First, there should be some type of self-report measurement of obsessive ideation. This should consist of paper and pencil inventories, interview ratings, daily self-monitoring, or some combination. Specific measurement of overt ritualistic behavior is best obtained through direct behavioral observations as illustrated by the Turner et al. (1979, 1980) studies. Unfortunately, such direct observations are not always practical. Therefore, some form of self-report or interview ratings might also be necessary.

When direct observational data cannot be obtained, one way to remedy the stituation is to employ a behavioral avoidance test similar to those used in phobic research. Anxiety should be measured in all three measurement channels. Self-report data can be obtained via daily ratings of tension, interview ratings, or paper and pencil inventories. Behavioral data can be obtained by direct observation of operationally defined anxiety behaviors (e.g., fidgeting or hand-wringing). Physiological processes are probably more appropriate in anxiety measurement than in any of the other aspects of obsessive-compulsive disorder. Such measures as heart rate and galvanic skin response (GSR) would be appropriate. However, in the obsessive-compulsive syndrome, another set of physiological measures is necessary if we are to understand the mechanism by which drug effects are obtained. These are biochemical measures such as the ones employed in the Thorén (1980) and Rachman et al. (1979) studies. Depression can be measured by a number of self-report scales. It can also be measured by interview ratings, and through direct behavioral observation. Finally, some type of measurement of social functioning should be employed to assess all relevant social role areas. Such social functioning data should be obtained from the patient himself as well as from significant others. An outline of the use of the tripartite measurement system in obsessive-compulsive disorder is presented in Table 1.

Prior studies in obsessive-compulsive disorder had typically grouped all of the obsessional states together and treated them with drugs or some other form of treatment. Yet, it appears from the clinical literature that subgroups of obsessive-compulsive patients might exist. If there are in

Table 1

Assessment Strategy for Obsessive-Compulsive Disorder*

	Obsessive-Compulsive Symptoms				
	Subjective Distress	Rituals/Avoidance Behavior	Anxiety	Depression	Social / Interpersonal Functioning
Self-Report	X	X	X	X	X
Behavioral		X	X	X	
Physiological**			X	X	

*The channel of measurement that can be employed will vary to some extent with the nature of the problem.

**Physiological measures include biochemical assays.

fact important differences among types of obsessives, it is essential to begin developing classification systems so that the effects of treatments can be clearly defined. For example, Mavissakalian (1980) proposed a "functional" classification of obsessive-compulsive phenomena (*see* Table 2). Although the clinical and theoretical value of this system has not been established, it is a beginning in an area that has lacked serious investigation.

Considerable evidence has accumulated to suggest that antidepressants such as clomipramine are an effective treatment agent for obsessive-compulsive disorder. Moreover, there is recent evidence to suggest that a specific dose range is more effective than others, and that the proposed mechanism of change is suppression or the reuptake of serotonin. Yet, it was suggested above that the measurement strategies employed in previous studies were not wholly adequate. Therefore, it is difficult to assess the value of drug treatments at this time. Finally, a word of caution is also in order concerning the sample size used in experimental studies. Given the number of measures needed to adequately assess the obsessive-compulsive syndrome (*see* Table 1), it is evident that multivariate procedures may be required, or at least adjustment of significance levels. Moreover, in order to obtain adequate statistical power (cf. Agras & Jacob, 1981) when comparisons of active treatments are made, sample sizes far in excess of what typically is employed will be required. The presence of obsessive-compulsive disorder is consistently estimated to be low in comparison to other anxiety disorders. Therefore, in order to conduct a study with with the proper sample size, multicenter studies might be necessary.

Table 2

Functional Classification of Obsessive-Compulsive Phenomena

Obsessions—noxious cognitive stimuli such as intrusive thoughts, images, feelings and impulses

Obsessions Plus Compulsions (Anxiety Reducing)—behaviors which attempt to neutralize obsessions and reduce anxiety, discomfort (washing, checking, other cognitions, etc.)

Obsessions Plus Obsessionalized Compulsions (anxiety augmenting)—development of obsessional secondary phenomena

Rituals (Autonomous Compulsions)—rituals are disassociated from the anxiety/discomfort producing obsessions

From Mavissakalian (1980), *Journal of Behavioral Assessment*. Reprinted by permission.

Clinical Trials of Neuropeptides in Psychiatric Disorders

Chair: Philip A. Berger, M.D.
Department of Psychiatry and Behavioral Sciences
Stanford University Medical School
Stamford, California

and

Jerome Levine, M.D.
Pharmacologic and Somatic Treatments Research Branch
National Institute of Mental Health
Rockville, Maryland

Effect of Des-Tyr-γ-Endorphin in Schizophrenia
Herbert Meltzer, Daniel A. Busch, John Lee, and Yiannis Papaçostas
University of Chicago, Chicago, IL and SUNY at Stony Brook, NY

*Des-Tyr-γ-Endorphin: Clinical Experience in Depression
Thomas Meehan, Lynn Johnson, Yiannis Papacostas, and Max Fink
SUNY at Stony Brook, Stony Brook, NY

Vasopressin Studies in Alzheimer's Disease
Carol Tamminga, Raymon Durso, Paul Fedio, and Thomas N. Chase
Maryland Psychiatric Research Center and University of Maryland School of Medicine and National Institutes of Health

---

*Denotes paper was presented at NCDEU meeting but not received before going to press.

Effect of Des-Tyr-γ-Endorphin in Schizophrenia

Herbert Y. Meltzer, M.D.,[1] Daniel A. Busch, M.D.,[2] John Lee, M.D.,[3] and Yiannis Papacostas, M.D.[3]

Des-tyr-gamma-endorphin (DTγE) is a peptide which may occur endogenously, (Verhoef, Loever, Burbach, et al., 1980), and which has been shown in animal studies to have some behavioral, biochemical, and electrophysiological effects which are comparable to those of classical neuroleptics (de Wied, Bohus, van Ree, et al., 1978; Nickolson, & Berendsen, 1980; Pedigo, Schallert, Overstreet, et al., 1979; Schoemaker, & Nickolson, 1980). There are also significant differences between DTγE and neuroleptics, such as inability to produce catalepsy or block apomorphine-induced stereotypy (de Wied, Kovacs, Bohus, et al, 1978; Weinberger, Arnsten, & Segal, 1979). This profile has led to a series of clinical trials designed to determine if DTγE has antipsychotic properties in man. As with many antipsychotic compounds, early results were very favorable, indicating that doses as low as 1 mg/day intramuscularly (i.m.) for as brief a period as 3 days produced considerable improvement in both chronic and acute schizophrenic patients, although the results were far from uniform

---

[1] University of Chicago School of Medicine and Illinois State Psychiatric Institute, Chicago, IL 60637.
[2] Illinois State Psychiatric Institute, Chicago, IL 60637.
[3] State University of New York, Stony Brook, NY 11794.

(Emrich, Zandry, Zerssen, et al., 1980; van Ree, de Wied, Verhoeven, & van Praag, 1980; Verhoeven, van Praag, Botter, et al., 1978; Verhoeven, van Praag, van Ree, & de Wied, 1979). No extrapyramidal side effects were noted. More recently, entirely negative results have been reported in schizophrenic patients with and without tardive dyskinesia (Casey, Korsgaard, Gerlach, et al., 1981; Tamminga, Tighe, Chase, et al., 1981).

Method

This study included two groups of subjects. The first consisted of eight newly hospitalized schizophrenic patients at the Illinois State Psychiatric Institute who were diagnosed schizophrenic according to Research Diagnostic Criteria (Spitzer, Endicott, & Robins, 1977). Six were chronic, one subacute, and one acute. There were five males and three females; the mean age was 24.8 years. Following admission, the patients were kept off active medication for a period of 9 to 25 days. There was no appreciable symptom change during this time. Treatment with DTγE was begun with an initial dose of 1 mg i.m. daily for at least 3 days. The dose was randomly adjusted on an open basis to 3-10 mg/day for the rest of the 12-day treatment period. The maximum dose was 3 mg/day in four patients, 5 mg/day in two patients, and 10 mg/day in two patients. Following treatment with DTγE, patients were not given active medication for at least a week. Clinical change was assessed with the Schedule for Affective Disorders and Schizophrenia (SADS) (Spitzer & Endicott, 1980), the Global Adjustment Scale (GAS) (Endicott, Spitzer, Fleiss, & Schen, 1976), and the Nurses' Observation Scale for Inpatient Observation (NOSIE) (Honigfeld, Gillis, & Klett, 1966).

The Hoffman-reflex (H-reflex) recovery curve (Metz, Busch, & Meltzer, 1981) and platelet monoamine oxidase (MAO) activity (Jackman & Meltzer, 1980) were determined at the end of the placebo period as well as during and after the post-DTγE treatment period. Serum prolactin levels were determined by radioimmunoassay.

The second group of subjects consisted of seven patients hospitalized at the Veterans Administration Hospital or University Hospital at Stony Brook. Seven schizophrenic patients were treated with DTγE in doses of 1-4 mg/day for 14-21 days. Clinical evaluation was by means of the Brief Psychiatric Rating Scale (Overall & Gorham, 1962) and the Clinical Global Scale.

Results

The overall clinical impression of the research staff was that two of the eight Chicago patients showed marked clinical improvement, four showed minimal to moderate improvement, and two showed no change. Changes in GAS scores were in the direction of improvement in seven of eight patients (*see* Figure). These improvements were slight, but of the order of magnitude noted in other schizophrenic patients in the author's research unit who have been treated with classical neuroleptic treatment for a comparable period. Improvement was mainly in the area of social functioning. Patients became less withdrawn and more sociable and cooperative. Reports of delusions and hallucinations decreased in the responses given during SADS interviews, but clinical staff did not believe meaningful improvement occurred in these areas. Improvement in social functioning began within the first 3-7 days of treatment and did not appear to be dose-related. No extrapyramidal or other side effects were noted. After discontinuation of DTγE, six of eight patients showed deterioration. Considerably greater improvement was noted in these patients during the neuroleptic treatment period which followed DTγE. One of the two apparent good responders to DTγE failed to show any improvement on DTγE when treated with a subsequent course of DTγE upon rehospitalization 6 months later.

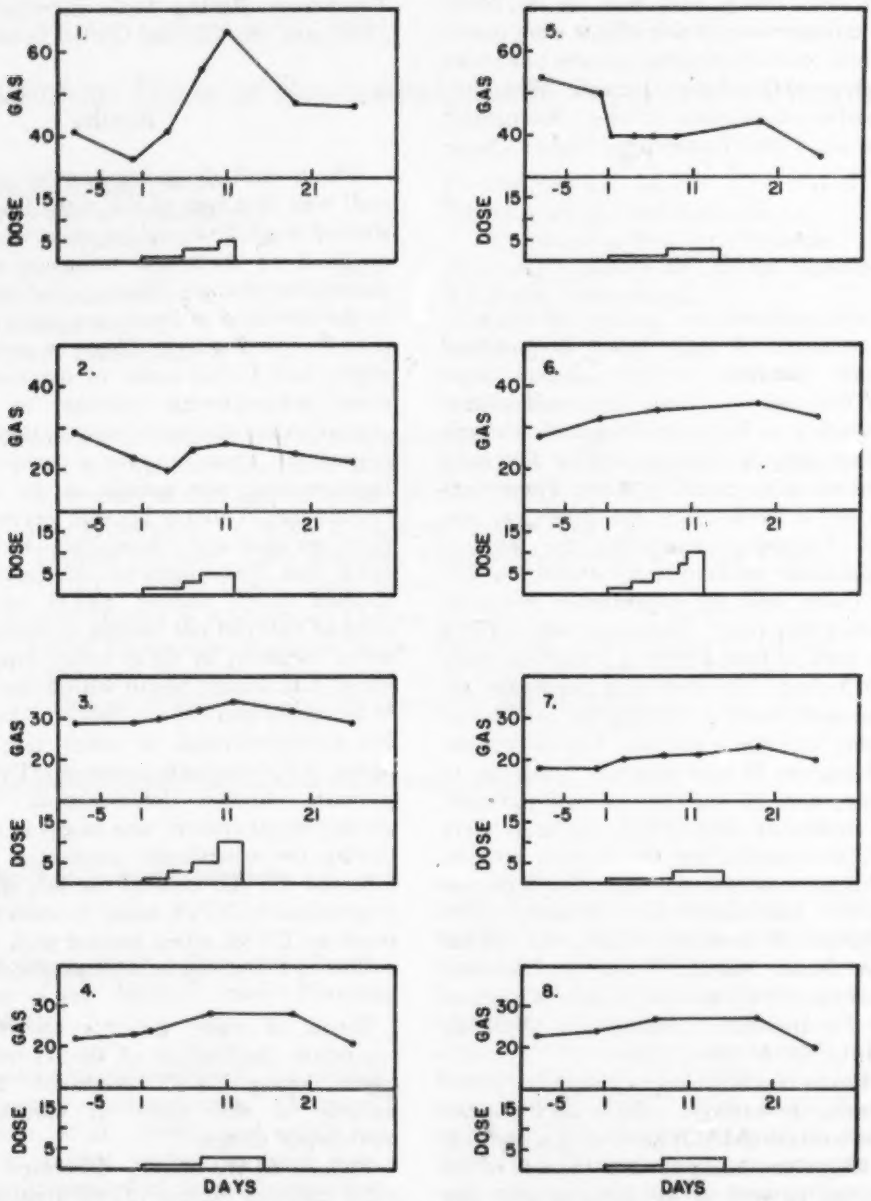
Seven of eight patients showed decreased secondary facilitation of the H-reflex recovery curve during DTγE treatment. This is comparable to the effect of clinically effective neuroleptic drugs.

Platelet MAO activity decreased in six of the eight patients during DTγE treatment. This is also comparable to the effect of neuroleptic drugs.

No change in serum prolactin levels was observed for up to 4 hours after injection of 1 mg DTγE.

Of the seven Stony Brook patients, one chronic

GLOBAL ASSESSMENT SCALE BEFORE, DURING AND AFTER DTGammaE



schizophrenic patient who had failed to respond to neuroleptic treatment showed marked, persistent clinical improvement of both positive and negative symptoms, and two showed moderate but transient improvement. No effect of DTγE on serum prolactin levels was noted.

Discussion

The clinical change during the period of treatment with DTγE was not impressive on an overall basis. An open study such as this has significant biases toward a type II error because of the high expectations of patients and staff of a novel antipsychotic agent. The major clinical improvement was noted in areas of behavior which are least objective to assess and most sensitive to high expectations for some improvement. The failure to obtain improvement in positive symptoms comparable to that produced by neuroleptic treatment is suggestive that DTγE is less effective than classical neuroleptic drugs if indeed it is active at all.

We did find two biological measures of activity of DTγE: the H-reflex and platelet MAO. The effects on these parameters were those produced by classical neuroleptic drugs. This is encouraging in that there may indeed be an in vivo neuroleptic effect of DTγE.

A double-blind, placebo-controlled study of DTγE for longer periods of time in a larger sample seems indicated, despite the meager clinical improvement demonstrated here because of the evidence of biological effects of DTγE. It may be that only a small proportion of subjects would respond clinically to this peptide because of heterogeneity of schizophrenia or because of differences in absorption and metabolism of DTγE.

References

Casey, D.R., Korsgaard, S., Gerlach, J., et al. Effect of des-tyrosine-γ-endorphin in tardive dyskinesia. *Arch. Gen. Psychiatry*, 38:158-160,1981.

de Wied, D., Bohus, B., van Ree, J.M., et al. Neuroleptic-like activity of (des-tyr^1)-γ-endorphin in rats. *Lancet*, 1:1046-1047, 1978.

de Wied, D., Kovacs, G.L., Bohus, B., et al. Neuroleptic activity of the neuropeptide β-LPH 62-77. *Eur. J. Pharmacol.*, 49:427-436, 1978.

Emrich, H.M., Zaudig, M., Zerssen, D.V., et al. Des-tyr^1-γ-endorphin in schizophrenia. *Lancet*, 9:1364-1365, 1980.

Endicott, J., Spitzer, R.L., Fleiss, J.L., et al. The Global Assessment Scale. *Arch. Gen. Psychiatry*, 33:766-771, 1976.

Honigfeld, G., Gillis, R.D., and Klett, C.J. NOSIE-30: *A Treatment Sensitive Ward Behavior Scale*, Report No. 66, Central Neuropsychiatric Research Laboratory, Perry Point, Maryland, 1966.

Metz, J., Busch, D.A., and Meltzer, H.Y. Des-tyrosine-γ-endorphine: H-reflex response similar to neuroleptics. *Life Sci.*, 28:2003-2008, 1981.

Nickolson, V.J., and Berendsen, H.H.G. Effects of the potential neuroleptic peptide des-tyrosine^1-γendorphin and haloperidol on apomorphine-induced behavioural syndromes in rats and mice. *Life Sci.*, 27:1377-1385, 1980.

Overall, J.E., and Gorham D.R. Brief Psychiatric Rating Scale (BPRS). *Psychol. Rep.*, 10:799-812, 1962.

Pedigo, N.W., Ling, N.C., Reisine, T.D., et al. Examination of des-tyrosine^1-gamma-endorphine activity at [^{3}H]-spiroperidol binding sites in rat brain. *Life Sci.*, 24:1645-1650, 1979.

Pedigo, N.W., Schallert, T., Overstreet, D.H., et al. Inhibition of in vivo [^{3}H]-spiperone binding by the proposed antipsychotic des-tyr^1-γ-endorphin. *Eur. J. Pharmacol.*, 60:359-364, 1979.

Schoemaker, H., and Nickolson, V.J. Effects of des-tyr^1-γ-endorphin on dopamine release from various brain regions *in vitro*. *Life Sci.*, 27:1371-1376, 1980.

Spitzer, R.L., and Endicott, J. *Schedule for Affective Disorders and Schizophrenia (SADS)*, 3d ed., New York State Psychiatric Institute, Biometrics Research, 1977.

Spitzer, R.L., Endicott J., and Robins, E. *Research Diagnostic Criteria*, 3d ed., New York State Psychiatric Institute, 1977.

Tamminga, C.A., Tighe, P.J., Chase, T.N., et al. Des-tyrosine-gamma-endorphin administration in chronic schizophrenics. *Arch. Gen. Psychiatry*, 38:167-168, 1981.

van Ree, J.M., de Wied, D., Verhoeven, W.M.A., et al. Antipsychotic effect of γ-type endorphin in schizophrenia. *Lancet*, 1363-1364, 1980.

Verhoef, J., Loberg, J.G., Burbach, J.P.H., et al. α-Endorphin, γ-endorphin, and des-tyrosine fragments in rat pituitary and brain tissue. *Life Sci.*, 26:851-859, 1980.

Verhoeven, W.M.A., van Praag, H.M., Botter, P.A., et al. (Des-tyr^1)-γ-endorphin in schizophrenia. *Lancet*, 1:1046-1047, 1978.

Verhoeven, W.M.A., van Praag, H.M., van Ree, J.M., et al. Improvement of schizophrenic patients treated with (des-tyr^1)-gamma-endorphin. *Arch. Gen. Psychiatry*, 36: 294-298, 1979.

Weinberger, S.B., Arnsten, A., and Segal, D.S. Des-tyrosine^1-γ-endorphine and haloperidol: Behavioural and biochemical differentiation. *Life Sci.*, 24:1637-1644, 1979.

Vasopressin Studies in Alzheimer's Disease

Carol A. Tamminga, M.D.,[1] Raymon Durso, M.D.[1] Paul Fedio, Ph.D.[1] and Thomas N. Chase, M.D.[1]

Recent advances in peptide pharmacology are suggesting areas for therapeutic application of exogenous peptides in human disease. Vasopressin, identified since 1950 as a cyclic-nine amino-acid peptide involved in sodium excretion and smooth muscle contraction, has been shown to facilitate animal learning and memory in behavioral testing. Peripherally administered vasopressin delays extinction of learned behaviors in a variety of animal learning paradigms (Ader & de Wied, 1972; Bohus, Gispen, & de Wied, 1973; de Wied, 1971; de Wied, Greven, Lande, & Witter, 1972). Furthermore, Brattleboro rats, which on a genetic basis lack vasopressin, learn behaviors more slowly and extinguish learned behaviors faster than control rats; this defect is corrected by the exogenous administration of vasopressin (de Wied, Bohus, & Wimersma, 1975). Moreover, analogues of vasopressin have been shown to block the effects of CO_2-induced retrograde amnesia in rats tested in a passive avoidance task (Rigter, Riezen, & de Wied, 1974). Recent uncontrolled trials of vasopressin in human memory-losing disorders (Weingartner, Gold, Ballenger, et al. 1981; Oliveros, Jandali, Timsit-Berthier, et al. 1978; LeBoeuf, Lodge, & Eames, 1978; Blake, Dodd, & Evans, 1978) as well as in normal individuals (Weingartner et al., 1981; Legros, Gilot, Seron, et al. 1978) have encouraged further controlled testing.

Method

Lysine vasopressin was administered in a double-blind, placebo-controlled design to patients with mild to moderate symptoms of Alzheimer's-type dementia. Patients were included if they had a progressive history of memory loss and cognitive deficit, documented by the Wechsler Adult Intelligence Scale (WAIS) and the Wechsler Memory Scale (WMS), without any evidence of focal brain impairment or other diagnosable cause of dementia. The study design was a non-crossover type using seven patients in each of two groups, one of which received 16 units per day of vasopressin administered intranasally, the other, an equivalent quantity of nasal spray carrier for 10 days. Subjects were evaluated with memory and performance tests prior to, during, and for 7 days following the intranasal treatment. The tests administered were selected to measure aspects of learning, memory, attention, and perception in each of the patient participants. At baseline, the WAIS and the WMS were done to confirm the diagnosis of Alzheimer's disease, and the initial battery of learning tests was applied. The specific learning and memory tests carried out were: 1) word list learning with free recall and selective reminding; 2) paired associate learning for immediate and delayed recall; 3) memory retention for a 20-item paragraph-long prose passage in immediate and delayed recall; 4) memory retention for photographs of common objects; 5) reaction time using a standard key-press machine with either fixed or variable forewarning period; and 6) perception capacity with a tachistoscope projecting patterns and words to the central visual field.

Results and Discussion

Results showed no difference in learning or memory between lysine vasopressin (LVP)-treated and placebo-treated subjects. Immediate recall and learning were unchanged in word list and paired associate learning and in the memory retention tests. Delayed recall testing, included to measure aspects of memory storage and recall, also remained unchanged. However, the tests of fixed alerting-interval reaction time showed that the subjects who received vasopressin reacted faster than those who received placebo. When a variable alerting-interval was used, no difference in reaction time was apparent between the vasopressin and placebo-treated groups.

We report that lysine vasopressin failed to enhance memory or learning in human subjects with Alzheimer's disease, while it did improve reaction time. The fixed-interval reaction time test indicates either an enhancement of motor response or attention or both. Our results suggest a nonspecific activating effect of vasopressin. This effect, similar to that expected with other central nervous system stimulants, like amphetamine, may well enhance learning and/or memory in noncognitively impaired individuals. The basal organic impairment of this patient group may account for their failure to respond to vasopressin.

---

[1] National Institute of Neurologic and Communicative Disorders and Stroke, Bethesda, MD 20205, and Maryland Psychiatric Research Center, Baltimore, MD 21228.

References

Ader, R., and De Weid, D. Effects of lysine vasopressin in passive avoidance learning. *Psychonomic Science*, 29:46-48, 1972.

Blake, R.D., Dodd, M.J., and Evans, J.G. Vasopressin in amnesia. *Lancet*, March 18:608, 1978.

Bohus, B., Gispen, W.H., and De Weid, D. Effect of lysine vasopressin and $ACTH_{4-10}$ on conditioned avoidance behavior of hypophysectomized rats. *Neuroendocrinology*, 11:137-143, 1973.

de Wied, D. Longterm effect of vasopressin on the maintenance of a conditioned avoidance in rats. *Nature*, 232:58-60, 1971.

de Wied, D., Bohus, B., and Wimersma Greidanus, T.J.B. Memory deficit in rats with hereditary diabetes insipidus. *Brain Res.*, 85:152, 1975.

de Wied, D., Greven, H.M., Lande, S., and Witter, A. Dissociation of the behavioural and endocrine effects of lysine vasopressin by tryptic digestion. *Br. J. Pharmacol.*, 45:118-122, 1972.

LeBoeuf, A., Lodge, J., and Eames, P.G. Vasopressin and memory in Korsakoff syndrome. *Lancet*, Dec. 23 & 30: 1370, 1978.

Legros, J.J., Gilot, P., Seron, X., et al. Influence of vasopressin on learning and memory. *Lancet*, Jan. 7:41-42, 1978.

Oliveros, J., Jandali, M.K., Timsit-Berthier, M., et al. Vasopressin in amnesia. (Letter) *Lancet*, 8054:42, 1978.

Rigter, H., Riezen, H. van, and de Wied, D. The effects of ACTH and vasopressin analogs on CO_2-induced retrograde amnesia in rats. *Physiol. Behav.*, 13:381, 1974.

Weingartner, H., Gold, P., Ballenger, J.C., et al. Effects of vasopressin on human memory functions. *Science*, 211: 601-603, 1981.

Psychoactive Drug Treatment in Retarded Populations

Chair: Robert L. Sprague, Ph.D.
Institute for Child Behavior and Development
University of Illinois
Champaign, Illinois

and

Robert Lipman, Ph.D.
Pharmacologic and Somatic Treatments Research Branch
National Institute of Mental Health
Rockville, Maryland

Effects of Phenytoin Withdrawal on Matching to Sample and Workshop Performance of Mentally Retarded Individuals – A Brief Report
Vicky J. Davis
Western Psychiatric Institute and Clinic, Pittsburgh, PA

Effects of Neuroleptic Drugs on the Intellectual and Habilitative Behaviors of Mentally Retarded Persons
Donald G. Ferguson
Mental Retardation Division, Brainerd State Hospital, Brainerd, MN

An Applied Dose-Response Curve of Thioridazine with the Mentally Retarded: Aggressive, Self-stimulatory, Intellectual, and Workshop Behaviors – A Preliminary Report
Stephen E. Breuning
Western Psychiatric Institute and Clinic, Pittsburgh, PA

An Analysis of Institutionalized Retarded Residents Using DIS-CO
Robert L. Sprague
Institute for Child Behavior and Development, University of Illinois, Champaign, IL

Tardive Dyskinesia in Mentally Retarded Children, Adolescents, and Young Adults: North Carolina and Michigan Studies
C. Thomas Gualtieri, Stephen E. Breuning, Steven R. Schroeder, and Dana Quade
University of North Carolina, Chapel Hill, NC and Western Psychiatric Institute and Clinic, Pittsburgh, PA

Comment on Neuroleptic Serum Levels in Mentally Retarded Boys
James C. Harris, Larry E. Tune, Michael Kurtz, and Joseph T. Coyle
Johns Hopkins University School of Medicine, Baltimore, MD and
University of Pennsylvania School of Medicine, Philadelphia, PA

Effects of Phenytoin Withdrawal on Matching to Sample and Workshop Performance of Mentally Retarded Individuals—A Brief Report[1]

Vicky J. Davis, M.A.[2]

Phenytoin is used with about 40% of institutionalized and non-institutionalized mentally retarded individuals and has been the medication of choice for the control of seizures with all types of populations. Despite its widespread use, only recently have studies begun to examine the effects of phenytoin on measures of learning, performance, and adaptive behavior with the mentally retarded. The present investigation was designed to examine the behavioral effects of phenytoin withdrawal on two procedural tasks with institutionalized mentally retarded individuals: a matching to sample (MTS) color discrimination task and a workshop bicycle brake assembly (Bendix RB-2) task.

The subjects were two female (D & L) and one male (E) institutionalized mentally retarded individuals who had each been receiving phenytoin for at least three consecutive years. Criteria for phenytoin withdrawal was the absence of observed seizures during this 3-year period. None of the subjects were receiving any other antiepileptic or neuroleptic medications. Subjects D, L, and E were 27, 23, and 16 years old, respectively. Subject D was receiving 100 mg oral dose of phenytoin, while Subjects L and E were each receiving 300 mg (100 t.i.d.) oral doses at the beginning of the study. Baseline phenytoin/serum levels for D, L, and E were 3.0 μg/ml, 4.1 μg/ml, and 3.5 μg/ml, respectively.

Method

Matching to Sample

The zero delay matching to sample (MTS) procedure involved a simple discrimination procedure using color stimuli. Each subject was seated in front of the intelligence panel where the center response window was illuminated with one of three colors (sample stimulus). Pressing the center window terminated its illumination and simultaneously resulted in the illumination of the two side windows (comparison stimuli). One of the side windows was illuminated with the same color (matching stimulus) as the center window (sample stimulus) and the other was illuminated with a different color (non-matching stimulus). Randomization of color assignments for each window occurred, with each color appearing equally often as sample, matching, and non-matching stimuli.

A matching response resulted in the delivery of one consumable reinforcer, and an 0.5 sec, 1000 hz tone. A non-matching response or no response within 30 sec terminated the side window illuminations for a 10-sec timeout prior to the onset of the next trial (i.e., illumination of the center window). The failure to emit a response within 30 sec was counted as an error. Five sec after reinforcement delivery or 10 sec after an incorrect reponse (error), the center window was illuminated to begin the next trial. Each incorrect response resulted in the stimulus being repeated until a correct response was emitted. The dependent variable was the percentage of correct responses per session. Each subject participated in two or three sessions per week with each session consisting of 30 trials. The first three sessions were pretraining sessions where the matching-to-sample procedure was followed and the subjects were given vocal and physical prompts that were gradually faded out until the subjects were able to respond independently. The fourth session began the experiment proper, in which phenytoin doses were systematically reduced following a multiple-baseline-across-subjects design (Baer, Wolf, & Risley, 1968). Subject D received one dose reduction (100 mg to 0 mg) while Subjects L and E received two reductions (300 mg to 150 mg to 0 mg). The number of daily phenytoin administrations remained consistent as dose reductions oc-

---

[1] This study was partially supported by USPHS Grant MH-32206 from the National Institute of Mental Health. A complete version of this paper appears in the *Journal of Nervous and Mental Disease* (Davis, V.J., Poling, A.D., Wysocki, T., and Breuning, S.E. Effects of phenytoin withdrawal on matching to sample and workshop performance of mentally retarded persons 169(11): 718-729, 1981).

[2] Substance Abuse Clinic, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261.

curred, and an inactive placebo was administered once 0 mg was reached.

Workshop

A retrospective analysis of Subjects D and L's performance on a workshop assembly task was performed once the matching to sample sessions were completed. The workshop task involved the assembly of a 15-part coaster bicycle brake assembly (Bendix RB-2) (Gold, 1972, 1973). Each brake was assembled individually by each subject utilizing a 15-compartment tray for sequential assembly. The three response measures recorded were percentage of time on task, number of assemblies completed, and number and type of prompts required from teacher or aides. Interobserver agreement checks by the workshop supervisor were completed on 15% of the teachers' and aides' ratings. The mean percentage of agreement was 89.6% with a range of 79.4% to 98.6% across sessions.

Serum Levels—EEG Assesments

Both phenytoin serum levels (gas liquid chromatography) and electroencephalogram (EEG) assessments were completed prior to baseline (within 5 days of Session 1) and the final reduction (10 to 14 days after matching to sample Sessions 13, 42, and 55 for Subjects D, L, and E; and workshop Sessions 19 and 54 for Subjects D and L, respectively). An additional phenytoin/serum level EEG was completed 4 days after the onset of the 150 mg dose for Subjects L and E (MTS Sessions 22 and 30, respectively, for L and E, and workshop Session 33 for L). Seizure monitoring procedures were in effect throughout the study. Double-blind procedures were implemented throughout; neither ward staff, workshop staff, nor subjects were aware of the phenytoin dose reductions or placebo administrations.

Results

The results of the study empirically demonstrate that doses of phenytoin considerably lower than the suggested optimum therapeutic level of 10-20 μg/ml (Rall & Schleifer, 1980) can impair the performance of mentally retarded individuals on both matching to sample and work assembly tasks. As the doses were reduced for each of the three subjects, there were increases in matching to sample task, with the highest percentage correct being obtained after, and only after, the 0 mg dose was reached. The greatest number of brake assemblies completed and lowest numbers brake assemblies completed and lowest numbers of prompts required in the workshop setting occurred only after the 0 mg dose was reached. There was no substantial change in the percentage of time-on-task for either subject in the workshop setting. Also, there were no EEG changes across withdrawal, and the results correlated with serum level changes.

Conclusion

The findings from this study have serious implications for the mentally retarded who receive phenytoin. While the subjects in the study are perhaps not typical of most epileptics receiving phenytoin, there are a great number of mentally retarded individuals receiving phenytoin of whom they are representative. It is not unreasonable to generalize the present findings to other mentally retarded individuals who are receiving phenytoin and have been seizure free for extended periods of time. For example, recent estimates suggest that about 28% of all the mentally retarded receiving phenytoin have not had observed seizures (Davis, Cullari, & Breuning, in press). This suggests that large numbers of the mentally retarded are experiencing an unnecessary drug-induced impairment in performance. However, it is important to mention that even though none of the subjects showed evidence of a clinical seizure while receiving phenytoin or following withdrawal, this certainly does not indicate that all mentally retarded individuals receiving phenytoin, but remaining seizure free for an extended period of time could be successfully titrated off of the drug. Probably some could not. However, given the possibility of behavior and impairment, conservative use of phenytoin is warranted.

References

Baer, D.M., Wolf, M.M., and Risley, T.R. Some current dimensions of applied behavior analysis. *JAMA*, 1, 91-97, 1968.

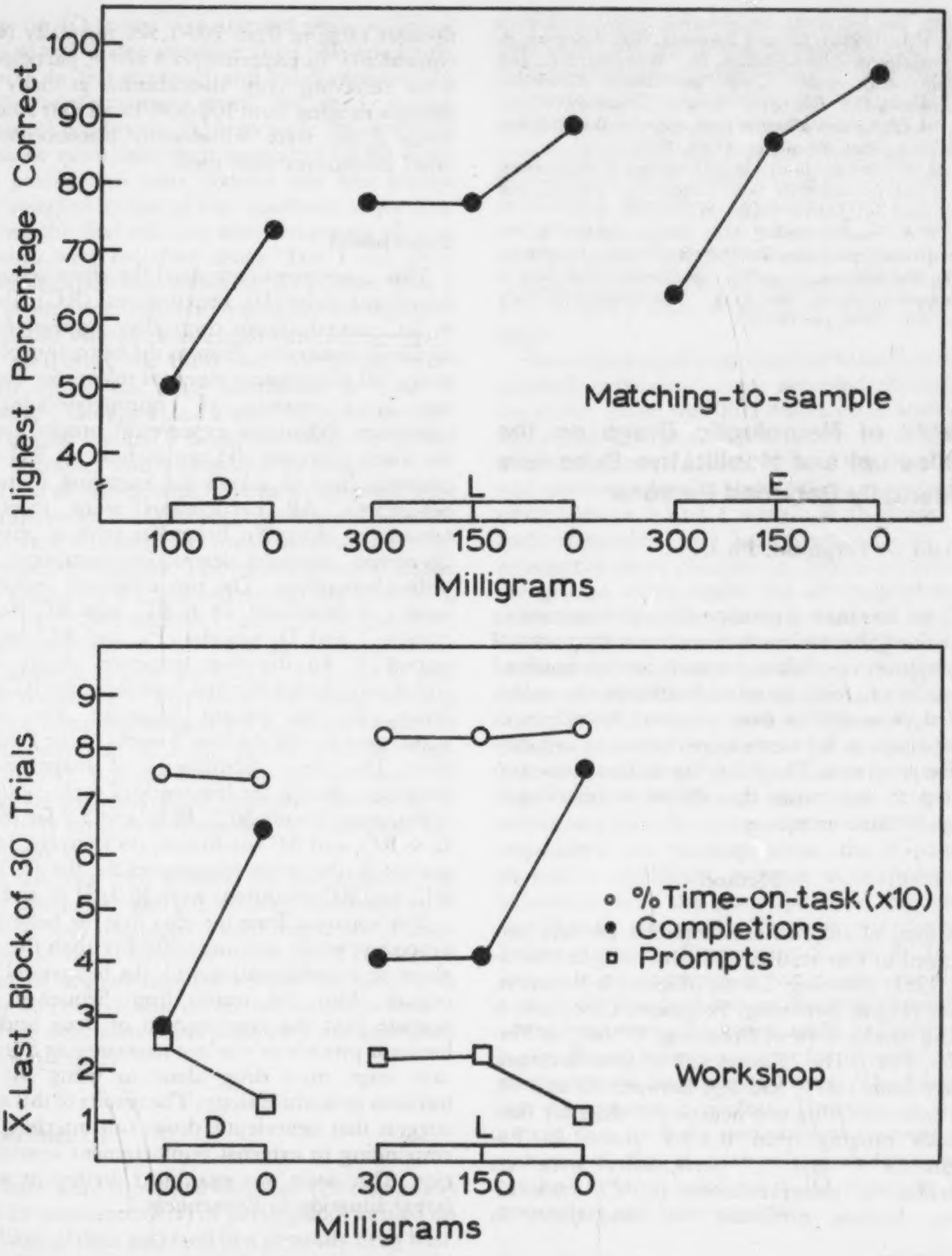


FIGURE. The Figure summarizes the matching to sample and workshop performance of Subjects D, L, E and D, and L, respectively.

Davis, V.J., Cullari, S., and Breuning, S.E. Drug use in community foster-group homes. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation*. Springfield, IL: Charles C Thomas. (In press)

Gold, M.W. Factors affecting production by the retarded: Base rate. *Ment. Retard.*, 11, 41-45. 1973.

Gold M.W. Stimulus factors in skill training of the retarded on a complex assembly task: Acquisition, transfer, and retention. *Am. J. Ment. Defic.*, 76, 517-526, 1972.

Rall, T.W., and Schleifer, L.S. Drugs effective in the therapy of epilepsies. In: Gilmar, A.G., Goodman, L.S., and Gilman, A. (eds.), *The Pharmacological Basis of Therapeutics*, 6th ed. New York: MacMillan Publishing Co., Inc., 1980, pp. 448-474.

Effects of Neuroleptic Drugs on the Intellectual and Habilitative Behaviors of Mentally Retarded Persons[1]

Donald G. Ferguson, Ph.D.[2]

There has been a paucity of studies examining behavioral alternatives to neuroleptic drug control of inappropriate behaviors with institutionalized mentally retarded persons. Furthermore, only a few of these studies have assessed the effects of these drugs on IQ scores or performance in habilitative programs. The following studies were conducted to determine the effects of neuroleptic drugs in these areas.

Method

A total of 162 mentally retarded persons participated in four studies (i.e., Breuning & Davidson, 1981; Breuning, Davis, Matson, & Ferguson, under review; Breuning, Ferguson, Davidson, & Poling under review; Breuning, O'Neill, & Ferguson, 1980). The 79 males and 83 females ranged in age from 11-71, had IQs between 19 and 64, and were receiving one neuroleptic drug for time periods ranging from 0.1-3.7 years. In Experiments 1 and 2, participants were on thioridazine, chlorpromazine (CPZ), mesoridazine, lithium carbonate, or haloperidol in dosages ranging from 200-1,500 mg daily (CPZ equivalent). In Experiments 3 and 4, participants were receiving only thioridazine in daily mg dosages ranging from 100-800. In all four studies, when drugs were withdrawn, placebo/double-blind procedures were used.

Experiment 1

This experiment compared the effectiveness of neuroleptic drug (D), response-cost (RC), and D + RC procedures for controlling aggressive and psychotic behaviors. Prior to the beginning of this study, all participants received tokens for engaging in a variety of appropriate/adaptive behaviors. When the experiment proper began, the token economy did not include an RC contingency (loss of tokens for engaging in target behaviors). All participants were receiving neuroleptic drugs for behaviors such as physical aggression, property destruction/disruption, and yelling/screaming. The two treatment sequences were: D (base-line), D + RC, and RC for Sequence 1 and D, placebo (P), and RC for Sequence 2. In the first sequence, drugs were withdrawn during the first 3 weeks of the RC condition. In the second sequence they were withdrawn during the first 3 weeks of the P condition. The mean frequencies of inappropriate behaviors during the last week of each condition of Sequence 1 were 50.2, 49.6, and 5.2 for the D, D + RC, and RC conditions, respectively. In Sequence 2, the mean frequencies for the D, D + RC, and RC conditions were 46.3, 51.3, and 3.7.

It is apparent from the data that the behavioral procedure alone was more effective than the drug alone or in combination with the behavioral procedure. Also, the results from Sequence 2 illustrate that the combination of drug and behavioral procedure was not necessary as a transition stage from drug alone to using the behavioral procedure alone. The results of this study suggest that neuroleptic drugs can interfere with responding to external reinforcement contingencies. This issue was examined further in a different situation in Experiment 2.

Experiment 2

In this experiment, the effect of neuroleptic drugs on IQ scores was assessed when residents were tested under standard (i.e., following procedures in test manual) and reinforcement (an edible reinforcement given for each correct response) conditions. IQ tests were administered on three occasions, each separated by 60 days. The participants were divided into four groups and assigned to one of four condition sequences. During the first two test administrations all participants were receiving drugs. Test 1 was given under standard conditions for all groups. Test 2 was given under standard conditions for Groups 1 and 3 and reinforcement conditions for Groups 2 and 4. During the third test, the groups were tested under the same conditions as Test 2. However, Groups 1 and 2 were taken off medication during the first 3 weeks following the second test. Groups 3 and 4 remained on drug.

---

[1] This study was partially supported by USPHS Grant MH-32206 from the National Institute of Mental Health.

[2] Developmental Disabilities Program Division, Brainerd State Hospital, Box 349, Brainerd, MN 56401.

While all four groups were on drugs there were no differences in IQ scores, regardless of whether tests were administered under standard or reinforcement conditions. The mean IQ scores for the four groups on the first and second test were 24.8, 27.6, 24.2, 26.3 and 25.7, 24.5, 24.0, and 26.9, respectively. On the third test the mean IQ scores for the four groups were 32.6, 54.7, 24.2, and 25.4, respectively. The two groups tested off drug showed mean increases of 6.9 IQ points (standard conditions) and 30.2 IQ points (reinforcement conditions). But the other two groups tested on drugs showed only slight changes. The results of this study support and extend the findings of Experiment 1.

In the first two studies, all participants had been previously selected for drug discontinuation because they displayed a high frequency of inappropriate behavior while on drug. Therefore it could be argued that the results are specific to those individuals who do not respond to neuroleptic drug treatment. This possibility was examined in a third study.

Experiment 3

There were two equal divisions (20 responders and 20 nonresponders) of participants formed on the basis of data gathered in a prestudy drug trial. The 20 responders were individuals showing decreased frequencies of inappropriate behaviors (at least 60%) while on thioridazine and 20 nonresponders were individuals showing no change (less than 10%) or increased frequencies of inappropriate behaviors while on drug. The prestudy drug trial used an ABA design (on-drug, off-drug, on-drug). Both the responders and nonresponders were each divided into four groups and exposed to the same condition sequences as described for Experiment 2. However, the time periods between test administrations were not equal. Tests 1 and 2 were separated by 8 weeks and Tests 2 and 3 were separated by 12 weeks. Drugs were titrated over a 3-week period from Week 10 to Week 13 of the study.

The frequency of inappropriate behaviors (e.g., physical aggression) were recorded throughout the study. There was little difference in scores for any of the groups on the first two tests. On the third test, Groups 1 and 2 of both the responders and nonresponders had been off drugs for 9 weeks while Groups 3 and 4 remained on drugs. For both responders and nonresponders, the only substantial score changes on Test 3 occurred in the groups tested under the off-drug/reinforcement condition. The mean increase in IQ score for these groups was 26.5 and 24.4 IQ points for responders and nonresponders, respectively. Mean test score changes for all other groups ranged from *−2.9* to *+4.1* points. There was little change in the frequency of inappropriate behaviors while all the groups were receiving thioridazine. However, when the drug was withdrawn from the two groups in each division of responders and nonresponders, the responders showed a significant increase in inappropriate behaviors, and the nonresponders frequencies significantly decreased. There is one disparate finding between Experiment 2 and 3. In the former study, increases in test scores were found under both standard and reinforcement conditions when drugs were withdrawn, while in Experiment 3 significant increases were found only under reinforcement conditions off-drug. The basis for this discrepancy is unclear. However, it is apparent that in both studies reinforcement procedures in the absence of neuroleptic drugs resulted in large increases in IQ scores for both responders and nonresponders.

Experiment 4

The final experiment was designed to assess the effect of thioridazine on the performance of a workshop task (assembly of a 15-part bicycle coaster brake). In addition, the effect of gradual vs. abrupt drug withdrawal and drug initiation was assessed. The study was conducted over a 29-week period. The conditions were abbreviated as follows: D-drug; ND-no drug; A-abrupt; withdrawal (end of Week 10); G-drug discontinued gradually over a 3-week period (Weeks 20-22). The groups were designated D-D, D-NDA, D-NDG, ND-D, and ND-ND where the letters before the hyphen refer to the first 10 weeks of the study and the letters after the hyphen refer to Weeks 11-29. Although three response measures were taken (time-on-task, number of prompts, and number of completions), the clearest drug effects were observed on the last measure and only they will be discussed.

Analyses showed that by the tenth week the two groups not receiving drugs (ND-D and ND-ND) were completing more assemblies than the others. On Weeks 12-15 the two groups not receiving drug (ND-ND, D-NDA performed significantly different than the other groups. Group ND-ND continued to improve while group D-NDA's performance deteriorated. The same was true of group ND-D. Throughout the remainder of the study, group ND-ND performed significantly better than all the other groups. The performance of group D-NDA gradually improved over a period of about 10 weeks and eventually surpassed their performance during the first 10 weeks of the study. Group D-NDG showed a decrease in performance during drug withdrawal, but the level of performance recovered much faster than was observed in group D-NDA. Group ND-D's performance, after an initial decrease, rapidly recovered to a level comparable to that observed during the first 10 weeks. Group D-D's performance remained fairly constant throughout the entire study and in the final weeks of the study was lower than the performance of all the other groups.

Both drug discontinuation and initiation disrupted performance. The most severe and longest lasting deficits were produced by abrupt withdrawal. The group that did not receive drugs at any time during the study (ND-ND) performed superior to all of the other groups.

The results of these four studies taken collectively indicate that neuroleptic drugs administered to institutionalized mentally retarded individuals 1) in many instances do not reduce inappropriate behaviors; 2) interfere with responding to reinforcement contingencies; and 3) interfere with the performance of workshop tasks. These effects are observed in both responders and nonresponders. Given the results of the above studies and other published reports (e.g., Breuning, Ferguson, & Cullari, 1980), it is apparent that the possible deleterious effects of neuroleptic drugs must be carefully assessed before they are administered to mentally retarded individuals. Finally, the results of these studies have possible legal ramifications. It is stated in the *Minimum Constitutional Standards for Adequate Habilitation of the Mentally Retarded* that neuroleptic drugs will not be used "...in quantities that interfere with a residents, habilitative *program*..." The interpretation of these standards with regard to drug responders is complex; since inappropriate behaviors are being effectively controlled there is no problem concerning excessive doses, but it is obvious that even with these individuals drugs interfere with habilitative processes. The case against the use of these drugs with nonresponders is very clear. When there is no evidence of a therapeutic effect and habilitative processes are clearly interfered with, neuroleptic drug use should be considered excessive and unnecessary.

References

Breuning, S.E., and Davidson, N.A. Effects of psychotropic drugs on the intelligence test performance of institutionalized retarded adults. *Am. J. Ment. Defic.*, 85:575-579, 1981.

Breuning, S.E., Davis, V.J., Matson, J.L., and Ferguson, D.G. Effects of thioridazine and withdrawal dyskinesias on workshop performance of mentally retarded young adults. (Manuscript under review)

Breuning, S.E., Ferguson, D.G., and Cullari, S. Analysis of single- and double-blind procedures, maintenance of placebo effects, and drug—induced dyskinesia with mentally retarded persons. *Appl. Res. Ment. Retard.*, 1:175-192, 1980.

Breuning, S.E., Ferguson, D.G., Davidson, N.A., and Poling, A.D. Effects of thioridazine on the intelligence of mentally retarded drug responders and non-responders. (Manuscript under review)

Breuning, S.E., O'Neill, M.J., and Ferguson, D.G. Comparison of psychotropic drug response-cost, and psychotropic drug plus response-cost procedures for controlling inappropriate behaviors of institutionalized retarded persons. *Appl. Res. Ment. Retard.*, 1:253-268, 1980.

An Applied Dose-Response Curve of Thioridazine with the Mentally Retarded: Aggrssive, Self-Stimulatory, Intellectual, and Workshop Behaviors—A Preliminary Report[1]

Stephen E. Breuning, Ph.D.[2]

Neuroleptic drugs are frequently prescribed for the mentally retarded in an attempt to suppress a plethora of unwanted behaviors. Surveys spanning the past decade have consistently shown that 40-50% of the institutionalized mentally retarded receive such drugs (*see* Breuning & Poling, in press, for a review). Most recently it has been found that similar use of neuroleptic drugs occurs in community foster homes and group homes for the mentally retarded (i.e., Davis, Cullari, & Breuning, in press). In both institutional and community settings thioridazine is by far the most prescribed neuroleptic with this population, as it accounts for 60-70% of all neuroleptic drug prescriptions.

Despite its wide use, little is known about the therapeutic and contratherapeutic effects of thioridazine. In three recent reviews it was concluded that thioridazine *may* be useful in reducing aggression, general motor activity, and self-stimulation with the mentally retarded (Aman, in press; Breuning & Poling, in press; Ferguson & Breuning, in press). However, these reviews also point out that evidence of therapeutic effect is the exception, not the rule, with thioridazine and the mentally retarded. The issue of therapeutic effect is further confounded by data from several recent reports which suggest that even when there is a reduction in symptomatology, there may well be a concomitant reduction or disruption (increased variability) in adaptive/habilitative behaviors (e.g., Breuning & Davidson, 1981; Breuning, O'Neill, & Ferguson, 1980; Singh & Aman, 1981).

While these findings have consistently been replicated in methodologically sound studies, only one study (Singh & Aman, 1981) has attempted to examine thioridazine effects in a dose-dependent manner. It was found that a low dose of thioridazine was as effective as a much larger dose in controlling self-stimulatory behaviors. The present report represents the initial findings of a study designed to further the findings of Singh and Aman (1981) by assessing the dose-response properties of thioridazine with mentally retarded individuals across four response measures, nine dose levels, and a placebo condition.

Method

Subjects

The subjects were 84 non-autistic, institutionalized, mentally retarded individuals between the ages of 13 and 27 and with IQs ranging between 34 and 59. Informed consent was obtained for each subject and there were approximately equal numbers of males and females. In total, there were 14 responders and 14 nonresponders assessed for aggressive behaviors, and 16 responders and 16 nonresponders assessed for self-stimulatory behaviors. For the intellectual and workshop behaviors there were 14-14 and 15-15 responders and nonresponders, respectively. Most of the individuals being assessed for the aggressive or self-stimulatory behaviors were also individuals receiving either the intellectual or workshop tasks. There were no individuals assessed on both adaptive measures, and those assessed for aggressive behaviors were not emiting self-stimulatory behaviors and vice versa.

Procedure

Each dose and placebo condition lasted for 8 weeks with half of each group (e.g., 7 of 14 responders) receiving conditions in an ascending order and half in a descending order (8-7 or 7-8 for workshop). Because of the clinical nature of the study, these subject assignments were not prepared randomly. Rather, half of the subjects had reached the highest dose as part of clinical treatment and were now withdrawn. The remaining half were determined clinically appropriate for initiation of neuroleptic treatment because of the above-mentioned symptomatology. Double-blind conditions were in effect throughout, as neither

---

[1] This study was supported in part by USPHS Grant MH-32206 from the National Institute of Mental Health.

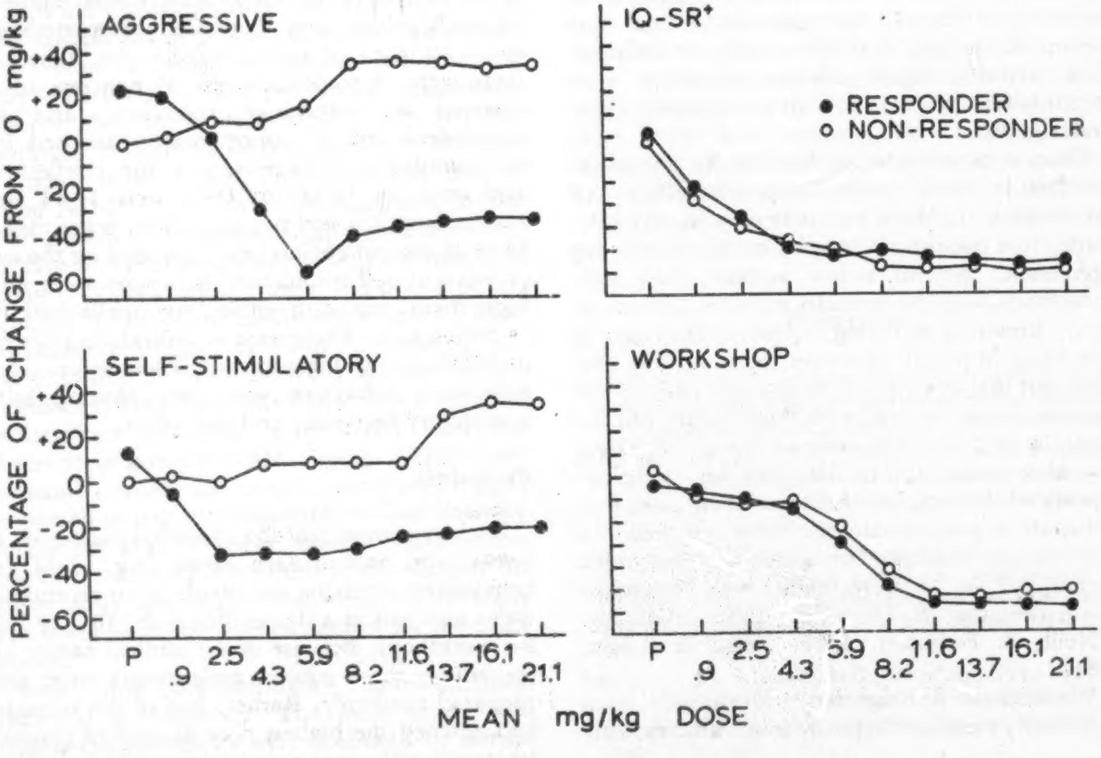
[2] Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261.

staff nor subjects were aware of conditions or dose. There were two equal dose administrations daily.

Definitions of aggression and self-stimulation were in observable and measurable terms and recorded by staff in 30-minute intervals, 24 hours per day (*see* Breuning, O'Neill, & Ferguson, 1980). Reliability checks were made by independent observers on a random selection of four 30-minute intervals per day. Mean reliability was 87.4% with a range of 76.3% to 92.4% across days. Intellectual behaviors were assessed using the procedure described by Breuning and Davidson (1981). Briefly, subjects received intellectual testing (Stanford-Binet, Form LM) under conditions where correct responses were reinforced with edible reinforcers selected on an individual basis. Workshop behaviors were assessed using procedures described by Davis, Poling, Wysocki, and Breuning (1981). In short, the number of 15-part coaster bicycle brakes (Bendix RB-2) assembled on an individual basis were counted. Completion of 0-7 of the 15 parts counted as 0 completion, 8-14 of the parts as one-half completion, and 15 parts as one completion.

Results and Discussion

The Figure shows the results from each response measure separately for responders and nonresponders. Data were analyzed using split-plot analyses of variance (one per response measure) with repeated measures and *post hoc* comparisons following Tukey's honestly significant difference (HSD) method (*see* Kirk, 1968).



FIGURE

Percentage of change from the off-drug condition (0 mg) plotted separately for responders and nonresponders and each response measure across the placebo condition (P) and nine doses.

Data in the Figure are plotted as percentage of change from the off-drug condition (0 mg) across the placebo (P) condition and nine doses. Data for the aggressive and self-stimulatory behaviors reflect daily frequencies; intellectual behaviors (IQ-SR+) reflect intelligence test scores; and workshop behaviors reflect the number of parts completed per session. Dose levels are plotted as means with no subject having more than a + or − 4% deviation from the mean.

For the responders, a dose of 5.9 mg/kg/day was optimal for reducing aggressive behaviors and a dose of 2.5 mg/kg/day was optimal for reducing self-stimulatory behaviors ($p < .01$). Higher doses had little additional effect except for a loss of behavioral control; i.e., increased frequencies of target behaviors ($p < .01$). For the nonresponders, the frequencies of aggressive and self-stimulatory behaviors showed no substantial changes at the lower doses ($p > .05$) but began to worsen as thioridazine doses increased ($p < .01$). For both responders and nonresponders, there were significant decreases in intellectual and workshop behaviors at even low doses ($p < .01$) and a continued worsening as the dose was increased ($p < .01$). Performance in the IQ-SR+ task was substantially more sensitive to dose changes than with the workshop task. For all response measures and both responders and nonresponders, identical dose effects were obtained regardless of ascending or descending order of conditions ($p > .05$).

The results from this study are clear. Mentally retarded individuals showing a beneficial response to thioridazine treatment (responders) will likely have the greatest suppression of aggressive behaviors occur at a moderate dose (about 6.0 mg/kg/day) and the greatest suppression of self-stimulatory behaviors occur at a fairly low dose (about 2.5 mg/kg/day). Regardless, it is also likely that there will be a concomitant decrease in adaptive/habilitative behaviors. For nonresponders, there may not only be a failure to show suppressed inappropriate behaviors but also a worsening of these behaviors (behavioral toxicity) along with a decrease in adaptive/habilitative behaviors.

There are two additional points worth making. First, preliminary correlational and discriminant function analyses show no significant relationship between psychiatric diagnosis or other possible predictor variables and whether or not an individual was a responder or nonresponder. Second, the equal numbers of responders and nonresponders in this study should not be interpreted to mean that 50% of the mentally retarded receiving neuroleptics will be responders. The reviews cited earlier suggest that only 10-15% of the mentally retarded receiving a neuroleptic will show a beneficial response.

References

Aman, M.G. Psychoactive drugs in mental retardation. In: Matson, J.L., and Andrasik, F. (eds.), *Treatment Issues and Innovations in Mental Retardation.* New York: Plenum Press. (In press)

Breuning, S.E., and Davidson, N.A. Effects of psychotropic drugs on the intelligence test performance of institutionalized mentally retarded adults. *Am. J. Ment. Defic.*, 85:575-579, 1981.

Breuning, S.E., and Poling, A.D. Pharmacotherapy with the mentally retarded. In: Matson, J.L., and Barrett, R.P. (eds.), *Psychopathology of the Mentally Retarded.* New York: Grune and Stratton. (In press)

Breuning, S.E., O'Neill, M.J., and Ferguson, D.G. Comparison of psychotropic drug, response cost, and psychotropic drug plus response cost procedures for controlling inappropriate behaviors of institutionalized retarded persons. *Appl. Res. Ment. Retard.*, 1:253-268, 1980.

Davis, V.J., Cullari, S., and Breuning, S.E. Drug use in community foster and group homes. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation.* Springfield, IL: Charles C Thomas. (In press)

Davis, V.J., Poling, A.D., Wysocki, T., and Breuning, S.E. Effects of phenytoin withdrawal on matching to sample and workshop performance of mentally retarded persons. *J. Nerv. Ment. Dis.*, 169:718-725, 1981.

Ferguson, D.G., and Breuning, S.E. Antipsychotic and antianxiety drugs. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation.* Springfield, IL: Charles C Thomas. (In press)

Kirk, R.E. *Experimental Design Procedures for the Behavioral Sciences.* Belmont, CA: Brooks/Cole, 1968.

Singh, N.N., and Aman, M.G. Effects of thioridazine dosage on the behavior of severely mentally retarded persons. *Am. J. Ment. Defic.*, 85:580-587, 1981.

An Analysis of Institutionalized Retarded Residents Using DIS-CO[1]

Robert L. Sprague, Ph.D.[2]

It is likely that tardive dyskinesia is as common among institutionalized populations of mentallyretarded peoples, due to extensive use of neuroleptic drugs (Davis, Cullari, & Breuning, in press; Sprague, 1977), as it is in psychiatric populations of patients. No systematic assessment using standardized instruments of such a population has been conducted, although surveys have been made (Baldessarini, 1979; Paulson, Rizvi, & Crane, 1975). In addition to the usual complications that persistent tardive dyskinesia causes any person, recent research has shown that even mild to moderate dyskinesia can interfere with performance on sheltered workshop tasks in which a large percentage of retarded residents participate as a therapeutic program (Breuning, Davis, Matson, & Ferguson, in press). When the fact that a serious side effect also actively interferes with ongoing programs is brought to the attention of a court, the court usually issues orders restricting use of such drugs (Sprague, in press).

Considering these two issues solely, the time for a systematic investigation of tardive dyskinesia in institutionalized populations of mentally retarded residents is long overdue. With these aims in mind, a project was undertaken to systematically assess the populations of two state-operated institutions for the mentally retarded in the midwest. In one institution it was possible to assess each resident, but in the other institution numerous problems such as budget cuts reducing staff and resignations prevented assessing the entire population. Consequently, emphasis is given in this report to the first institution in which the entire population of 519 residents participated in the study with less emphasis on the second facility where 67 residents were studied for a total of 586 residents.

A survey of the literature on rating scales of dyskinesia revealed that only one instrument, the Abnormal Involuntary Movement Scale (AIMS), had some reliability and validity data (Smith, Kucharski, Eblen, et al. 1979; Smith, Kucharski, Oswald, & Waterman, 1979), but it was felt that the items were of such a global nature that one might not be able to distinguish between tardive dyskinesia and the numerous movement disorders due to neurological disease, brain damage, and long-term social isolation, problems which can be readily found in institutionalized populations. Thus, a new scale was developed which contained 34 items subdivided into 10 body areas. Because the scale is too long to publish in this journal, copies are available from the author. Preliminary pilot studies were conducted on the wording of items which were changed to be readily understandable to nurses and licensed practical nurses. The scale was given the name Dyskinesia Identification System-Coldwater (DIS-CO).

After intensive inservice training and pilot ratings on some residents, nurses at one institution were asked to personally examine and rate every resident in the institution. Where possible, i.e., two nurses familiar with the residents in a ward, two independent assessments of the same residents were made to obtain interrater reliability correlations. Also, when possible, two different assessments about 1 month apart by the same nurse for the same resident were made to obtain stability correlations.

Each item was rated on a five-point scale: not present - 0, minimal - 1, mild - 2, moderate - 3, and severe - 4 with NA (not assessed) used when it was not possible to rate that particular item.

In the Table are listed the means and standard deviations for each of the 10 body areas with the number of items per body area in parentheses, the reliability correlation between two independent raters, and the stability correlations over about a 1-month period of time. Totals for each body area were summed over the number of items for that area to obtain the data included in the Table. In a similar fashion, the overall total was obtained. The overall mean rating was 8.8 (possible range 0 to 132) with a standard deviation of 6.8. All of the reliability and stability correlations are highly significantly different from zero.

---

[1] This research was supported in part by USPHS Grant No. MH-32206 from the National Institute of Mental Health.

[2] Institute for Child Behavior and Development, University of Illinois, Champaign, IL 61820.

Note: Anyone wishing a copy of the DIS-CO Scale should write to the author at: Institute for Child Behavior and Development, University of Illinois, 51 E. Gerty Drive, Champaign, IL 61820.

Table

Means and Standard Deviations for Each Body Area and Interrater and Stability Correlations for One Institution

Body Region	Descriptive			Reliability		Stability	
(number of items)	*N*	Mean	*SD*	*N*	Correlation	*N*	Correlation
Face (2)	519	1.1	1.3	177	.61†	160	.55†
Ocular (2)	519	.6	1.0	177	.64†	160	.48†
Oral (8)	517	2.2	2.6	177	.79†	160	.48†
Lingual (8)	428	2.0	2.7	177	.84†	160	.68†
Head/neck (2)	516	.3	.8	177	.48†	160	.52†
Trunk (2)	475	.2	.5	177	.21*	160	.31†
Upper limb (4)	513	1.6	1.9	177	.67†	160	.71†
Lower limb (4)	318	1.3	1.6	177	.67†	160	.45†
Gross body (1)	487	.2	.6	169	.14*	147	.15*
Ambulation (1)	343	.5	1.0	133	.41†	116	.64†
TOTAL (34)	519	8.8	6.8	177	.78†	160	.77†

*Significant at $p <$ .005
†Significant at $p <$ .001

It should be obvious that this reported data represents only the first step of a project if tardive dyskinesia is to be accurately and reliably assessed repeatedly in retarded populations and its relationship to neuroleptic drug administration determined. The DIS-CO instrument will be refined on the basis of this data; the refined instrument related to 4 years of drug history now available on the residents and, finally, a withdrawal of neuroleptic drugs study is underway to ascertain the effects of withdrawal on the ratings of abnormal movement as shown by this scale. Clearly, much remains to be done, but the issues are crucial to the welfare of mentally retarded people.

Acknowledgment: The author wishes to thank his colleagues Stephen E. Breuning, Vicky J. Davis, Donald Ferguson, John E. Kalachnik, and Rina Ullmann for their help in this study.

References

Baldessarini, R.J. (Chair) *Tardive dyskinesia.* Washington, D.C.: American Psychiatric Association, 1979.

Breuning, S.E., Davis, V.J., Matson, J.L., and Ferguson, D.G. Effects of thioridazine and withdrawal dyskinesias on workshop performance of mentally retarded young adults. (Submitted, 1981).

Davis, V.J., Cullari, S., and Breuning, S.E. Drug use in community foster-group homes. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation.* Springfield, IL: Charles C Thomas. (In press)

Paulson, G.W., Rizvi, C.A., and Crane, G.E. Tardive dyskinesia as a possible sequel of long-term therapy with phenothiazines. *Clin. Pediatr. (Phila.),* 14:953-955, 1975.

Smith, J.M., Kucharski, L.T., Eblen, C., et al. An assessment of tardive dyskinesia in schizophrenic outpatients. *Psychopharmacology (Berlin),* 64:99-104, 1979.

Smith, J.M., Kucharski, L.T., Oswald, W.T., and Waterman, L.J. A systematic investigation of tardive dyskinesia in inpatients. *Am. J. Psychiatry,* 136:918-922, 1979.

Sprague, R.L. Overview of psychopharmacology for the retarded in the United States. In: Mittler, P. (ed.), *Research to Practice in Mental Retardation,* Vol. III. Baltimore, MD: University Park Press, 1977.

Sprague, R.L. Litigation, laws, and regulations regarding psychoactive drug use. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation.* Springfield, IL: Charles C Thomas. (In press)

Tardive Dyskinesia in Mentally Retarded Children, Adolescents, and Young Adults: North Carolina and Michigan Studies

C. Thomas Gualtieri, M.D.,[1] Stephen E. Breuning, Ph.D.,[2] Steven R. Schroeder, Ph.D.,[2] and Dana Quade, Ph.D.[2]

Although neuroleptic drugs are frequently prescribed for behavior control and alleviation of psychiatric symptoms in mentally retarded children, adolescents, and young adults (Lipman, DiMascio, Reatig, & Kirson, 1978; Davis, Cullari, & Breuning, 1982), no systematic or methodologically acceptable studies of the occurrence of tardive dyskinesia (TD) in mentally retarded patients have appeared in the literature (Gualtieri & Hawk, 1980). Two parallel studies of TD and other problems associated with neuroleptic withdrawal were conducted: the North Carolina study (Gualtieri and Schroeder) was primarily concerned with clinical factors associated with TD; the Michigan study (Breuning) was primarily concerned with the course of TD symptoms after neuroleptic withdrawal.

Method

Subjects

Subjects were referred by treating physicians who felt that a trial neuroleptic withdrawal should be a routine part of each patient's clinical management. Inclusion criteria were: a) IQ less than 75, functional diagnosis of mental retardation (American Association of Mental Deficiency criteria); b) stable living environment; c) appropriate educational or workshop placement; d) good general health, with no active neurologic disease, or history of neurologic disorder which might be associated with dyskinesia; and e) continuous neuroleptic treatment of at least 6 months' duration.

North Carolina Study. Thirty-eight subjects (age 5 to 47, mean = 19.4 ± 1.7 [SEM]) were studied at four clinical sites: a psychiatric hospital, a pediatric psychopharmacology clinic, and two residential facilities for the mentally retarded. The mean age at which subjects began neuroleptic treatment was 10.9 (± 1.0) years. The mean duration of treatment was 8.3 (± 6) years, and total lifetime exposure to neuroleptics, expressed in chlorpromazine (CPZ) equivalents (Davis, 1976) ranged from 13.5 to 11,188 grams (mean = 1,046.7 ± 344.3).

Michigan Study. Fifty-seven subjects were studied at the Coldwater Regional Center. Subjects in the Michigan study were older than the North Carolina group ($p < .02$), had higher IQ scores ($p < .001$), and were treated with higher neuroleptic doses immediately prior to withdrawal ($p < .001$) (*see* Table). Because so many subjects in the Michigan group had been treated with neuroleptics for substantial periods of time as outpatients, comprehensive neuroleptic drug histories are not available for this group. All subjects, however, had been treated continuously with neuroleptics for at least 1.3 years prior to entry into this study.

Procedure

Subjects received comprehensive neurologic and developmental assessments prior to neuroleptic withdrawal. Special attention was given to neurologic or developmental problems (e.g., cerebral palsy, autism) which might be associated with dyskinetic movements, stereotypies, or psychotic mannerisms which may have anteceded neuroleptic treatment. After baseline evaluation, subjects were withdrawn from neuroleptic drugs, with serial examinations for dyskinesia, behavior change, or nondyskinetic withdrawal symptoms.

North Carolina Study. Subjects were assessed at weekly or biweekly intervals at baseline, during and after withdrawal, and until 8 weeks after complete discontinuance of neuroleptics. The Abnormal Involuntary Movement Scale (AIMS) exam and rating scale were used (Guy, 1976). Subjects who continued to manifest dyskinesia at 8 weeks were subsequently reexamined at monthly intervals. Mean interrater reliability among three physician raters on the AIMS rating scale was 0.83 (0.74-1.00) (Cohen's Kappa).

---

[1] Biological Sciences Research Center, Department of Psychiatry, and the Department of Statistics, University of North Carolina, Chapel Hill, NC 27515.

[2] Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261.

Table

Demographic and Outcome Data

	N.C.	Mich.	Total
N	38	57	95
Sex: Male	28	28	56
Female	10	29	39
Age (Yrs)	19.4	25.7	
(Mean ± *SD*)	± 10.3	± 12.6	
Age Range	5-47	12-71	5-71
IQ	31.2	40.4	
	± 15.9	± 14.8	
IQ Range	9-69	14-74	9-74
Drugs: Thioridazine	28 (74%)	27 (47%)	55 (58%)
Other neuroleptics	10	30	40
Mean Daily Dose	239.9	688.6	
(CPZ* equivalents)	± 293.8	± 310.2	
	48.3(SEM)	41.1	
Outcome:			
No problems	12 (32%)	19 (33%)	31 (33%)
Withdrawal-related problems	13 (34%)	20 (35%)	33 (35%)
Tardive dyskinesia	13 (34%)	18 (32%)	31 (33%)
Mild	5 (13%)	3 (5%)	8 (8%)
Moderate-severe	8 (21%)	15 (26%)	23 (24%)
Maintenance onset	3 (8%)	4 (7%)	7 (7%)

*Chlorpromazine

Michigan Study. Dyskinetic movements were assessed at weekly intervals at baseline, during withdrawal, and for 80 weeks thereafter. The Withdrawal Emergent Symptom Checklist (WESC) rating scale and examination were used (Engelhardt, 1974), and interrater reliability was 0.79 (Cohen's Kappa).

Results

Four outcome categories were considered according to diagnostic criteria that have been described elsewhere (Gualtieri, Sprague, Breuning, & Campbell, 1981): 1) no problems associated with neuroleptic withdrawal; 2) transient withdrawal problems, that is, withdrawal dyskinesia, nondyskinetic withdrawal symptoms, or acute behavior deterioration; beginning during neuroleptic withdrawal or immediately thereafter, and lasting less than 16 weeks after complete withdrawal; 3) mild TD; and 4) moderate or severe TD. In spite of the clinical differences between the two groups, the outcome of both studies are remarkably similar (*see* Table).

One-third of the total group ($N = 95$) experienced no problems prior to, during, or for at least 8 weeks after neuroleptic withdrawal; one-third experienced only transient withdrawal-related problems; and one-third had TD. Most of the cases of TD were characterized by moderate or severe movements. Of 31 cases of TD, only 7 were apparent while patients were on maintenance doses of neuroleptics. Six of the 7 cases of maintenance onset TD were characterized by dyskinesia that was rated as moderate or severe.

Thioridazine (THD) was the neuroleptic most commonly prescribed in both locations (58% of subjects). There was no association between the use of THD or any other particular neuroleptic and the development of TD.

North Carolina Study

The following were considered in a stepwise regression analysis of variables which might be associated with the development of moderate to severe tardive dyskinesia: location, age, race, sex, age at which neuroleptic treatment was begun, IQ, duration of treatment, total lifetime neuroleptic exposure, mean daily dose, and use of THD as the primary neuroleptic. The single variable that was most highly correlated with the development of moderate or severe TD was total lifetime exposure (analyzed as log of the total lifetime dose, $R^2 = 0.38$ for a one-variable regression). The regression analysis selected three independent variables, total lifetime exposure (log dose), IQ, and the age at which neuroleptic treatment began that were most highly correlated with moderate or severe TD ($R^2 = 0.65$, $F = 18.82$, 3 and 31 *df*), and each independent variable contributed significantly to the regression. Since treatment duration was highly correlated with total lifetime exposure ($r = +0.69$) adding it to the analysis did not increase R^2. None of the other variables contributed significantly to the equation. Nonparametric correlations (Goodman-Kruskal) also showed total lifetime exposure to be the variable most highly correlated with TD ($G = .531 \pm .120$, $p < .0001$).

Michigan Study

Dyskinetic movements were maximal at 4 weeks after neuroleptic withdrawal, when 36 of 57 patients (63%) exhibited symptoms. Dyskinetic movements were noted in 30 patients (53%) at 16 weeks, and in 18 patients (32%) at 52 and 80 weeks. This remission pattern was similar for movements of the tongue, lips and face, and head, limbs, and trunk. Facial dyskinesias which were rated as mild at 4 weeks were more likely to remit, and those which were rated as moderate or severe at 4 weeks were more likely to persist at 80 weeks (chi-square analysis, $p \leq .05$ and $\leq .025$, respectively). Dyskinetic movements which were apparent prior to neuroleptic withdrawal were invariably persistent.

Discussion

Moderate to severe, persistent TD is a cause for concern and a serious problem in mentally retarded children, adolescents, and young adults treated with neuroleptic drugs, a finding that must stand in sharp contrast to the dearth of empirical data to support the clinical use of neuroleptics in this group. The occurrence of TD is, not surprisingly, related to the patient's total lifetime exposure to neuroleptics. Dyskinetic movements that "break through," i.e., that are manifest on maintenance neuroleptic doses, predict a particularly severe and persistent course. However, the large majority of cases of TD — even severe and persistent TD — may not be apparent while patients continue to receive neuroleptic drugs. One may surmise, then, that epidemiologic surveys of TD that do not include trial neuroleptic withdrawal periods will necessarily underestimate the frequency of TD. On the other hand, a substantial number of the dyskinetic movements which arise within 4 weeks of neuroleptic withdrawal will remit spontaneously; such cases are better classified as "withdrawal dyskinesias."

Clearly, although advanced age may increase the risk of TD (Smith & Baldessarini, 1980), youth, at least in combination with mental retardation, does not confer protection from TD. In light of this serious risk, it is noteworthy that very few of the patients in these two samples actually needed to be on neuroleptic medication. In the North Carolina group, only 11 of 38 patients had to return to neuroleptic treatment; in the Michigan group, none returned. When behavior problems following neuroleptic withdrawal did arise, they were usually time limited, or readily controlled using behavioral or programmatic approaches. Many of these behavior problems appeared to be concentrated in the immediate postwithdrawal period, suggesting that a period of behavioral instability occurs following withdrawal. Physicians who withdrew mentally retarded patients from neuroleptic drugs should not take this postwithdrawal behavior deterioration as a mandate to immediately resume treatment with neuroleptics.

References

Davis, J.M. Comparative doses and costs of antipsychotic medication. *Arch. Gen. Psychiatry*, 33:858-861, 1976.

Davis, V.J., Cullari, S., and Breuning, S.E. Drug use in community foster-group homes. In: Breuning, S.E., and Poling, A.D. (eds.), *Drugs and Mental Retardation*. Springfield, IL: Charles C Thomas, 1982.

Engelhardt, D.M. WESC — Withdrawal Emergent Symptoms Checklist, Unpublished Ms., 1974. Available from Dr. David M. Engelhardt, Dept. of Psychiatry/Psychopharmacology, Downstate Medical Center, State University of New York, 450 Clarkson Avenue, Brooklyn, NY 11203.

Gualtieri, C.T., and Hawk, B. Tardive dyskinesia and other drug-induced movement disorders among handicapped children and youth. *J. Appl. Res. Ment. Retard.*, 1:55-69, 1980.

Gualtieri, C.T., Sprague, R., Breuning, S.E., Campbell, M. A centralized data system for studies of tardive dyskinesia in children, adolescents, and the developmentally handicapped. (Submitted, 1981)

Guy, W. ECDEU Assessment Manual for Psychoparmacology, Revised, 1976. U.S. DHEW, PHS, ADAMHA, NIMH, Psychopharmacology Research Branch, Rockville, MD.

Lipman, R.S., DiMascio, A., Reatig, N., and Kirson, T. Psychotropic drugs and mentally retarded children. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress*. New York: Raven Press, 1978.

Smith, J.M., and Baldessarini, R.J. Changes in prevalence, severity, and recovery in tardive dyskinesia with age. *Arch. Gen. Psychiatry*, 37:1368-1373, 1980.

Neuroleptic Serum Levels in Mentally Retarded Boys

James C. Harris, M.D.,[1] Larry E. Tune, M.D.,[1] Michael Kurtz, M.D.[2] and Joseph T. Coyle, M.D.[1]

This is a preliminary report on the measurement of serum neuroleptic levels in mentally retarded children and adolescents. The investigators have measured neuroleptic levels in 60 patients on a variety of neuroleptics (haloperidol, chlorpromazine, trifluoperazine, molindone, thioridazine). However, a summary of neuroleptic blood levels in 9-15 year-old boys taking thioridazine for behavior management is the subject of this report.

Until recently there had been no simple procedure for the measurement of neuroleptic serum activity levels. However, a radioreceptor assay described by Snyder and Creese (1977) based on competition of neuroleptics in plasma or serum for the binding of [^{3}H]-spiroperidol to dopamine receptors may serve this function. The assay measures dopamine receptor blockade and, therefore, detects active metabolites as well as parent drug activity. This is a distinct advantage for thioridazine which has several active metabolites.

Previous reports by Tune, Creese, Depaulo, Slavney, Coyle, and Snyder (1980) and Cohen, Lipinski, Pope, Harris, and Altesman (1980) have demonstrated a correlation between serum levels of neuroleptics and therapeutic response in acutely psychotic patients during an acute episode. Both studies showed poor correlations between oral dosage and serum level.

Myers, Tune, and Coyle (1980) have used this assay to manage schizophrenia in childhood at Johns Hopkins. The current investigators are now studying the use of the radioreceptor assay in the retarded where both thioridazine and haloperidol are approved for use in the management of behavior disorders.

Method

Sixteen moderately to severely retarded 9-15 year-old boys taking thioridazine as a single treatment participated in the study. All are residents in a well-staffed and well-supervised behaviorally oriented institutional setting and are considered to be patients who are the most difficult to manage. Each subject had been on the same dosage of medication for at least 2 weeks.

Five milliliters of blood were drawn from each member of the study population 2 hours after supervised oral administration of the medication to obtain peak blood levels. Specimens were cooled and allowed to clot over a 2-hour period, centrifuged, and the serum frozen at 70° C in glass tubes. Assays were performed in triplicate.

On the day before the blood specimen was obtained, the Sprague Resident Behavior Checklist was completed by the case manager.

---

[1] The Johns Hopkins University School of Medicine and Hospital, Baltimore, MD 21205.

[2] The University of Pennsylvania School of Medicine, Philadelphia, PA 19104.

Results

The serum drug levels were looked at as total dosage and as mg/kg/day. Drug levels were recorded as haloperidol equivalents (ng/ml). In each instance, when a resident was on a given daily dosage of drug there was variability in blood level at that dosage. Thus, for the four residents on a total daily dosage of 50 mg, levels ranged from 13-102 ng/ml haloperidol equivalents and for the four residents on 75 mg/day the range was from 37-199 ng/ml haloperidol equivalents. In two residents on 100 mg/day, the range was from 65-122 ng/ml haloperidol equivalents. So, on a given dose there was up to an eightfold variation in drug level.

If the dosage is looked at as mg/kg of thioridazine, when the dosage reached 2.0 mg/kg considerable variability in level was evident. For example, at a dosage range of 2.0-2.3 mg/kg the level varied from 20-199 ng/ml haloperidol equivalents, a tenfold difference in level. The four residents on higher dosages from 3.2-14.8 mg/kg had levels over 95 ng/ml haloperidol equivalents.

The Sprague Resident Behavior Rating Scale was completed on each resident. No specific correlations were demonstrated between drug level and total score or individual scores on specific behavioral items. Since intense aggression and assaultive behavior is a common indication for drug treatment, global ratings of aggression were reviewed carefully. There was no correlation between drug level and severity of aggressive behavior, although the most physically aggressive boys were on the highest dosages of neuroleptics, 4.8 and 8.8 mg/kg, respectively.

Conclusions

In this group of retarded boys we have demonstrated variability in the neuroleptic level of thioridazine 2 hours after oral administration, as was previously reported in adults by Tune et al. (1980) and Cohen et al. (1980). Further work will need to be done to demonstrate the usefulness of the assay in patient management and to determine whether there is a threshhold neuroleptic level in the management of target symptoms in the retarded, especially in aggressive behavior. However, current findings may be pertinent to the possible relationship of high neuroleptic levels and long-term complications such as dyskinesias and for thioridazine, retinopathy.

The assay may provide a useful tool for future monitoring of drug therapy in the retarded and be of use in the treatment of medication nonresponders.

References

Cohen, B.M., Lipinski, J.F., Pope, H.G., et al. Neuroleptic blood levels and therapeutic effect. *Psychopharmacology, (Berlin)*, 70:191-193, 1980.

Myers, B.J., Tune, L.E., and Coyle, J.T. Clinical response and serum neuroleptic levels in childhood schizophrenia. *Am. J. Psychiatry*, 137:(4):483-484, 1980.

Snyder, S.H., and Creese, I. A simple and sensitive radioreceptor assay for antischizophrenic drugs in blood. *Nature*, 270(5633):180-182, 1977.

Sprague, R.L. Sprague Resident Behavior Checklist. Institute for Child Behavior and Development, University of Illinois at Urbana-Champaign. Champaign, IL.

Tune, L.E., Creese, I., Depaulo, J.R., et al. Clinical state and serum neuroleptic levels measured by radioreceptor assay in schizophrenia. *Am. J. Psychiatry*, 137(2):187-189, 1980.

Free Communications—Session A

Chair: Eugene S. Paykel, M.D.
Department of Psychiatry
St. George's Hospital Medical School
London, England

and

Paul D. Leber, M.D.
Division of Neuropharmacological Drug Products
Food and Drug Administration
Rockville, Maryland

* An Open, Uncontrolled Clinical and Pharmacokinetic Study with LM 5008: A New Antidepressant
M. Amin, R. Khalid, and H.E. Lehmann
Lakeshore General Hospital, Pointe Claire, Quebec, Canada

Efficacy of Mianserin in Mildly Depressed Patients
Jonathan W. Stewart, Frederic M. Quitkin, Patrick J. McGrath, Michael R. Liebowitz, and Donald F. Klein
New York State Psychiatric Institute, New York, NY

The Effect of Mianserin on Cardiac Conduction: A Controlled Study
Patrick J. McGrath, Frederic M. Quitkin, David Blood, Michael R. Liebowitz, Jonathan W. Stewart, Abby Fyer, and Donald F. Klein
New York State Psychiatric Institute and Columbia Presbyterian Medical Center, New York, NY

Double-Blind Comparison of Bupropion vs. Amitriptyline in Depressed Outpatients
Nancy Harto-Truax, Joanne van Wyke Fleet, and Warren C. Stern
Department of Clinical Research, Burroughs Wellcome Company, Research Triangle Park, NC

Wellbatrin Studies
Baron Shopsin and Gregor Laakmann
Creedmoor Psychiatric Center, Queens Village, NY. and Universität München, München, West Germany

Atypical Depressives: A Preliminary Report of Antidepressant Response and Sleep Patterns
Frederic M. Quitkin, David Schwartz, Michael R. Liebowitz, Jonathan R. Stewart, Patrick J. McGrath, Frieda Halpern, Joaquim Puig-Antich, Elaine Tricamo, Edward J. Sachar, and Donald F. Klein
New York State Psychiatric Institute, New York, NY

Biological and Clinical Studies of Tardive Dyskinesia
Robert C. Smith, Richard Allen, Jack Gordon, Chandra Misra, Joseph Schoolar, Judith Wolff, and Beng T. Ho
Texas Research Institute of Mental Sciences, Texas Medical Center, Houston, TX

Results from a Prospective Study of Tardive Dyskinesia Development: Preliminary Findings over a 2-year Period
John M. Kane, Margaret Woerner, Paul Weinhold, and James Wegner
Long Island Jewish-Hillside Medical Center, Glen Oaks, NY

Impairment of Swallowing, Tardive Dyskinesia, and Anticholinergic Drug Use
Thomas J. Craig, Mary Ann Richardson, Nigel M. Bark, and Roman Klebanov
Rockland Research Institute, Orangeburg, NY; New York University and Columbia University, New York, NY; and New York Medical College, Valhalla, NY

Lecithin Treatment of Tardive Dyskinesia—A Progress Report
Brian G. Anderson, Dean Reker, Miodrag Ristich, Eitan Friedman, and Jan Volavka
New York University, Ward's Island and New York, NY

Effects of AMPT on Tardive Dyskinesia and Psychosis
Henry A. Nasrallah, Robert E. Smith, Frederick J. Dunner, and Mona McCalley-Whitters
VA Medical Center and University of Iowa College of Medicine, Iowa City, IA

Receptor Sensitivity Modification in the Treatment of Tardive Dyskinesia
Murray Alpert, Florence Diamond, and Arnold J. Friedhoff
New York University Medical Center, NY

Efficacy of Mianserin in Mildly Depressed Patients

Jonathan W. Stewart, M.D.,[1] Frederic M. Quitkin, M.D.,[1] Patrick J. McGrath, M.D.,[1] Michael R. Liebowitz, M.D.,[1] and Donald F. Klein, M.D.,[1]

Mianserin is a tetracyclic antidepressant with demonstrated efficacy (Brogden, Heel, Speight, & Avery, 1978). Since mianserin appears to have a different mechanism of action from the tricyclic antidepressants (TCAs)(Brogden et al., 1978), it seemed useful to investigate the efficacy of mianserin in patients with relatively mild depression, a population similar to that previously studied using desipramine (DMI) (Stewart, Quitkin, Liebowitz, et al., 1981.)

The study design was identical to that previously utilized for DMI (Stewart et al., 1981). Basically, patients aged 18-65 with Hamilton Depression Scores (HAM-D) less than 19 who met Research Diagnostic Criteria (RDC) (Spitzer, Endicott, & Robbins, 1978) for depression were placed on placebo for 10 days single-blind. Patients who responded were removed from further study. Those who maintained their level of depression were randomized to double-blind treatment with mianserin or placebo for 6 weeks. At reevaluation after 10 days of placebo and after 6 weeks' double-blind treatment, response was defined as a Clinical Global Impression (CGI) score of 1 or 2 ("very much improved" or "much improved"). Nonresponse was a CGI score of 3 or higher ("minimally improved," "unchanged," or "worse").

Initial mianserin dose was 30 mg/d, increased twice weekly to 150 mg/d unless side effects prevented such regular increases. Previous studies had used 60-90 mg/d as a maximal dose of mianserin (Coppen, Ghose, et al., 1977; Wheatley, 1977). As this dose of mianserin had been compared with 150 mg/d of amitriptyline, it was felt that a higher dose of mianserin might be more comparable to 300 mg of a TCA. In addition, a pilot study (McGrath, Quitkin, Stewart, et al., 1981) had suggested additional benefit as dose was raised to 150 mg/d. Hence, the latter was selected as a maximal dose to attempt to maximize likelihood of response. Statistical analysis included the chi-square test without Yates correction to 2 × 2 tables using two-tailed tests.

The mean age of 127 patients entering the study was 43 ± 12 (range, 21-65). There were 72 men and 55 women. Twenty-seven patients dropped out and 17 responded during the initial 10 days of placebo. Of the 83 patients completing the randomization trial, 54% (21/39) responded to mianserin, 27% (12/44) to placebo ($X^2=6.64$, $p<.02$). According to RDC diagnoses, patients with definite diagnosis for major depressive disorder demonstrated a 50% (10/20) response to mianserin, 14% (3/22) to placebo, a statistically significant difference ($X^2=6.48$, $p<.02$). Patients with intermittent depressive disorder did not demonstrate this difference, 64% (7/11) responding to mianserin, 40% (4/10) to placebo

---

[1] New York State Psychiatric Institute, New York, NY 10032.

($X^2 = 1.17$, n.s.). There were not enough patients with minor depressive disorder ($N = 6$) to test for significance.

Differential response among RDC major depressives was entirely accounted for by those with endogenous subtype. Thus, patients with endogenous subtype had a 77% (10/13) response to mianserin, 9% (1/11) to placebo ($X^2 = 11.50$, $p < .001$). By contrast, major depressives without endogenous depression had an 18% (2/11) response to mianserin, 31% (5/16) to placebo ($X^2 = 0.58$, n.s.). Major depressives with endogenous depression were significantly more likely to respond to mianserin than major depressives without endogenous subtype ($X^2 = 8.22$, $p < .01$).

Most of the subtypes of major depressive disorder which had appreciable numbers demonstrated at least a trend for significant drug-placebo response differences. In each case, however, this difference seemed entirely accounted for by those who also had endogenous subtype. For example, among major depressives with simple subtype, 50% (9/18) improved on mianserin, 14% (3/21) on placebo ($X^2 = 5.80$, $p < .02$). However, patients with simple subtype who also had endogenous subtype had an 82% (9/11) response rate to mianserin, 9% (1/11) to placebo ($X^2 = 11.73$, $p < .001$). Patients with simple subtype who did not meet criteria for endogenous had a 0% (0/7) response to mianserin, 20% (2/10) response to placebo ($X^2 = 1.59$, n.s.). Response to mianserin was significantly more likely among the simple subtype if they were also endogenous than if not ($X^2 = 11.45$, $p < .001$).

Among patients with situational subtype of major depression, 30% (6/20) improved on placebo. While this was not significantly greater than placebo response of major depressives without situational subtype (13%, 1/8, $X^2 = 0.9$, n.s.), this had been the group in the previous study (Stewart et al., 1981) which demonstrated increased response. Combining placebo responses from the two studies yielded a significantly increased placebo response among major depressives with situational subtype when compared to those without situational subtype ($X^2 = 7.13$, $p < .05$, $df = 2$).

Regardless of diagnosis, differential response occurred among patients with more severe illness. That is, patients at or above the median Day 10 HAM-D score of 13 had a 60% (12/20) response to mianserin, 27% (7/27) to placebo ($X^2 = 5.54$, $p < .02$). Patients with Day 10 HAM-D score below 13 had a 47% (9/19) response to mianserin, 29% (5/17) to placebo ($X^2 = 1.22$, n.s.).

These results demonstrate the efficacy of mianserin in this population of mild- to moderately depressed outpatients. In particular, patients with endogenous subtype of major depressive disorder seemed to account for the mianserin-placebo response difference found. Major depressives without endogenous subtype may do poorly on mianserin. No group was found to have increased placebo response. These differential responses according to RDC subtype partially validate this system as being useful for the treatment of affective illness.

Differential response according to presence or absence of endogenous subtype suggests that RDC major depression defines a heterogeneous population, some of whom improve due to specific mianserin effects, some who are unresponsive to this medication, and a few of whom improve due to nonspecific factors. For both research and clinical purposes, RDC major depression with endogenous subtype may define a fairly homogeneous population in which to use mianserin.

Although placebo response of major depressives with situational subtype was not significantly greater than those without situational subtype, combining these results with those from the previous study (Stewart et al., 1981) did suggest increased placebo response among situational depressives. This again suggests that some patients with clear-cut psychosocial precipitants may improve without the need for medication.

While many of these results were similar to those found previously with DMI, mianserin may not have the same spectrum of action as DMI. In the present study, 65% (7/11) of patients with intermittent depressive disorder responded to mianserin. While this was not significantly greater than the placebo response in this group, it does compare favorably with the 13% (1/8) response rate of this group to DMI in the earlier study. Since placebo response in this group was little different in the two studies (4/11 vs. 2/8), this suggests that mianserin might be beneficial for some intermittent depressives, while DMI is not.

As in the DMI study (Stewart et al., 1981) it

TABLE

Response by Diagnosis and Severity of Illness

Research Diagnostic Criteria**	% Response to Mianserin	% Response to Placebo	χ^2	Significance
Major Depressive Disorder	50 (12/24)*	23 (7/31)	4.50	$p<.05$
with endogenous subtype	77 (10/13)[a]	13 (2/15)	11.50	$p<.001$
without endogenous subtype	18 (2/11)[a]	31 (5/16)	0.58	n.s.
Simple subtype	50 (9/18)	14 (3/21)	5.80	$p<.02$
with endogenous subtype	82 (9/11)[b]	9 (1/11)	11.73	$p<.001$
without endogenous subtype	0 (0/7)[b]	20 (2/10)	1.59	n.s
with situational subtype	36 (5/14)	30 (6/20)[c]	0.12	n.s.
without situational subtype	63 (5/8)	13 (1/8)[c]	4.27	$p<.05$
Minor depressive disorder	67 (2/3)	33 (1/3)	—	—
Intermittent depressive disorder	64 (7/11)	36 (4/11)	1.64	n.s.
Severity of Illness				
Day 10 Hamilton ≥ 13	60 (12/20)	27 (7/27)	5.54	$p<.02$
Day 10 Hamilton < 13	47 (9/19)	29 (5/17)	1.22	n.s.
TOTAL	54 (21/39)	27 (12/44)	6.64	$p<.02$

*in parentheses are proportion responding.

**definite diagnoses only

Within Mianserin Contrasts:

a = Major Depressive Disorder with Endogenous Subtype vs. without Endogeneus Subtype, $\chi^2 = 8.22$, $p<.01$.

b = Major Depressive Disorder Simple Subtype with Endogenous Subtype vs. without Endogenous Subtype, $\chi^2 = 11.45$, $p<.001$.

Within Placebo Contrasts:

c = Major Depressive Disorder with Situational Subtype vs. without Situational Subtype, $\chi^2 = 0.93$, n.s.

was patients above the median of pre-randomization HAM-D scores who demonstrated specific medication response. This was true, however, only for Day 10 HAM-D, not for initial HAM-D (results not shown). Thus, patients who maintain their depression at a certain level for 10 days may be good candidates for either mianserin or DMI. Conversely, few patients with Day 10 HAM-D below 13 may be expected not to respond to either DMI or mianserin. Such patients may require other antidepressants, such as monoamine oxidase inhibitors, or psychotherapy in order to improve.

References

Brogden, R.N., Heel, R.C., Speight, T.M., and Avery, G.S. Mianserin: A review of its pharmacological properties and therapeutic efficacy in depressive illness. *Drugs*, 16:273-301, 1978.

Coppen, A., Ghose, K., Rama Rao, V.A., et al. Mianserin in the prophylactic treatment of bipolar affective illness. *Int. Pharmacopsychiatry*, 12(2):95-99, 1977.

McGrath, P.M., Quitkin, F., Stewart, J.W., et al. Novel antidepressants: A clinical trial of mianserin. *Psychopharmacol. Bull.*, 17:21-23, 1981.

Spitzer, R., Endicott, J., and Robbins, E. Research diagnostic criteria. *Arch. Gen. Psychiatry*, 35:773-782, 1978.

Stewart, J.W., Quitkin, F., Liebowitz, M.E., et al. Efficacy of desipramine in mildly depressed patients: A double-blind placebo-controlled trial. *Psychopharmacol. Bull.*, 17:136-8, 1981.

Wheatley, D. Controlled trial of a new antidepressant (DRG GB 94) of novel chemical formulation. *Curr. Ther. Res.*, 18:849-854, 1975.

The Effect of Mianserin on Cardiac Conduction: A Controlled Study

Patrick J. McGrath, M.D.,[1] Frederic M. Quitkin, M.D.,[1] David Blood, M.D.,[2] Michael R. Liebowitz, M.D.,[1] Jonathan W. Stewart, M.D.,[1] Abby Fyer, M.D.,[1] and Donald F. Klein, M.D.[1]

A variety of studies have shown that tricyclic antidepressants (TCAs) can affect the heart and particularly cardiac conduction at toxic dosages. The typical electrocardiographic (ECG) changes seen include tachycardia, prolongation of the PR interval, and widening of the QRS complex (Bigger, Kantor, Glassman, & Perel, 1978). These are associated with a variety of arrhythmias. The PR prolongation is thought to represent inhibition of conduction in the ventricular specialized conducting system, especially in the Bundle of His (Vohra, Burrow, Hunt, & Sloman, 1978). There is less clarity about how much effect the TCAs have on cardiac conduction when used at therapeutic dosage in the normal heart. In patients with preexisting conduction defects, there appears to be general agreement in the literature that the TCAs can aggravate these disturbances and cause significant cardiac toxicity (Kantor, Bigger, Glassman, et al. 1975). One of the features of interest of newer antidepressant compounds is the possibility of less cardiac toxicity. This is clinically important both because of the contribution this makes to the drugs' lethality in overdose as well as drug safety in patients with heart disease.

This investigation was undertaken to explore the cardiac effects of mianserin, a tetracyclic antidepressant. Crome and Newman (1977) reported a series of cases of poisoning with either maprotiline (Ludiomil) or mianserin (Bolvidon). In 20 cases of mianserin overdose, no arrhythmias similar to those seen in TCA overdose were observed. Kopera and Schenk (1977) monitored the clinical ECG of 54 patients who had preexisting "gravely disturbed" ECGs who were treated with 30 to 60 mg daily of mianserin. These studies suggested that mianserin had little or no cardiac toxicity.

Method

Depressed patients between the ages of 18 and 65 with no significant medical illness were recruited from ongoing studies at the New York State Psychiatric Institute. All 48 patients had normal routine clinical ECGs. Each patient had a high-speed, high-fidelity ECG done while drug free. A second high-speed ECG was done after each patient was stabilized on drug or placebo treatment. These were recorded after 4 to 6 weeks of treatment after at least 1 week on the maximum dose of medication they received during the drug trial. Electrocardiograms were interpreted by an experienced cardiologist (D.B.) who was blind to treatment status of the patients. Statistical analysis was done using analysis of covariance with baseline scores as the covariate. Treatments were then compared by *t*-test.

Results

The mean daily drug dosages (mg/day) were 142 ± 16.9 for mianserin, 222 ± 71.2 for amitriptyline (AMI), and 225 ± 65.5 for imipramine (IMI)(*see* Table). Both AMI and IMI produced a significant increase in heart rate over baseline compared to placebo, while mianserin did not. The PR interval during drug treatment was significantly prolonged compared to placebo IMI but not for AMI, although there was a trend for the latter. Mianserin treatment did not

Table

Corrected ECG Variables by Treatment Compared to Placebo (Pre/Post Treatment Score)

	Placebo ($N = 12$)	Mianserin ($N = 19$)	Amitriptyline ($N = 9$)	Imipramine ($N = 8$)
Heart Rate (Beats/min)	70.9/72.5 -	77.8/79.8 N.S.	68.0/89.7 $p = .0003$	71.3/89.4 $p = .002$
PR Interval (msec)	148.3/144.4 -	147.8/149.5 N.S.	154.9/150.8 $p = .08$	145.3/161.9 $p = .0007$
QRS Interval (msec)	90.9/92.8 -	89.8/87.2 N.S.	83.7/91.7 $p = .04$	89.9/99.3 $p = .11$
QT Interval (msec)	418.3/427.0 -	427.8/430.3 N.S.	408.2/435.4 $p = .04$	431.2/445.9 $p = .06$

---

[1] New York State Psychiatric Institute, New York, NY 10032.

[2] Columbia Presbyterian Medical Center, New York, NY 10028.

significantly change the PR interval. There was a trend for IMI to prolong the QRS interval, while mianserin and AMI did not. Prolongation of the QT_c interval was seen with AMI and IMI but not with mianserin treatment.

Conclusion

In a sample of medically healthy depressed patients with normal pretreatment ECGs treated with mianserin, no changes in cardiac conduction could be detected using high-speed, high-resolution ECG, compared to patients randomly assigned to placebo. Patients treated with IMI or AMI showed significant increase in heart rate as well as prolongation of the PR and QT_c intervals. The conduction changes, though clearly significant, would not have been demonstrated using routine clinical ECGs. The investigators conclude that mianserin, even when used in a dosage which is higher than has previously been employed clinically, shows little effect on cardiac conduction. If this is confirmed in further studies, trials of mianserin in depressed patients with disease of the cardiac conducting system would be warranted. If shown to be as effective an antidepressant as the tricyclics, it may be a drug of choice for patients with cardiovascular disease. Additionally, the method of high-speed ECG was suggested as being a sensitive screening technique to get evidence of the effects of new drugs on cardiac conduction in patients. This can be studied easily and evidence of the drug's effect shown, even though there are no clinically significant changes in the routine clinical ECG.

References

Bigger, J.T., Kantor, S.J., Glassman, A.A., and Perel, J.M. Cardiovascular effects of tricyclic antidepressant drugs. In: Lipton, M.A., DiMascio, A. A., and Killam, K. (eds.), *Psychopharmacology: A Generation of Progress*. New York: Raven Press, 1978, pp. 1033-1046.

Crome, P., and Newman, B. Poisoning with malprotiline and mianserin. *Br. Med. J.*, 23, July 1977.

Kapcra, A., and Schenk, A. Poisoning with antidepressants. *Br. Med. J.*, 17 September, 1977.

Kantor, S.J., Bigger, J.T., Glassman, A.H. et al. Imipramine-induced heart block: A longitudinal case study. *JAMA*, 231:1364-1366, 1975.

Vohra, J., Burrows, G.D., Hunt, D., and Sloman, G. The effect of toxic and therapeutic doses of tricyclic antidepressant drugs on intracardiac conduction. *Eur J. Cardiol.*, 3:219-227, 1975.

Double-Blind Comparison of Bupropion vs. Amitriptyline in Depressed Out-patients

Nancy Harto-Truax, B.S.,[1] Judith Van Wyck Fleet, B.A.,[1] and Warren C. Stern, Ph.D.[1]

Bupropion HCl (Wellbutrin®) is a novel antidepressant with a structure shown in Figure 1. Potential antidepressant properties of bupropion were first suggested by its antagonism of tetrabenazine-induced ptosis and sedation in the mouse (Soroko, Mehta, Maxwell, et al. 1977). Bupropion's neurochemical and pharmacological profile is distinct from that of tricyclic and monoamine oxidase (MAO) inhibitor antidepressants. Bupropion has minimal effects on blocking neuronal reuptake of norepinephrine or serotonin, and does not inhibit MAO (Ferris, Maxwell, Cooper, & Soroko, 1981). Although bupropion weakly inhibits the reuptake of dopamine (Ferris et al., 1981), the neurochemical mode of the antidepressant action of bupropion must still be elucidated. In animals, bupropion does not possess anticholinergic, antihistaminergic, antiserotonergic, or cardiotoxic properties (Soroko et al., 1977; Wang, Parker, & Maxwell, 1981).

The antidepressant properties of bupropion were previously demonstrated in two double-blind, placebo-controlled inpatient trials (Stern & Harto-Truax, 1980). Bupropion produced significantly greater improvement than placebo starting at 8 days in one study (using doses of 300-750 mg/d) and at 3 weeks in the other study (doses of 300-450 mg/d). The side-effect profile of bupropion in both studies was similar to that of placebo with a notable absence of anticholinergic, cardiotoxic, or sedating side effects. In view of these initial efficacy findings and a low side-effect profile, it was appropriate to further assess the efficacy and safety of bupropion relative to a tricylic antidepressant.

In the present interim report, the antidepressant activity and safety of bupropion were compared to that of amitriptyline in a six-center out-

---

[1] Department of Clinical Research, Burroughs Wellcome Company, Research Triangle Park, NC 27709.

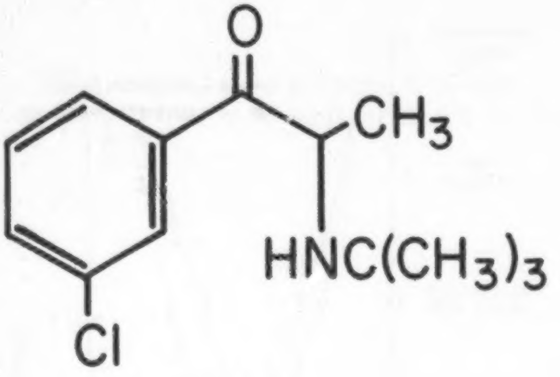


FIGURE 1. Structure of bupropion.

patient investigation (*see* Acknowledgments). A double-blind, randomized, parallel treatment design study with a 2:1 ratio of bupropion ($N=$ 81) to amitriptyline ($N=$ 42) treated patients was conducted. Treatment was scheduled for up to 15 weeks, the first week consisting of a single-blind placebo period. Responders to placebo during the initial week, as judged by an improvement of more than 10 points on the Hamilton Depression Scale or a Hamilton Depression rating of less than 18 on Day 7, were dropped from the study. Patients were then treated for up to 13 weeks with an ascending dosage regimen of either bupropion (300-450 mg/d, administered t.i.d.) or amitriptyline (75-150 mg/d, administered q.h.s.). The final week of the study consisted of a drug-free, posttreatment, followup period to assess possible withdrawal effects.

Entrance criteria required that each patient satisfy the diagnostic criteria for major affective disorder as defined by the FDA guidelines (1977); be 18-65 years old; have a current depressive episode duration of 4 weeks to 2 years; have a minimum Hamilton Depression total score of 18; have at least a moderate rating on the Clinical Global Severity Scale; have acceptable baseline values on vital signs, EKG, physical, and clinical laboratory examinations; and be withdrawn from other psychoactive medication. Patients who had a history or evidence of a seizure disorder, intestinal obstruction, glaucoma, significant cardiovascular disease, or thyroid dysfunction; alcoholism, alcohol abuse, or drug abuse within the past 2 years; or intolerance to amitriptyline were excluded from the study. Patients who were currently suicidal; schizophrenic or schizoaffective; receiving guanethidine or an other agent whose effects are known to be blocked or enhanced by tricyclic antidepressants; or who were pregnant, lactating, or did not agree to employ contraception to avoid pregnancy during the study were also excluded.

Comparison of the bupropion and amitriptyline groups with respect to demographic characteristics indicated that the majority of the patients were females (70% and 62%, respectively), and caucasian (94% and 98%). The average age was 39.7 years for the bupropion group and 36.0 years for the amitriptyline group. Of the 98 patients included in the efficacy analyses, the majority were diagnosed as either manic-depressive, depressed (70%), or with depressive neurosis (23%) according to the Diagnostic and Statistical Manual-II (American Psychiatric Association, 1968). None of the patients had received prior hospitalization for a depressive episode, and the mean duration for the current episode of depression was 6.0 and 7.2 months for the bupropion and amitriptyline patients, respectively.

The efficacy of bupropion was compared to amitriptyline using the Clinical Global Severity of Illness and Improvement Scales (Figure 2), and the Hamilton Depression and Anxiety Scales (Figure 3). Both bupropion and amitriptyline patients showed a significant ($p < 0.05$) improvement from baseline in their severity of illness and Hamilton Depression scores starting on Day 7 of active drug treatment (Study Day 14). Significant improvement from baseline in the Hamilton Anxiety scores occurred starting on Day 14 of bupropion treatment and Day 7 of amitriptyline treatment. For both treatment groups, all subsequent assessments on each scale differed significantly from baseline. Similar equivalency of results were obtained with the Zung Self-Rating Depression and Anxiety Scales. Except for Treatment Day 7 (Study Day 14) on the Hamilton Depression Scale, there were no significant differences in efficacy at any of the nine assessment points for each rating scale between the bupropion and amitriptyline groups. At termination of treatment, 85% of the bupropion and 81% of the amitriptyline patients were rated much or very much improved on the Clinical Global Improvement Scale.

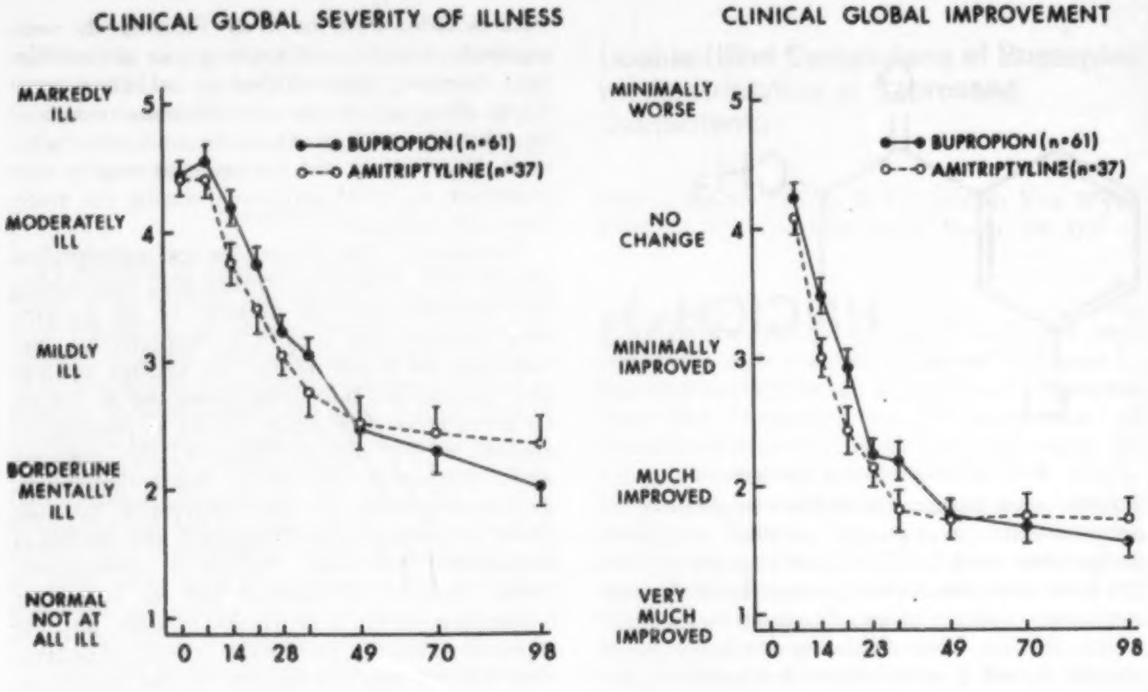


FIGURE 2. Comparison of bupropion vs. amitriptyline on the Clinical Global Severity of Illness and Improvement Scales. (Improvement is judged relative to baseline.)

With respect to safety, bupropion treatment was associated with fewer drug-related side effects than amitriptyline treatment. Side effects were recorded at each assessment day using a modified Treatment Emergent Symptom Scale format (Guy, 1976). Two of the 81 bupropion patients were discontinued due to adverse events (rash) as was one of the 42 amitriptyline patients (disturbed concentration, confusion, and agitation). During treatment, there were five adverse experiences whose relative frequencies, both in terms of percent patient and report incidence, were differentially associated with either amitriptyline or bupropion. Blurred vision, dry mouth, dizziness, and nightmares occurred more often in amitriptyline patients (in 11-27% more patients); whereas, only decreased appetite occurred more frequently in bupropion patients (in 15% more patients). During the posttreatment week, no withdrawal effects were noted in either group. Analyses of mean change in body weights between baseline and termination of treatment showed a mild weight loss (2.1 pounds) by bupropion patients in contrast to a mild weight gain (2.4 pounds) by amitriptyline patients. With respect to vital signs, bupropion treatment resulted in no clinically significant cardiovascular changes, whereas amitriptyline produced significant ($p < 0.05$) increases in supine and standing pulse rates (5 and 6 beats/min, respectively), and a number of reports of orthostatic hypotension.

In conclusion, during a six-center, double-blind outpatient investigation, bupropion (300-450 mg/d) produced antidepressant activity comparable to amitriptyline (75-150 mg/d) with both groups showing significant improvements in their depression scores after 7 days of treatment. Bupropion treatment was associated with fewer drug-related side effects, particularly fewer sedative, anticholinergic, and cardiovascular-related adverse events than those observed with amitriptyline.

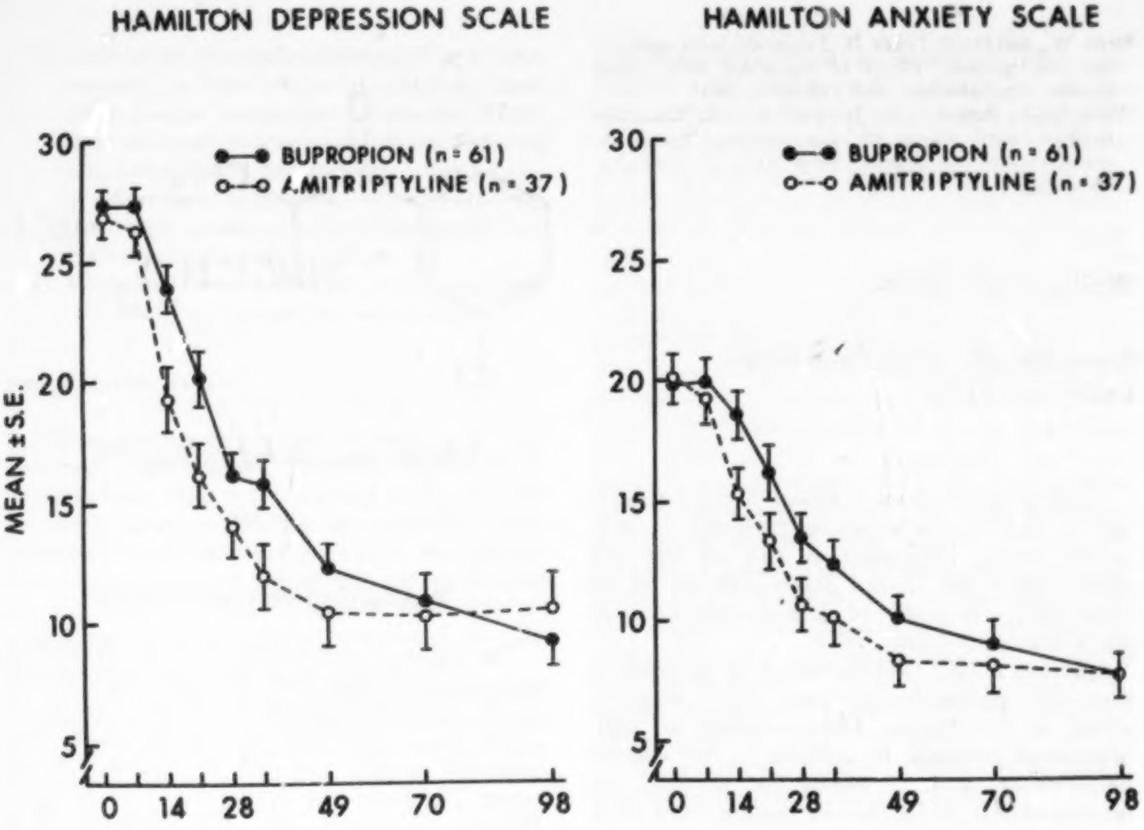


FIGURE 3. Comparison of bupropion vs. amitriptyline on the Hamilton Depression and Anxiety Scales.

Acknowledgment: Investigators contributing data to this multicenter evaluation of the efficacy and safety of bupropion versus amitriptyline included: R.A. Remick, M.D., Vancouver, British Columbia; A.J. Cooper, M.D., Sarnia, Ontario; J. Mendels, M.D., Philadelphia, Pennsylvania; A.N. Singh, M.D., and B. Saxena, Ph.D., Hamilton, Ontario; M.M. Amin, M.D., Pointe Claire, Quebec; and G. Chouinard, M.D., Montreal, Quebec.

References

Diagnostic and Statistical Manual of Mental Disorders (DSM-II). Washington, D.C.: American Psychiatric Association, 1968.

Ferris, R.M., Maxwell, R.A., Cooper, B.R., and Soroko, F.E. Neurochemical and neuropharmacological investigations into the mechanisms of action of bupropion HCl, a new atypical antidepressant agent. In: Costa, E., and Racagni, G. (eds.), *Advances in Biochemical Psychopharmacology.* Vol. 1. *Typical and Atypical Antidepressants: Molecular Mechanisms.* New York: Raven Press. (In press)

Guidelines for the Clinical Evaluation of Antidepressant Drugs. HEW (FDA) 77-3042. Rockville, MD: U.S. Dept. of Health, Education, and Welfare, Food and Drug Administration, 1977.

Guy, W. *ECDEU Assessment Manual for Psychopharmacology.* Rockville, MD: U.S. Dept. of Health, Education, and Welfare, 1976.

Soroko, F.E., Mehta, N.B., Maxwell, R.A., et al., Bupropion hydrochloride [(±)"-t-butylamino-3-chlorpropiophenone HCl]: A novel antidepressant. *J. Pharm. Pharmacol.*, 29: 767-770, 1977.

Stern, W., and Harto-Truax, N. Two multicenter studies of the antidepressant effects of bupropion HCl versus placebo. *Psychopharmacol. Bull.*, 16:43-46, 1980.

Wang, C.M., Parker, C.H., Jr., and Maxwell, R.A. Electrophysiological effects of antidepressants on mammalian hearts and crayfish giant axon. *J. Cardiovasc. Pharmacol.*, 3:101-112, 1981.

Wellbatrin Studies

Baron Shopsin, M.D.,[1] and Gregor Laakmann, M.D.[2]

Among the 30 or more newer "second generation" antidepressant molecules reviewed by us in recent years, bupropion is one of the few discovered in the United States and one of the more unique in profile of clinical activity (Shopsin, Cassano, & Conti, 1981).

Bupropion HCl (Wellbatrin) is an antidepressant of the propiophenone class, with a structure shown in the Figure. Demonstrating an antidepressant potential in animals in the learned helplessness and tetrabenazine models, its neurochemical profile remains distinct from other standard/marketed antidepressants of the tricyclic-monoamine oxidase (MAO) inhibitor classes. Included in the pharmacological profile of bupropion is an absence of anticholinergic, antihistaminergic, and antiserotonergic properties. At the time of writing, its central chemical mode of antidepressant action awaits clarification (Maxwell, Mehta, Tucker, et al. 1981; Stern, Harto-Truax, Rogers, & Miller, 1981).

This paper is an abstract of data presented at the 1981 NCDEU meeting which focused on three separate studies: a single-blind comparison of Wellbatrin vs. imipramine in depressed outpatients; long-term maintenance or prophylactic effects in both unipolar as well as bipolar manic-depressives; and neuroendocrine studies carried out to help clarify its potential mechanism of action.

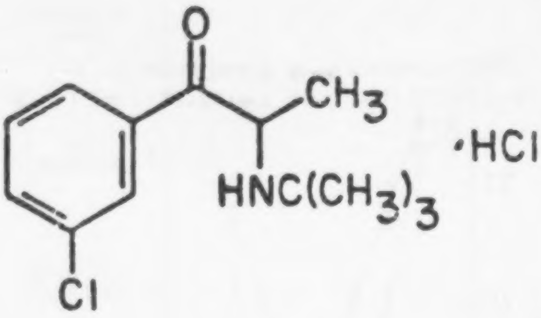


FIGURE. Bupropion HCl (Wellbatrin™)

Wellbatrin-Imipramine Study

The efficacy and safety of three Wellbatrin regimens (150 mg/d, 300-450 mg/d, and 300-900 mg/d) and one imipramine regimen (up to 300 mg/d) were compared in a single-blind, randomized, parallel trial with 40 depressed outpatients. The study was carried out at the Affective Disorder-Lithium Clinic, NYU-Bellevue Hospital Center under conditions of written informed consent. The number of patients examined was limited (10 patients in each drug group), so that conclusions from a biometric standpoint must be circumspect. Within these methodological constraints, it may be concluded that:

1) Both high-dose Wellbatrin and imipramine showed a comparable and statistically significant antidepressant action in endogenously depressed outpatients. These findings were documented using a battery of standard National Institute of Mental Health-Pharmacologic and Somatic Treatments Research Branch (NIMH-PST) objective rating devices including patient self-rating scales. Most patients in the low and mid-dose range groups required switching to high dose medication (i.e., 300-900 mg/d range) after 2 weeks.
2) The speed/onset of action was similar for both compounds and reached statistical significance by the end of the second week.

---

[1] New York University School of Medicine, New York, NY 10016,
[2] Psychiatrische Klinik und Poliklinik, Universität München, West Germany.

3) Wellbatrin was well tolerated. There were virtually no side effects recorded for these drug groups irrespective of dosage. There were no anticholinergic side effects; the drug was nonsoporific and did not cause fatigue or drowsiness. Imipromine was accompanied by a high incidence of anticholinergic and central nervous system effects.
4) Vital signs and laboratory tests remained essentially unchanged for both drugs.

Prophylactic Trials

Those patients responding to Wellbatrin, who also had a documented history of illness recurrence at least once yearly during the 2 years immediately prior to Wellbatrin treatment, were continued in an open trial for 1 year. All unipolar and bipolar patients remaining on medication showed no illness relapse and were able to sustain a reduction in dosage and an absence of any side effects (Shopsin, Cassano, & Conti, 1981).

None of the unipolar or bipolar patients showed a swing to mania and none needed the addition of lithium carbonate to prevent or stabilize any such behavioral toxicity.

Three bipolar patients who had never before responded to antidepressant drugs without a swing into a manic state, also did well for a 1-year period on Wellbatrin alone. All three cases were known to us in the clinic for many years. Prior psychoactive treatment responses of these patients were either poor or unsustained, and lithium was unable to prevent or satisfactorily attenuate continued recurrences of high or low mood states. This, then, was the first occasion that any of the three bipolar patients showed any prophylactic response for a 1-year period. There were no attendant side effects.

All patients, unipolar as well as bipolar, relapsed into depression (all unipolar and two bipolar) or mania (one bipolar) within 6 months of discontinuing Wellbatrin; all patients were placed on other medication when Wellbatrin was discontinued because of their history of recurrences, except for the bipolar patient who became manic.

Neuroendocrine Studies

The effect of bupropion on the secretion of growth hormone (GH) and prolactin (PRL) was studied in six healthy male subjects and another six male hyperprolactinemic patients, using a randomized double-blind paradigm. The collaborative study was carried out in Germany at the Outpatient Pscyhiatric Clinic, University of Munich. The six "normal" subjects and six psychiatric patients each received placebo (one dose) and 200 mg bupropion (one oral dose) under conditions of written informed consent. The patient group was pretreated with a neuroleptic drug, haloperidol. The studies with both healthy volunteers and psychiatric patients occurred at an interval of 1 week. After administration of the test substances (i.e., either placebo or bupropion), blood was drawn to measure GH or PRL up to 240 minutes (i.e., 4 hours) thereafter. The data presented clearly indicate that bupropion, in the dose administered, leads to no change in the secretion of GH or PRL in humans. The findings hold both in the normal volunteers and with psychiatric patients pretreated with haloperidol (i.e., rendered hyperprolactinemic). There was no change in the thyroid-releasing hormone (TRH)-induced stimulation of PRL in either the normal volunteers or psychiatric patients (Laakmann, Hoffmann, & Hofschuster, in press).

Conclusion

The present single-blind study data support open trails and double-blind comparisons to the effect that Wellbatrin is an effective antidepressant drug whose clinical response in psychiatric patients is not accompanied by anticholinergic or CNS effects. (Stern, Harto-Truax, Rogers, & Miller, in press). It appears particularly suited for patients with psychomotor retardation. Preliminary data in both unipolar as well as bipolar patients suggest a prophylactic effect for bupropion against acute recurrences of either mania or depression. Finally, in efforts to clarify its potential mechanism of action, we carried out neuroendocrine studies to examine the potential effects of bupropion on central noradrenergic and dopaminergic mechanisms. Our negative findings fail to enhance our understanding of the possible mechanism of action of this new and exciting antidepressant drug.

References

Laakmann, G., Hoffmann, N., and Hofschuster, H. The effect of bupropion HCl on the secretion of growth hormones and prolactin in humans. *Life Sci.* (In press)

Maxwell, R.A., Mehta, N.B., Tucker, W.E., Jr., Schroeder, D.H., and Stern, W.C. Bupropion. In: Goldberg, M.E. (ed.), *Pharmacological and Biochemical Properties of Drug Substances*. Vol. 3. Washington, D.C.: American Pharmaceutical Association, Academy of Pharmaceutical Sciences. (In press)

Shopsin, B., Cassano, G.B., and Conti, L. An overview of new "second generation" antidepressant compounds: Research and treatment implications. In: Enna, S.J., et al. (eds.), *Antidepressants, Behavioral, and Clinical Perspectives*. New York: Raven Press, 1981, ps. 222 and 235.

Stern, W.C., Harto-Truax, N., Rogers, J., and Miller, L. Clinical profile of the novel antidepressant bipropion. In: Costa, E., and Racagni, G. (eds.), *Advances in Biochemical Psychopharmacology, Typical and Atypical Antidepressants, Neuroendocrine and Clinical Aspects*. Vol. 2. New York: Raven Press. (In press)

Atypical Depressives: A Prelminary Report of Antidepressant Response and Sleep Patterns

Frederic M. Quitkin, M.D.,[1] David Schwartz, Ph.D.,[1] Michael R. Liebowitz, M.D.,[1] Jonathan R. Stewart, M.D.,[1] Patrick J. McGrath, M.D.,[1] Frieda Halpern, M.A.,[1] Joaquim Puig-Antich, M.D.,[1] Elaine Tricamo, R.N.,[1] Edward J. Sachar, M.D.,[1] and Donald F. Klein, M.D.[1]

Although tricyclic treatment for severe depressive disorder was adopted as a standard by 1970, there was still no agreement on the best method of treating the large number of mildy or moderately depressed patients seen in outpatient settings.

In an effort to render antidepressant drug treatment more uniformly effective, investigators began to reconsider two aspects of the problem: refinement of diagnostic classification and alternative treatment strategies. Accumulating evidence now suggests that meaningful subtypes may differentially respond to alternative treatment. It was in this context that we have formulated the present investigation.

Subtypes of Depressive Disorder

It has been recognized that some depressed patients, especially among outpatients and those failing to respond to standard tricyclic treatment, show symptoms opposite to the traditional endogenous constellation. These nonendogenous symptoms include overeating and weight gain, initial insomnia without intermittent or early morning awakenings, and mood worsening in the evening. In addition, such patients are responsive to their social surroundings and can be temporarily cheered, although their dysphoric mood returns. This symptomatic picture is referred to as atypical depression (Klein, Gittelman-Klein, Quitkin, & Rifkin, 1980). We wished to test the hypothesis that atypical depressives are more likely to respond to monoamine oxidase inhibitors (MAOI) than tricyclic antidepressants.

Sleep polysomnography has been demonstrated to be altered in some depressive subgroups (Kupfer & Foster, 1978). To further understand the atypical syndrome, sleep studies of this patient group were initiated. All of this work is in the preliminary phase. Data from a treatment study and sleep polysomnography are presented.

Method

This is a 7-week drug study of atypical depressives comparing placebo, a tricyclic antidepressant (imipramine), and a MAO inhibitor (phenelzine). All patients received placebo single-blind for 10 days. Patients who were much improved during the initial placebo phase were removed from the study. Treatment and evaluation of progress after the initial placebo phase was done in a double-blind manner.

Subjects

To be eligible, subjects must meet the Research Diagnostic Criteria for major, minor, or intermittent depression (Spitzer, Endicott, & Robins, 1978). To be diagnosed as having an atypical depressive disorder, subjects must have the essential feature of reactivity of mood. They must also be rated as moderate to severe for at least two of four associated features, which include hypersomnia, overeating, fatigue and lethargy, and rejec-

---

[1] New York State Psychiatric Institute, New York, NY 10032.

tion sensitivity. Subjects are excluded if they meet Research Diagnostic Criteria for schizophrenia, schizoaffective disorder, unspecified functional psychoses, or criteria for endogenomorphic depression (Klein et al., 1980). Patients are excluded if they have been treated in the current episode with tricyclics (greater than 150 mg of imipramine/d or its equivalent) or MAOI (45 mg/d or more of phenelzine or its equivalent).

Medication

Each patient receives two bottles of medication. One bottle contains 15 mg phenelzine or matching placebo, and the other contains 50 mg imipramine or matching placebo. The patient will take the phenelzine or its matching placebo in the morning and the imipramine or its matching placebo at bedtime In no case will the patient receive both active medications. Thus, the dosage schedule is fixed up to 4 tablets/day of each medicine or its placebo. This schedule will be delayed, stopped,or reversed in the event of adverse reactions. The patients who have had a complete remission of symptoms will not have their dose increased beyond 4 tablets/day of each medicine or its placebo. However, for patients who have not responded, every attempt will be made to increase the dose to five or six pills of each medication (that is 75-90 mg phenelzine or 250-300 mg imipramine for patients on an active medication).

Results

This is a preliminary report of an ongoing study. To date, 44 patients have been entered into the study. During the initial 10-day single-blind placebo period, 6 were judged significantly improved and removed from the study; 12 patients were randomized to imipramine, 2 were judged significantly improved, 9 were unimproved, and 1 patient dropped out. Twelve patients were randomized to phenelzine, 7 were judged significantly improved, 3 were judged unimproved, and 2 patients dropped out. Thirteen patients were randomized to placebo, 3 were judged significantly improved, and 10 were judged not improved. This data is summarized in the Table.

Table

Preliminary Results: Randomization Phase

	Phenelzine	Imipramine	Placebo	Chi-Square
Improved	7	2	3	7.54*
Unimproved	3	9	10	

*Significant at .05 level.

Sleep Indexes of Atypical Depressives: A Preliminary Examination

Recent work suggests that the EEG sleep indexes of primary depressives differentiate them from other patients as well as normal controls.

Also reported is a preliminary examination of a pilot study of 10 nonbipolar, atypical depressives studied in our sleep laboratory. Data from Williams, Karacan, and Hursch (1974) as well as that from Kupfer, Foster, Coble, McPartland, and Ulrich (1978) were used to serve as a standard for comparing the sleep indexes of the atypical depressive. The use of data recorded in other laboratories for this purpose is viewed as a methodological shortcoming to be corrected in future studies.

The mean age of the 10 patients with atypical depression is 30.6. Their REMP latency on Night 1 is 69.61 min, SD 31.07; on Night 2, 53.05 min, SD 21.96; and on Night 3, 57.87 min, SD 39.60. Williams et al. (1974) reported normative data in the 30-40 age group, where the REMP latency is 82 minutes, SD 24.77. Kupfer et al. (1978) reported that the REMP latency for 47 patients (mean age 45.7 ± 1.9) with primary depression was 38.6, SEM 3.2 and for 47 patients with secondary depression (mean age 45.7 ± 1.9) it was 72.3, SEM 4.3. This would suggest that patients with atypical depression are different from "normals" and that their REMP latency may differentiate them from secondary as well as primary endogenous depressives.

We also examined other sleep measures in this study of atypical depressives. Total sleep time for atypical depressives was close to 400 min (range is 395-406 min on three nights). This is similar to Williams' et al. normals of 423 min and appears to be different from Kupfer's findings of approximately 304 to 336 min in primary and secondary depressives, respectively.

Summary and Conclusions

These preliminary results support the hypothesis that patients referred to as atypical depressives have a greater likelihood of responding to MAOI than to TCA or placebo. If this preliminary trend persists, it would have important clinical and heuristic implications.

It would suggest that MAOI is the treatment of choice for this patient group. Differential responsivity of MAOI supports the validity of the phenomenologic depressive subtype and suggests that the pathophysiology of this patient subgroup differs from endogenous depressives. It would also be relevant to determine if this response of atypical depressives is specific for hydrazine derivatives such as phenelzine, or whether it also occurs with nonhydrazine derivatives such as tranylcypromine, or specific MAOI such as deprenyl or clorgyline.

The shortened REM latency of atypical depressives suggests that they do share some of the characteristics of other depressive disorders. It might be concluded that this is a mild form of depressive illness. If that were the case, they should respond to TCA as well as MAOI. Since that does not appear to be the case, we think this may be a form of affective disorder whose treatment response and pathophysiology is distinctly different from patients with endogenous forms of the illness.

References

Klein, D.F., Gittelman-Klein, R., Quitkin, F., and Rifkin, A. *Diagnosis and Drug Treatment of Psychiatric Disorders*. Baltimore, MD: Williams and Wilkins, 1980.

Kupfer, D.J., and Foster, F.G. EEG, sleep, and depression. In: Williams, R., and Karacan, I. (eds.), *Sleep Disorders,Diagnosis and Treatment*. New York:John Wiley and Sons,1978.

Kupfer, D.J., Foster, F.G., Coble, P., et al. The applicationof EEG sleep for the differential diagnosis of affective disorders. *Am. J. Psychiatry*, 135:69-74, 1978.

Spitzer, R., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry*, 35:773-782, 1978.

Williams, R.L., Karacan, I., and Hursch, C.F. *EEG of Human Sleep*. New York: John Wiley and Sons, 1974.

Biological and Clinical Studies of Tardive Dyskinesia

Robert C. Smith, M.D., Ph.D.,[1] Richard Allen, D.P.H.,[1] Jack Gordon, M.D.,[1] Chandra Misra, Ph.D.,[1] Joseph Schoolar, M.D., Ph.D.,[1] Judith Wolff, R.N.,[1] and Beng T. Ho, Ph.D.[1]

A series of surveys, small treatment trials, and biological studies have been conducted on patients with tardive dyskinesia (TD). In all studies, TD was rated using the Smith-TRIMS TD scale which evaluates multiple symptom areas of dyskinetic and extra pyramidal type symptoms.

A prevalence study of TD was done in eight hospitals in the state of Texas using an age-stratified random sampling procedure (about 50% of the sample below and 50% above the age of 50). Most patients with at least minimal symptoms of TD on initial rating were evaluated for more definite dyskinesia with TD ratings on at least two occasions. On a selected sample of patients, a blood sample was drawn to measure plasma neuroleptics, measured by radio-receptor (RR) assay techniques, during an additional TD rating. For the diagnosis of a positive case of TD, a subject had to have a total TD score of at least 5 on the Smith-TRIMS TD scale on two occasions.

Using these rating procedures and criteria, 35.8% of patients in the sample had definite TD, with the rate about twice as high in patients over the age of 50 (47.1% positive cases) as in cases under the age of 50 (22% positive cases). The percent of patients with definite TD increased in a montonic fashion between the ages of 50 and 60 or 70 but did not increase further in the oldest age groups (Figure 1). Females had higher dyskinesia scores than males in the younger and middle age groups, but did not show a consistent trend for higher TD scores in patients above 60 or 70 years of age.

---

[1] Sections of Biological Psychiatry, Neurochemistry and Neuropharmacology, and Biological Psychiatry Research Team, Texas Research Institute of Mental Sciences, Texas Medical Center, Houston, TX 77030.

Note: Address communications to Dr. Smith, Chief, Biological Psychiatry.

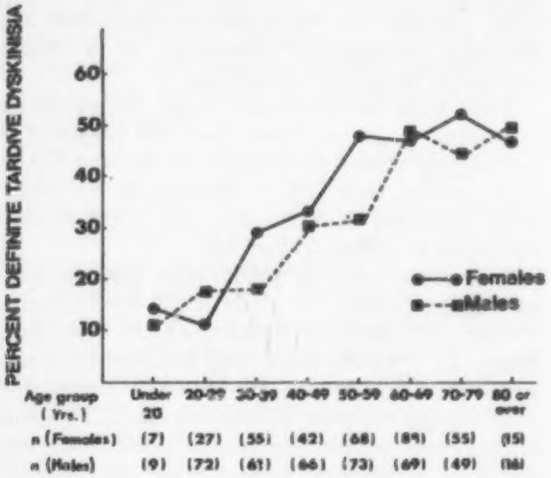


FIGURE 1. Effects of age and sex on the prevalence of tardive dyskinesia

Table

Lower Neuroleptic Plasma Levels in Patients with Definite Tardive Dyskinesia

	Mean Neuroleptic Plasma Level* (RR Assay)		
	Definite TD	No TD	TD Percent Decrease
All Patients	263 ± 35** (101)†	438 ± 98 (52)	−40%
Patients over 50 years	248 ± 42 (65)	450 ± 157 (22)	−45%
Patients 50 years or under	293 ± 65 (36)	430 ± 127 (30)	−32%

* Radio-receptor assay ng/ml chlorpromazine equivalence
**Each number is mean ± s.e.m.
† Number of patients

Radio-receptor plasma levels of neuroleptic drugs that the patients were receiving correlated significantly but negatively with TD scores. Patients who met criteria for a positive case of TD had about 40% lower plasma neuroleptic levels than patients without TD (*see* Table). A similar trend was found in patients under the age of 50 than in patients over the age of 50.

In a small sample of patients treated with lecithin (35 gm/d of 53% phosphatidylcholine) in a double-blind crossover design, lecithin did not have consistent or statistically significant effect in ameliorating TD severity scores; one or two patients showed improvement and one or two patients had a worsening of TD symptoms (Figure 2).

Patients with TD had significantly higher plasma pseudocholinesterase levels than controls (Figure 3), but they showed no significant difference in platelet monoamine oxidase compared to schizophrenic controls.

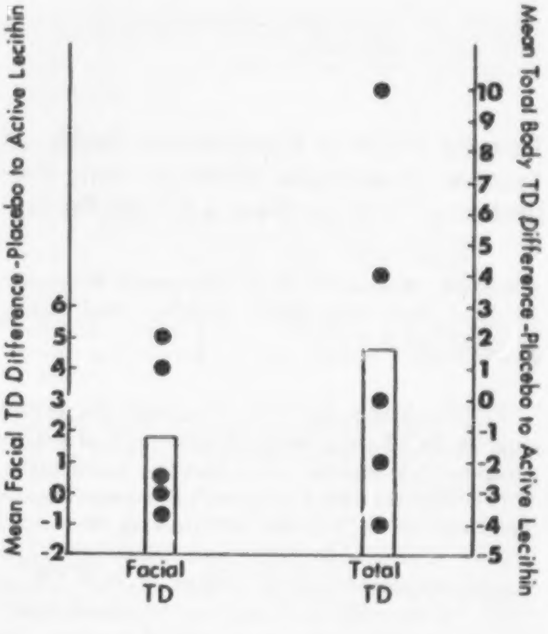


FIGURE 2. Effects of lecithin on tardive dyskinesia. Each point represents the mean difference of placebo minus lecithin scores; a higher score indicates improvement.

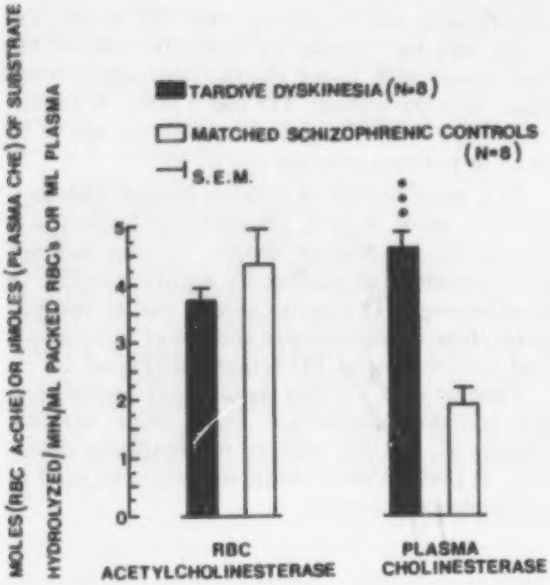


FIGURE 3. Plasma pseudocholinesterase values in patients with TD and control.

Results From a Prospective Study of Tardive Dyskinesia Development: Preliminary Findings Over a 2-Year Period[1]

John M. Kane, M.D.,[2] Margaret Woerner, Ph.D.,[2] Paul Weinhold, Ph.D.,[2] and James Wegner, M.A.[2]

Tardive dyskinesia (TD) remains a major concern in the pharmacological treatment of schizophrenia (American Psychiatric Association, 1979). The lack of a proven, safe, and effective treatment for TD makes attempts at prevention urgent. A review by Kane and Smith (1981) revealed prevalence rates ranging from 0.5% to 56% (mean = 20.1%) among 56 neuroleptic-treated samples. Among untreated samples, the prevalence of abnormal movements ranged from 0 to 36.7% (mean = 5.1%). Since these samples may have differed on many variables other than neuroleptic exposure, contrasting them is not ideal. Despite this, the epidemiological data implicating neuroleptic treatment as a major etiological factor are compelling.

Even with the enormous range in prevalence estimates, it seems clear that the majority of neuroleptic-treated patients do not develop TD. It is important, therefore, to identify factors which might increase vulnerability and then develop strategies to minimize the risk.

This report presents preliminary findings from an ongoing prospective study of TD development. To date, 777 psychiatric patients have entered the study; the majority have been followed for 1 to 3 years. Patients are examined every 3 months and rated on the Simpson Dyskinesia Scale, Simpson Angus Scale (for extrapyramidal side effects), and the Brief Psychiatric Rating Scale. Electroencephalograms and psychometric testing are done at baseline, and detailed histories of psychotropic medications are obtained. Ratings are made blind to treatment history.

Patients who develop "questionable" signs (defined globally) are seen monthly. Diagnosis of presumptive TD requires ratings of at least mild TD by three raters following separate examinations. TD cases are videotaped, discontinued from antipsychotic drugs if possible, and rated biweekly for at least 3 months.

The demographic characteristics of the first 328 patients who were at risk (neuroleptic-treated) include: mean age = 27 (*SD* 9); 59% male; 59% schizophrenic, 17% affective disorder, 12% schizoaffective on the Diagnostic and Statistical Manual-II (DSM-II). The majority had less than 1 year total cumulative neuroleptic exposure prior to study entry (mean exposure 21 months, median 10 months).

To date, 44 cases of presumptive TD have developed during the study. Their characteristics include: 50% male; mean age = 33 (*SD* 12); mean cumulative neuroleptic exposure 30 months (*SD* 31); 34% schizophrenic; 36% major affective disorder; 20% schizoaffective. These patients were classified according to the Research Diagnoses for Tardive Dyskinesia (RD-TD) (Schooler & Kane, 1981) as follows: 30 persistent TD (18 neuroleptic-free and 12 with concurrent neuroleptics);

---

[1] This project was supported by USPHS, NIMH Grant MH-32369.

[2] Long Island Jewish-Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004.

8 transient TD, 3 probable, and 3 withdrawal TD.

A life-table analysis employing the first 328 at risk subjects indicated a cumulative incidence of TD of 12% (95% confidence interval 6%-18%) at the end of 4 years of total cumulative neuroleptic exposure. Our effective sample size beyond 4 years is still too small to determine incidence beyond this point.

The patients who developed TD had a mean cumulative neuroleptic exposure prior to TD diagnosis of 158 weeks (*SD* 134) compared with 122 weeks (*SD* 122) for those without TD when last examined (two-tailed p value = .12).

Additional analyses of risk factors eliminated those who had shown any "questionable" signs of TD to provide a sharper distinction between those who developed TD and those who remained "clear" up to the most recent observation. In addition, to explore factors which might indicate those most vulnerable to TD development (Kane, Struve, Weinhold, & Woerner, 1980), TD cases were divided into two groups: those developing TD after less than 2 years of neuroleptic exposure (early TD) and those developing TD after more than 2 years (late TD).

The results indicated that TD cases had longer exposure to neuroleptic and antiparkinsonian drugs prior to study entry than did patients without TD. TD cases compared with non-TD patients were older at study entry, had had a longer psychiatric history, and had more often been treated with electroconvulsive therapy (ECT). Early and late TD cases did not differ significantly on these variables. Early TD cases had significantly lower maximum doses of neuroleptics than late TD cases, suggesting that early TD onset is not related to the use of higher doses of medication. The TD group as a whole, however, did receive significantly higher maximum doses than the non-TD group. Late TD cases had had more neuroleptic-free intervals of at least 1 month and were more likely to have taken combined neuroleptics than both the early TD and clear groups. However, the effects of the latter three variables may be mediated by length of neuroleptic treatment with which they are correlated.

Interestingly, the history of extrapyramidal side effects and the number of months of exposure to lithium prior to study entry were significantly related to the "early" onset of TD. The former has been suggested as a risk factor in the literature (Crane, 1972) and will be explored in more detail in subsequent analyses. The lithium finding may reflect a possible increased risk among patients with affective illness (Rosenberg, Niven, & Hanson, 1977; Davis, Berger, & Hollister, 1976) or may involve unknown long-term neurochemical effects of lithium.

The ECT finding also suggests that diagnosis may be a factor. We found no relationship between DSM II-diagnosis and TD development; however, further exploration using Research Diagnostic Criteria (RDC) diagnoses for matched TD and non-TD cases may prove more fruitful.

Other variables showing no relationship to TD development were: sex, psychometric test scores, history of CNS injury or dysfunction, medication at study entry, potency of predominant neuroleptic, total exposure to tricyclic antidepressants, monoamine oxidase inhibitors, minor tranquilizers, and anticonvulsants.

It is important to emphasize the preliminary nature of these findings. Many risk factors are intercorrelated, and a larger number of TD cases will be necessary in order to carry out more meaningful analyses.

References

American Psychiatric Association. Tardive dyskinesia. *Task Force Report 18*. Washington, D.C.: APA, 1979.

Crane, G.E. Pseudoparkinsonism and tardive dyskinesia. *Arch. Neurol.*, 27:426-430, 1972.

Davis, K.L., Berger, P.A., and Hollister, L.E. Tardive dyskinesia and depressive illness. *Commun. Psychopharmacol.*, 2:125-130, 1976.

Kane, J., and Smith, J.M. Tardive dyskinesia: Prevalence and risk factors, 1959-1979. (Submitted, 1981)

Kane, J., Struve, F., Weinhold, P., and Woerner, M. Strategy for the study of patients at high risk for tardive dyskinesia. *Am. J. Psychiatry*, 137:1265-1267, 1980.

Rosenbaum, K.M., Niven, R.G., Hanson, N.P., et al. Tardive dyskinesia: Relationship with primary affective disorder. *Dis. Nerv. Syst.*, 38:423-427, 1977.

Schooler, N., and Kane, J. Research diagnoses for tardive dyskinesia (RD-TD). (Submitted, 1981)

Impairment of Swallowing, Tardive Dyskinesia, and Anticholinergic Drug Use

Thomas J. Craig, M.D., M.P.H.,[1,2] Mary Ann Richardson, M.A.,[1] Nigel M. Bark, M.D.,[1,3] and Roman Klebanov, M.D.[4]

The influence of psychotropic medication on the swallowing mechanism has been a source of controversy since the mid-1950s when case reports of choking deaths among medicated psychiatric patients began to appear (Feldman, 1957; Hollister, 1957; Plachta, 1965; Wardell, 1957). A recent case-control study of choking deaths revealed that patients who choked to death were twice as likely to be receiving two or more drugs with significant anticholinergic effects than matched controls (Craig, 1980). An unpublished report (Moore & Book, 1970) claimed that 40% of an unselected sample of psychiatric patients were found to have an impairment of the gag reflex in contrast to only 9% of "normals." Case studies of two patients with tardive dyskinesia indicated a difficulty in swallowing (Brandon, McClelland, & Protheroe, 1971; Gilbert, 1969.) These findings plus experimental evidence (Bieger, Giles, & Hockman, 1977) implicating dopaminergic mechanisms in the pharyngeal phase of swallowing led to the present study.

Method

The present study was conducted using a nonrandom sample of long-term psychiatric patients in a large state hospital. All but one patient were diagnosed schizophrenic by the treating clinician using Diagnostic and Statistical Manual-II criteria. A research scientist with extensive experience carried out ratings of tardive dyskinesia using the Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976), and the Simpson Abbreviated Rating Scale (ADS) (Simpson, Lee, & Zouback, 1979), and of parkinson-like symptoms using the Neurological Rating Scale (NRS) (Simpson & Angus, 1970). The scoring of the NRS and the ADS were adapted to conform with the AIMS ratings of 0 = absent, 1 = minimal or questionable, 2 = mild, 3 = moderate, and 4 = severe. Separate from this examination but within the same time period, two research psychiatrists independently assessed each patient's gag reflex. The technique and ratings described were developed after a study of the literature and consultation with local experts in neurology and otorhinolaryngology plus a pilot test in patients not included in the study. Inter-rater agreement for this gag reflex rating was acceptably high (Kappa = 0.76, $Z = 7.05$). After both clinical procedures were completed on all patients, a history of current medication usage was obtained from each patient's clinical chart by the research scientist. Data analysis was carried out using the chi-square statistic (Fleiss, 1973) and the log-linear model technique (Fienberg, 1978).

Results

A total of 56 patients were studied of whom 34 (60.7%) were men, 21 (36.2%) were less than 50 years old, and 43 (76.8%) were continuously hospitalized for more than 10 years. Thirty-three (58.9%) of the patients were rated normal on gag reflex with 8 (14.3%) rated variable, and 15 (26.8%) impaired. Initial analyses were carried out with the three dependent variable groups (Normal, Variable, Impaired). However, since the Variable and Impaired groups were virtually identical in their characteristics, these groups were combined in later analyses. There were no significant differences among the groups on the variables of age, sex, length of stay, extrapyramidal symptoms, or neuroleptic use as measured in chlorpromazine equivalents.

The Table shows the prevalence of gag reflex impairment among patients classified according to both presence or absence of tardive dyskinesia (using the ADS and AIMS) and use of anticholinergic medication. As indicated, the proportion of patients with gag reflex impairment is roughly

---

[1] Rockland Research Institute, Orangeburg, NY 10962.

[2] Department of Psychiatry, New York University, New York, NY 10016.

[3] Columbia University, New York, NY 10028.

[4] New York Medical College, Valhalla, NY 10595.

Address correspondence to Dr. Craig at 40 Woodbine Road, New City, NY 10956.

similar for patients with one or neither of these conditions, ranging from 12.5-33.3%. In striking contrast, almost three-fourths of those patients with tardive dyskinesia and using anticholinergic drugs showed gag reflex impairment, suggesting an interaction effect among these factors.

Discussion

Due to the highly selective nature of the patient population studied (long-stay schizophrenics exposed to long-term medication use), the generalizability of the present findings to more acute patient populations with heterogeneous drug use and diagnoses requires further replication. However, the prevalence of impaired gag reflex in these patients (41.4%) is remarkably similar to the figure found in the only previous report addressing this issue (Moore & Book, 1970).

The present findings suggest an interrelationship among tardive dyskinesia, the use of anticholinergic drugs, and impairment of the gag reflex. It is generally accepted that the use of anticholinergic agents aggravates the signs of tardive dyskinesia once the latter have been established (Gerlach, Reisby, & Randrup, 1974; Klawans, Goetz, & Perlik, 1980). The association of both these variables with impairment of the gag reflex is not as well defined.

Neurotransmitters involved in the gag reflex arc include glutamic acid (afferent impulses), dopamine (centrally), and nicotinic acetylcholine receptors at the afferent striated muscle motor end plate (DeJong, 1950; Kaelle, 1975). Dopamine has been shown in animal studies to both facilitate and inhibit swallowing under varying circumstances (Bieger, Giles, & Hockman, 1977). Thus, one possible explanation for the observed association among these three variables could be the hypothesis that the mechanism of impairment of the gag reflex is analogous to that of tardive dyskinesia, being a supersensitivity phenomenon related to prolonged block of dopamine receptors. The fact that the reflex is inhibited rather than exaggerated, which is the case in tardive dyskinesia, could suggest that there is a relative predominance in supersensitivity of inhibitory dopamine receptors over facilitating receptors which might be further enhanced by a central hypocholinergic effect induced by anticholinergic drugs. This hypothesis would be consistent with recent

Table

Tardive Dyskinesia, Anticholinergic Drug Use, and Pharyngeal Reflex

	Pharyngeal Reflex				
	Normal		Variable/ Impaired		
	No	%	No	%	Chi-square
Simpson ADS Global					
None/Questionable:					
No Anticholinergic Drugs ($N=9$)	7	77.8	2	22.2	.01 NS
Anticholinergic Drugs ($N=8$)	7	87.5	1	12.5	
Mild-Severe:					
No Anticholinergic Drugs ($N=20$)	14	70.0	6	30.0	5.80*
Anticholinergic Drugs ($N=19$)	5	26.3	14	73.7	
AIMS Global Severity					
None/Minimal:					
No Anticholinergic Drugs ($N=6$)	4	66.6	2	33.3	.18 NS
Anticholinergic Drugs ($N=4$)	3	75.0	1	25.0	
Mild-Severe:					
No Anticholinergic Drugs ($N=23$)	17	73.9	6	26.1	4.33†
Anticholinergic Drugs ($N=23$)	9	39.0	14	61.0	

*Significant at .02 level.

†Significant at .05 level.

evidence showing the existence of both inhibitory and facilitating dopamine receptors in various parts of the brain (Klawans et al., 1980).

Alternative hypotheses invoking a primary role for anticholinergic drugs in this mechanism seem less likely, in view of their relatively weak and inconsistent impact on the swallowing mechanism (Bieger et al., 1977), and the fact that they exert their influence only on muscarinic acetylcholine receptors, and thus should have no influence on the nicotinic receptors at the motor endplate (Richelson & Divinetz-Romero, 1977). The present data suggesting an interaction between tardive dyskinesia and anticholinergic drug use support this conclusion.

Whatever the underlying mechanism, the present study strongly suggests that patients with tardive dyskinesia receiving anticholinergic drugs are at extremely high risk of also having an impaired gag reflex. This finding reinforces the recommendation that anticholinergic agents be avoided in the treatment of patients with tardive dyskinesia although, as has been noted (Klawans et al., 1980), tardive dyskinesia and extrapyramidal symptoms can coexist and thus pose a therapeutic dilemma. It remains for further study to determine whether the discontinuation of these agents might result in a restoration of the gag reflex.

Acknowledgment: The authors wish to acknowledge the assistance of Morris Meisner, Ph.D., and Shang P. Lin, Ph.D., for statistical analysis, and Mary Herrmann and Frances Simpson for manuscript preparation.

References

Bieger, D., Giles, S. A., and Hockman, C. H. Dopaminergic influences on swallowing. *Neuropharmacology*, 16:245-252, 1977.

Brandon, S., McClelland, H.A., and Protheroe, C. A study of facial dyskinesia in a mental hospital population. *Br. J. Psychiatry*, 118:171-184, 1971.

Craig, T. J. Medication use and deaths attributed to asphyxia among psychiatric patients. *Am. J. Psychiatry*, 131:1366-1373, 1980.

DeJong, R. N. *The Neurologic Examination*. New York: Paul B. Hoeber, Inc., 1950.

Feldman, P.E. An unusual death associated with tranquilizer therapy. *Am. J. Psychiatry*, 113:1032-1033, 1957.

Fienberg, S. E. *The Analysis of Cross-Classified Categorical Data*. Cambridge, MA: MIT Press, 1978.

Fleiss, J. *Statistical Methods for Rates and Proportions*. New York: John Wiley and Sons, Inc., 1973.

Gerlach, J., Reisby, N., and Randrup, A. Dopaminergic hypersensitivity and cholinergic hypofunction in the pathophysiology of tardive dyskinesia. *Psychopharmacologia (Berlin)*, 34:21-35, 1974.

Gilbert, M. M. Haloperidol in severe facial dyskinesia (case report). *Dis. Nerv. Syst.*, 30:481-482, 1969.

Guy, W. *ECDEU Assessment Manual for Psychopharmacology*. Revised 1976. Washington, D.C.: U.S. Department of Health, Education, and Welfare, 1976.

Hollister, L.E. Unexpected asphyxial death and tranquilizing drugs. *Am. J. Psychiatry*, 114:366-367, 1957.

Kaelle, G.B. Microanatomy and pharmacology of cholinergic synapses. In: Brady, R. O. (ed.), *The Nervous System*. Vol. 1. *The Basic Neuro-sciences*. New York: Raven Press, 1975, pp. 363-373.

Klawans, H. L., Goetz, C. G., and Perlik, S. Tardive dyskinesia: Review and update. *Am. J. Psychiatry*, 137:900-908, 1980.

Moore, M. T., and Book, M. H. Sudden death in phenothiazine therapy. *Psychiatric Quart.*, 44:389-402, 1970.

Plachta, A. Asphyxia relatively inherent to tranquilization. *Arch. Gen. Psychiatry*, 12:152-158, 1965.

Richelson, E., and Divinetz-Romero, S. Blockade by psychotropic drugs of the muscarinic acetylcholine receptor in cultured nerve cells. *Biol. Psychiatry*, 12:771-785, 1977.

Simpson, G. M., and Angus, J. W. S. Drug-induced extrapyramidal disorders. *Acta Psychiatr. Scand. (Suppl.)*, 212:11-19, 1970.

Simpson, G. M., Lee, J. H., and Zouback, B. A. Rating scale for tardive dyskinesia. *Psychopharmacology, (Berlin)*, 64:171-179, 1979.

Wardell, D. W. Untoward reactions to tranquilizing drugs. *Am. J. Psychiatry*, 113:745, 1957.

Lecithin Treatment of Tardive Dyskinesia—A Progress Report

Brian G. Anderson, M.B., Ch.B.,[1] Dean Reker, R.N.,[1] Miodrag Ristich, M.D.,[1] Eitan Friedman, Ph.D.,[2] Miriam Banay-Schwartz, Ph.D.,[3] and Jan Volavka, M.D., Ph.D.[1]

Tardive dyskinesia (TD) is thought to be related to an imbalance between the dopaminergic and cholinergic systems in the striatum (1). It is believed that there may be a relative deficiency of acetylcholine (Ach) neurotransmission in this area. Some studies have reported beneficial effects in TD using Ach precursors or agonists such as choline, lecithin or physostigmine (2,3,5,6). Lecithin contains phosphatidylcholine (PC) which is metabolized to choline. Oral administration of lecithin elevates plasma choline levels (7) and may increase brain choline and Ach levels (4). Different commercial lecithins contain varying concentrations of PC and impurities, e.g., fatty acids and phosphatidylethanolamine. The authors report progress in a study attempting to replicate beneficial effects of lecithin in TD.

Method

Subjects

Nine female inpatients who gave informed consent served as subjects. Prerequisites to enter the study were: 1) a history of neuroleptic treatment and 2) moderate to severe TD on the Abnormal Involuntary Movement Scale (AIMS) as judged independently by two experienced raters. Age range was 32-77 years (mean 62 yrs), diagnosis by Diagnostic and Statistical Manual-III (DSM-III) criteria was chronic schizophrenia, and three patients also had mild dementia. Duration of neuroleptic treatment was 2-21 years (mean 6 yrs); patients receiving neuroleptics at the beginning of the study had been on the same dosage for 4-12 months (mean 6 mos) and were maintained on this dosage throughout the study. Three patients had been on no medication for 6, 7, and 24 months. TD was assessed using AIMS for 2-8 months before entering the study. The state of dentition was as follows: two subjects were edentulous, four were pre-edentulous (i.e., only 1 or 2 teeth present), and three had poor dentition (i.e., 4-26 teeth missing).

Procedure

This is a crossover, placebo-controlled, double-blind study. The treatment and placebo periods lasted 4 weeks with pretreatment, washout, and posttreatment periods of 2,4, and 2 weeks, respectively. Lecithin or placebo was given in a milk shake at 8 a.m. and 4 p.m. TD was assessed weekly at the same time of day using AIMS, by two blind raters who had an interrater correlation coefficient of 0.93; videotapes of the examinations and polygraph recordings of facial movements were also taken. Weekly plasma choline levels were assayed, using the Jendin-Handin gas liquid chromatography (GLC) method, from blood samples drawn before the 8 a.m. dose. Other parameters measured weekly were the Brief Psychiatric Rating Scale, the Hamilton Depression Rating Scale, and weight.

Results

The first trial involving seven subjects and using Phospholipon-100 (American Lecithin Co., soyabean extract) at a dose of 31.5 gm/70 kg/d showed no change in TD ratings in the presence of consistently elevated plasma choline levels while taking lecithin (Table). Phospholipon-100 was initially chosen because it has one of the highest concentrations (93.5%) of PC. There were no side effects. An attempt was then made to replicate the findings of Jackson, Nuttall, Ibe, and Perez-Cruet (1979), who reported improvement in TD using Type IXE lecithin (Sigma Chemicals, egg-yolk extract) which has 54% PC. The dosage of 50 gms/70 kg/d used by Jackson et al. (1979) was given to five subjects in the present study for 3

---

[1] New York University at Manhattan Psychiatric Center, Ward's Island, NY 10035.

[2] New York University, New York, NY 10028.

[3] Center for Neurochemistry, Rockland Research Institute, Ward's Island, NY 10035.

Correspondence should be addressed to Dr. Anderson.

weeks. Again, no improvement in TD was noted in the presence of consistently elevated plasma choline levels while receiving lecithin (Table). Because there were no adverse side effects from Phospholipon-100, a trial has been completed in three subjects using a higher dose of this lecithin, i.e., 50 gm/70 kg/d. These subjects all showed a reduction in AIMS scores during the second week of treatment, but this was not sustained throughout the 4-week treatment period (Table).

Table

AIMS Scores* and Plasma Choline Levels†

	Baseline 2 Wks Mean	Lecithin Treatment (Wks) 1	2	3	4	Placebo 4 Wks Mean
		Phospholipon-100 31.5 gm/70 kg/d				
AIMS ($N=7$)	15.6	15.8	16.6	16.8	16.4	15.7
Plasma Choline ($N=5$)	6.0	20.4	18.6	20.7	-	-
		Sigma IXE 50 gm/70 kg/d				
AIMS ($N=5$)	17.8	16.8	18.2	17.6	-	19.3
Plasma Choline ($N=2$)	8.6	20.9	27.8	31.6	-	8.6
		Phospholipon-100 50 gm/70 kg/d				
AIMS ($N=3$)	15.5	15.8	11.0	12.8	14.8	15.5
Plasma Choline ($N=3$)	8.4	32.9	33.3	-	28.8	-

*AIMS scores are the sums of items 1-7 on the AIMS scale and are shown as the average for *N*, the no. of subjects.

†Plasma choline levels are in *n* moles/ml. and are the averages for *N* subjects.

Discussion

The investigators were unable to show improvement in TD using two different lecithins. The patient group described here is similar to that of Jackson et al. in terms of diagnosis, age, and sex. However, there may be various subtypes of TD which are biochemically different but clinically indistinguishable from each other; such differences in patient selection may account for the failure to replicate Jackson's results. Furthermore, it is possible that patients vary in their permeability of the blood-brain barrier for choline and, therefore, raising plasma choline may have quite different effects on choline levels in the brain in different patients. Finally, the number of patients in the reported study, as well as in other reports, is still far too small for a conclusive statement; the investigators are studying additional patients.

References

Baldessarini, R.J., and Tarsy, D. Tardive dyskinesia. In: Lipton, M.A. DiMascio, A.,and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress.* New York: Raven Press, 1978.

Branchey, M.H., Branchey, L.B., Bark, N.M.,and Richardson, M.A. Lecithin in the treatment of tardive dyskinesia. *Commun. Psychopharmacol.* , 3(5):303-307, 1979.

Gelenberg, A.J., Doller-Wojcik, J.C., and Growden, J.H. Choline and lecithin in the treatment of tardive dyskinesia: Preliminary results from a pilot study. *Am. J. Psychiatry*, 136(6):772-776, 1979.

Hirsch, M.J., and Wurtman, R.J. Lecithin consumption increases acetylcholine concentrates in rat brain and adrenal gland. *Science*, 202:223-225, 1978.

Jackson, I.V., Nuttall, E.A., Ibe, O., andPerez-Cruet, J. Treatment of tardive dyskinesia with lecithin. *Am. J. Psychiatry*, 136(11):1458-1460, 1979.

Jeste, D.V., and Wyatt, R.J., In search of treatment for tardive dyskinesia: Review of the literature. *Schizophr. Bull.*, 5(2):251-293, 1979.

Wurtman, R.J., Hirsch, N.J., and Growden, J.H. Lecithin consumption elevates serum-free choline levels. *Lancet*, 2:68-69, 1977.

Effects of AMPT on Tardive Dyskinesia and Psychosis

Henry A. Nasrallah, M.D.,[1] Robert E. Smith, M.D.,[1] Frederick J. Dunner, M.D.,[1] and Mona McCalley-Whitters, B.S.N.,[1]

Dopamine (DA) receptor supersensitivity in the striatum after chronic neuroleptic intake is believed to be the basic pathophysiology of tardive dyskinesia (Klawans, 1973). In addition, DA receptor supersensitivity in the mesolimbic and mesocortical tracts has been suggested as possibly associated with psychosis (Davis & Rosenberg, 1979). DA antagonists such as receptor blockers (neuroleptics), stores depletors (reserpine), and synthesis inhibitors (alpha methyl paratyrosine) (AMPT) are known to mask tardive dyskinesia (Baldessarini & Tarsy, 1978).

AMPT has been shown to potentiate the antipsychotic effect of neuroleptics (Carlsson, Persson, Roos, & Walinder, 1972) but not in neuroleptic-resistant schizophrenic patients (Nasrallah, Donnelly, Bigelow,et al. 1977). AMPT has also been reported to improve the symptoms of tardive dyskinesia in about 50% of patients receiving 4 g/day for 3 days (Gerlach, Reisby, & Randrup, 1974; Gerlach & Thorsen, 1976).

In this study, the effects of AMPT on tardive dyskinesia and psychosis are described.

Method

Six patients with chronic schizophrenia or schizoaffective psychosis and persistent tardive dyskinesia of over 2 years' duration, consented to participate in the study. Their ages ranged from 26 to 71 years. Three patients were drug-free at the time of the study, while three others were receiving maintenance neuroleptic medication. Identical capsules of AMPT and placebo were given in a double-blind, crossover (placebo-active-placebo) design. Depending on body weight, patients received 1.5 to 3.0 g/d of AMPT for 4 weeks, with 2-3 weeks of placebo before and after. Weekly videotapes of the Abnormal Involuntary Movement Scale (AIMS) were randomized and rated blindly by two psychiatrists. Psychosis was rated weekly using the Brief Psychiatric Rating Scale (BPRS).

Results

The results are summarized on the Table. Five out of six patients had a reduction in their tardive dyskinesia AIMS scores after 2 weeks of AMPT. However, after 2 more weeks of treatment with AMPT, four patients showed worsening of tardive dyskinesia while two patients had sustained improvement.

As for the psychosis ratings, after 2 weeks of AMPT treatment the BPRS scores improved for one patient, worsened for two others, and were essentially unchanged for three patients. After 4 weeks of AMPT treatment, all three patients who were receiving maintenance neuroleptic medication showed improvement in the BPRS scores, while all three neuroleptic-free patients showed worsening of their psychosis ratings.

Discussion

The data suggest that AMPT improves tardive dyskinesia initially, probably by inhibiting DA synthesis and decreasing the availability of DA to supersensitive postsynaptic DA receptors. However, continued treatment with AMPT appears to cause a rebound increase in postsynaptic DA receptor supersensitivity (Nasrallah et al., 1977) associated with a reappearance of the dyskinetic symptoms. This suggests that AMPT may not be useful in the long-term treatment of tardive dyskinesia, and that inhibition of DA synthesis probably would not correct the underlying pathophysiology of tardive dyskinesia.

The effect of AMPT on psychosis in this study suggests that AMPT, given alone, may exacerbate psychosis, but if the patient is already on a regimen of antipsychotic medication, then the addition of AMPT seems to produce further improvement in psychosis ratings.

It is possible to postulate that prolonged treatment with AMPT alone in schizophrenic patients may induce DA receptor supersensitivity in both the nigrostriatal as well as mesolimbic DA tracts, which would clinically manifest as tardive dyskinesia and psychotic relapse, respectively.

---

[1] VA Medical Center and Department of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52240.

Table

Effects of AMPT On Tardive Dyskinesia (AIMS Scores) and Psychosis (BPRS Scores)

	Total AIMS Score				Total BPRS Score			
Patient No.	Placebo	AMPT (2 Weeks)	AMPT (4 Weeks)	Placebo	Placebo	AMPT (2 Weeks)	AMPT (4 Weeks)	Placebo
1*	12	8	10	9	19	17	42	27
2	10.5	5.5	10.5	14.5	25	23	18	23
3*	10	11	12.5	12.5	15	22	35	16
4*	17	14.5	8	21	24	28	36	34
5	5.5	1	0	2	12	12	9	2
6	7	2	3.5	3.5	20	8	7	8

*Patients who were neuroleptic-free prior to and during the AMPT trial.

References

Baldessarini, R.J., and Tarsy, D. Tardive dyskinesia. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progresss.* New York: Raven Press, 1978, pp. 993-1004.

Carlsson, A., Persson, A.T., Roos, B.E., and Walinder, I. Potentiation of phenothiazines by alpha-methyltyrosine in treatment of chronic schizophrenia. *J. Neurol. Transm.*, 33:83-90, 1972.

Davis, K.L., and Rosenberg, G.S. Is there a limbic system equivalent of tardive dyskinesia? *Biol. Psychiatry,* 14:699-703, 1979.

Gerlach, J., Reisby, N., and Randrup, A. Dopamine hypersensitivity and cholinergic hypofunction in the pathophysiology of tardive dyskinesia. *Psychopharmacologia (Berlin),* 34:21-25, 1974.

Gerlach, J., and Thorsen, K. The movement pattern of oral tardive dyskinesia in relation to anticholinergic and antidopaminergic treatment. *Int. Pharmacopsychiatry,* 11:1-7, 1976.

Klawans, H.L. The pharmacology of tardive dyskinesia. *Am. J. Psychiatry,* 130:82-86, 1973.

Nasrallah, H.A., Donnelly, E.F., Bigelow, L.B., et al. Inhibition of dopamine synthesis in chronic schizophrenia. *Arch. Gen. Psychiatry,* 34:649-655, 1977.

Receptor Sensitivity Modification in the Treatment of Tardive Dyskinesia[1]

Murray Alpert, Ph.D.,[2] Florence Diamond, M.S.,[2] and Arnold J. Friedhoff, M.D.[2]

Increase in dopamine receptor sensitivity is widely thought to underlie tardive dyskinesia (TD) (American Psychiatric Association, 1979). The increased sensitivity is postulated to be a compensatory reaction to the decreased access of dopamine to the postsynaptic receptors through the blocking action of neuroleptic drugs. This study explores a novel treatment approach to TD (Friedhoff & Alpert, 1978); testing the hypothesis that dopamine sensitivity can be down-regulated by temporarily increasing dopamine levels. To accomplish this, increasing doses of L-DOPA are gradually administered, waiting at each dose increment for evidence of adaptation. Following adaptation to a 1-month course of treatment at the target dose, the L-DOPA is discontinued. It is expected that improvement will persist if normal receptor sensitivity is reestablished, and transmitter levels are permitted to return to their usual levels.

Method

Subjects

Subjects were patients in state hospitals who met the following inclusion criteria: 1) a history of at least 2-years' neuroleptic medication; 2) no evidence of abnormal movements prior to receiving neuroleptic drugs; and 3) at least three ratings of mild or one rating of moderate severity of movements on Items 2 (lips), 3 (jaw), and 4 (tongue) of the Abnormal Involuntary Movement Scale (AIMS) (Guy, 1976). Initially only drug-free patients were included, but the study was extended to include patients requiring maintenance neuroleptics. Patients were followed for a period of at least 6 weeks prior to baseline during which they remained drug free or their neuroleptic medication remained unchanged. Anticholinergic drugs were not permitted. Inclusion Item 3 had to

---

[1] This study was supported by USPHS Grants MH-28892, MH-08618, and Research Scientist Award MH-14024 to A.J.F.

[2] Department of Psychiatry, New York University Medical Center, New York, NY 10016.

be satisfied at the baseline rating just prior to initiation of L-DOPA treatment.

Procedure

Patients were randomly assigned by a nonblind medicating psychiatrist to one of three target doses of carbidopa/L-DOPA as Sinemet: 30/300 mg/d, 50/500 mg/d, and 75/750 mg/d, which was administered orally in divided doses with meals. There was a dose-finding period of 4 weeks during which the dosage was increased as frequently as once a week, and the target dose was maintained for an additional 4 weeks. Increments in dosage were skipped and the dose-finding phase extended if the patient showed evidence of hypotension or significant activation of movement or behavior. In some cases, the target dose was continued to synchronize with the blind evaluators, visit. Patients were treated for an average of 72 days with a range of 56-126 days and received between 11.8 and 54 g of L-DOPA. Six patients received less than 21.9 g and nine patients received more than 33.9 g. These two groups will be reported as low-dose and high-dose groups.

The AIMS was administered as recommended by the Psychopharmacology Research Branch* of the National Institute of Mental Health (NIMH) (Guy, 1976) at baseline, weekly during L-DOPA treatment, and 4 weeks following termination of L-DOPA, which served as an outcome measure. Evaluators were blind as to dose and to where the patient was in the course of treatment. Sedatives were permitted throughout the trial but not within 12 hours of an AIMS rating.

The authors found that summing the AIMS scores is a less satisfactory reflection of pathology, and the data presented here have been derived by squaring the item score before summing. The rationale for squaring and the psychometric properties of the squared scores will be described separately (Alpert, Diamond, & Taleporos, Unpublished data). Intuitively, it may be seen that a patient with three scores of 1 should not be seen as showing equal pathology as a patient showing one score of 3. Squaring the scores, then summing, is a more adequate reflection of pathology.

Abnormal Movements of L-Dopa Treated (N=15) and Comparison Group of Equivalent Baseline Pathology (N=10). Second Rating Is Four Months After Baseline.

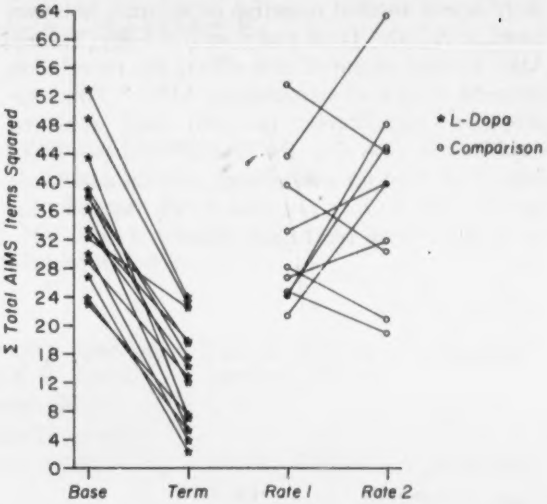


FIGURE 1

Results

Baseline and termination AIMS² Total for 15 patients treated with L-DOPA were compared with 10 patients who met the inclusion criteria but who were not treated with L-DOPA and were evaluated using the AIMS on two occasions approximately 12 weeks apart. The comparison group was matched with the experimental group for age, sex, and baseline AIMS score, but did not receive placebo. (Figure 1). Patients treated with L-DOPA uniformly showed some improvement at termination ratings and for about half the patients the change was clinically significant. Such changes were not apparent in the comparison group. One-way analysis of covariance for AIMS² Total, covarying baseline score, showed a reliable effect for L-DOPA treatment ($F = 25.90$, $p < .001$, *df* 2,22).

A comparison of low-dose ($N = 6$) and high-dose ($N = 9$) L-DOPA groups at baseline and termination AIMS² Total demonstrated relatively similar slopes, but the high-dose group showed more frequent "good" outcomes (Figure 2). It can be seen that the six lowest scores at termination were obtained by the high-dose group. Through randomization, the low-dose group may have had slightly higher baseline scores; in a multiple regression analysis examining the effect of dose, there was a modest negative correlation between baseline AIMS^2 Total and dose ($r = -.28$) (Table). After having removed this effect, the correlation between dose and termination AIMS^2 Total approached significance ($p = .08$) and achieved significance ($p = .05$) for Facial^2 scores. Since there was random assignment to dose and blind ratings, this finding provides further support for the suggestion of treatment efficacy.

---

*Now the Pharmacologic and Somatic Treatments Research Branch

Comparison of Outcome for Low and High Dose L-Dopa Treatment

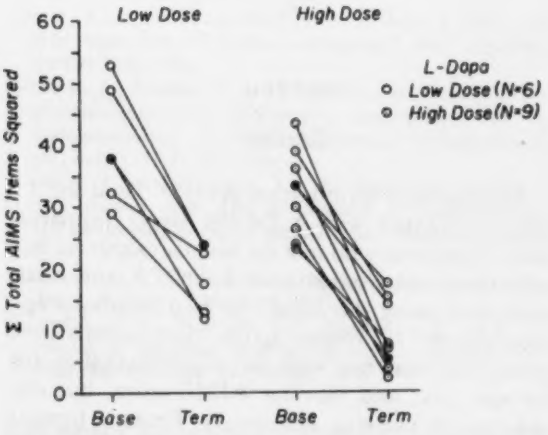


FIGURE 2

Discussion

This report describes a dose ranging study of a novel treatment approach to TD based on the assumption that the TD is related to an underlying pathogenic dopamine receptor supersensitivity, and that this supersensitivity may be reversed if dopamine levels are increased. In these trials it was found that dopamine levels may be safely increased in psychotic dyskinetic patients if incremental steps are carefully controlled. When this is done, there is some evidence that dyskinetic movements may be modestly exacerbated initially, especially for patients who are not receiving neuroleptic medication. With adaptation to the L-DOPA, the movements are reduced while the medication is continued. When the medication is stopped and the patients evaluated 4 weeks later, a reduction in dyskinetic movements was observed and about half the patients showed a marked improvement. Greater improvement was more likely in patients treated at higher doses. The level of improvement appears to be independent of whether the patient is also receiving a neuroleptic drug.

Table

Multiple Regression Analysis
Termination AIMS^2 Is the Dependent Variable
Base AIMS^2 and Total Dose are Stepped

		Total		Facial	
AIMS^2		r	F	r	F
1. Base AIMS^2	$r_{1.2}$	-.28		-.21	
2. Total Dose	$r_{1.3}$	.63		.72*	
3. Term AIMS^2	$r_{2.3}$	.51	3.01	.52	5.50*
	R^2	.52		.67	

*Contributes to prediction of Y p .05.
NOTE: AIMS^2 refers to the squared score referred to in the text.

References

Alpert, M., Diamond, F., and Taleporos, E. Unpublished data.

American Psychiatric Association Task Force Report on Tardive Dyskinesia. Washington, D.C.: American Psychiatric Association, December 1979.

Friedhoff, A.J., and Alpert, M. Receptor sensitivity modification as a potential treatment. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress*. New York: Raven Press, 1978, pp. 797-802.

Guy, W. *ECDEU Assessment Manual for Psychopharmacology-Revised 1976*. Washington, D.C.: DHEW Publication No. (ADM) 76-338, 1976.

Free Communications—Session B

Chair: **Thomas H. Crook, Ph.D.**
Center for Studies of the Mental Health of the Aging
Rockville, Maryland

and

Richard Marcus, Ph.D.
Clinical Service Research Review Branch
National Institute of Mental Health
Rockville, Maryland

*Differential Effects of Trazodone and Amitriptyline on Cognition in Normal Elderly
R.J. Branconnier, D.R. DeVitt, J.O. Cole, and K.F. Spera
Institute for Psychopharmacologic Research, Boston, MA

Combination Choline-Piracetam Treatment of Senile Dementia
Steven H. Ferris, Barry Reisberg, Eitan Friedman, Michael K. Schneck, Kathleen A. Sherman, Pervez Mir, and Raymond T. Bartus
New York University Medical Center, New York, NY

*Loxapine in Psychogeriatrics: A Placebo and Standard Controlled Clinical Study
W.M. Petrie, T.A. Ban, S. Berney, W. Guy, M. Ragheb, W.H. Wilson, and J.D. Schaffer
Tennessee Neuropsychiatric Institute and Vanderbilt University, Nashville, TN

Development and Prediction of Postpsychotic Depression in Neuroleptic-Treated Schizophrenic Patients
Joanne B. Severe, Michel R. Mandel, and Nina R. Schooler
National Institute of Mental Health, Rockville, MD, and Pacific Medical Center, San Francisco, CA

Plasma Levels of Thiothixene by Radioreceptor Assay and Clinical Outcome
Theodore van Putten, Philip R.A. May, Stephen R. Marder, and Jeffery N. Wilkins
Brentwood VA Medical Center and UCLA School of Medicine, Los Angeles, CA

The Effects of Psychotropic Drugs on Informed Consent
Barbara Stanley, Michael Stanley, Eric Peselow, Adam Wolkin, Steven Deutsch, Laura Platt, Julie Speicher, Lynn Golash, and Michael Kaufman
Wayne State University School of Medicine, Detroit, MI; New York University School of Medicine, New York, NY; and Massachusetts General Hospital, Harvard Medical School, Boston, MA

Research Use of the ECDEU Data Bank
John E. Overall and Howard M. Rhoades
The University of Texas Medical School, Houston, TX

DSM-III and the Children's Psychiatric Rating Scale
Betty Pfefferbaum and John E. Overall
The University of Texas Medical School, Houston, TX

---

* Denotes paper was presented at NCDEU meeting but not received before going to press.

Haloperidol in Autistic Children: Effects on Learning, Behavior, and Abnormal Involuntary Movements
Magda Campbell, Lowell T. Anderson, Ira L. Cohen, Richard Perry, Arthur M. Small, Wayne H. Green, Lillian Anderson, and William H. McCandless, Jr.
New York University Medical Center, New York, NY

A Controlled Study of Methylphenidate in Combination with Academic Instruction
Rachel Gittelman
New York State Psychiatric Institute, New York NY

Methylphenidate in Adults with Minimal Brain Dysfunction Symptomatology
Jeffrey A. Mattes, Lane Boswell, and Herman Oliver
Bronx VA Medical Center, Bronx, NY, and Long Island Jewish-Hillside Medical Center, Glen Oaks, NY

*The Long-Term Efficacy of Methylphenidate: Medicated vs. Unmedicated Hyperactive Boys at Adolescent Followup
J. Loney, J. Kramer, and T. Kosier
University of Iowa, Iowa City, IA

Combination Choline/Piracetam Treatment of Senile Dementia[1]

Steven H. Ferris, Ph.D.,[2] Barry Reisberg, M.D.,[2] Eitan Friedman, Ph.D.,[2] Michael K. Schneck, M.D.,[2] Kathleen A. Sherman, Ph.D.,[2] Pervez Mir, M.A.,[2] and Raymond T. Bartus, Ph.D.[2]

Despite the compelling rationale for precursor therapy of Primary Degenerative Dementia (PDD, also known as Alzheimer's disease) a large number of clinical trials have failed to demonstrate a consistent pattern of clinically significant effects for either choline or lecithin (Ferris, Sathananthan, Reisberg, & Gershon, 1979; Pomara, Reisberg, Ferris, & Gershon, 1981). Similarly, treatment with the "metabolic enhancer" Piracetam alone also does not appear to improve the cognitive symptoms of senile dementia (Reisberg, Ferris, Schneck, et al., 1981). However, the possibility exists that drugs which enhance brain metabolism might potentiate the effects of cholinergic precursors (Ferris, 1981; Gibson, Shimada, & Blass, 1978). Bartus, Dean, Sherman, & Friedman (1980) treated aged rats with both choline and Piracetam, and demonstrated a synergistic effect on memory retention. Since brain metabolism is reduced in aging and dementia (Ferris, de Leon, Wolf, et al., 1980; Smith, Goochee, Rapoport, & Sokoloff, 1980; Sokoloff, 1979), it may be that a general increase in metabolism improves the possibility of increasing acetylcholine synthesis. Piracetam may also have more direct cholinergic effects, since it increases the incorporation of ^{32}P into phosphatidyl choline (Woelk, 1979) thus suggesting an increase in phosphatidyl choline turnover. We therefore conducted an initial clinical trial in dementia with combination choline/Piracetam treatment.

Method

Subjects

A total of 15 outpatients, aged 60-85, with a Diagnostic and Statistical Manual-III (DSM-III) diagnosis of PDD completed the study. The patients all showed objective evidence of very mild to moderate cognitive impairment secondary to PDD. The diagnostic evaluation was based on DSM-III criteria and included a medical history,

---

[1] Supported by USPHS Grants MH-2959 and AGO-1344.

[2] Department of Psychiatry, New York University Medical Center, New York, NY 10016.

Development and Prediction of Postpsychotic Depression in Neuroleptic-Treated Schizophrenic Patients

Joanne B. Severe, M.S.,[1] Michel R. Mandel, M.D.,[2] and Nina R. Schooler, Ph.D.[1]

This paper concerns the emergence of depressive symptomatology in schizophrenic patients who were treated in the community with maintenance neuroleptic drugs. It has been reported by several investigators that schizophrenic patients demonstrate depressive symptoms at various times during their illness (Stern, Pillsbury, & Sonnenberg, 1972; McGlashan & Carpenter, 1976). However, there are problems in defining and describing these symptoms. Some investigators claim that such symptoms are part of the natural course of the disorder (Roth, 1970), others that they are side effects (akinesia) of neuroleptic drugs (Rifkin, Quitkin, & Klein, 1975), and still others feel that such symptoms call the diagnosis of schizophrenia into question (Goplerud & Depue, 1978).

Because of reports of postpsychotic depression (PPD) in the literature, data were examined which were available from a National Institute of Mental Health (NIMH) multicenter collaborative trial which specifically compared injectable fluphenazine (FPZ) decanoate with oral FPZ hydrochloride (HCl) in outpatient schizophrenics being maintained in the community for up to 1 year (Schooler, Levine, Severe, Brauzer, DiMascio, Klerman, & Tuason, 1980). This study was not designed to specifically address the question of PPD and therefore lacks the placebo control necessary to determine whether the emergence of depressive symptoms is a result of neuroleptic therapy or is a part of the natural course of the disorder. However, the data can address the following questions: What is the rate of emergence of depression in FPZ-treated schizophrenic outpatients over the course of 1 year? Is this rate higher in patients treated with FPZ decanoate than in those treated with oral FPZ HCl? Are patients who develop depressive symptomatology more likely to relapse? Can development of depression be predicted from presenting psychopathological symptoms at the time patients were acutely ill or from social, family, psychiatric, and treatment histories?

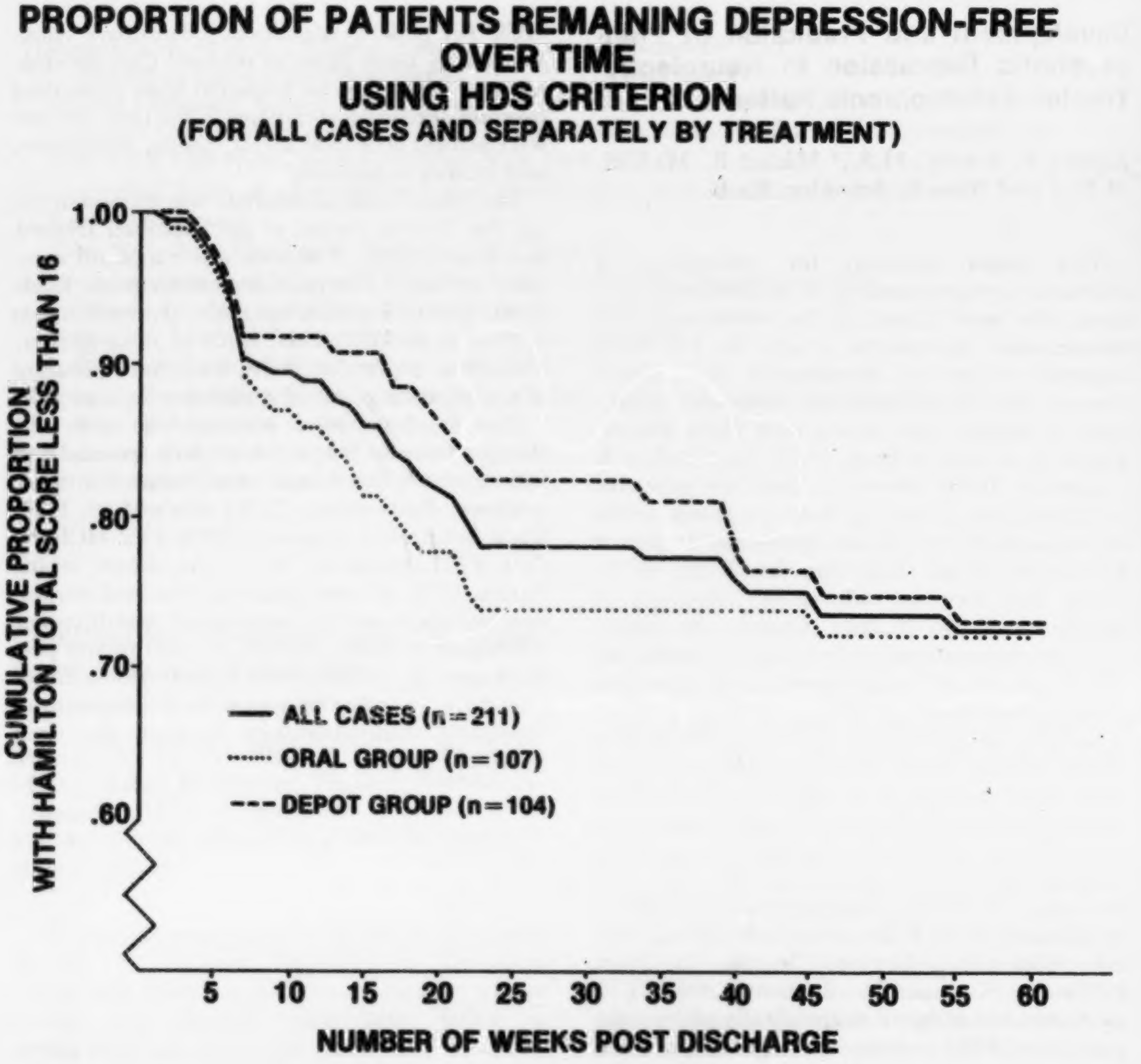
Depressive symptomatology was measured using the 22-item version of the Hamilton Depression Scale (HDS). The scale was completed at intake, at start of community maintenance treatment, and at 4-month intervals. Depression was defined as an HDS Total Score of 16 or greater. Therefore, depression, here, is not the equivalent of a clinical diagnosis of depressive disorder.

Two-hundred eleven patients who were discharged from the hospital depression free and had subsequent HDS ratings were included in these analyses. Forty-seven (22%) attained an HDS Total Score of 16 or greater (25% FPZ HCl and 22% FPZ decanoate, N.S.). As shown in the Figure, 73% of these patients remained depression free and most of the depression that did occur developed by about the fifth to sixth month post discharge. In addition, the Figure demonstrates that there were no differences in development of depressive symptomatology between the drug treatment groups.

---

[1] Pharmacologic and Somatic Treatments Research Branch, National Institute of Mental Health, Rockville, MD 20857.

[2] Department of Psychological Medicine, Pacific Medical Center, San Francisco, CA 94120.


PROPORTION OF PATIENTS REMAINING DEPRESSION-FREE OVER TIME USING HDS CRITERION (FOR ALL CASES AND SEPARATELY BY TREATMENT)

FIGURE

Comparison between the depressed and nondepressed patient groups revealed that the depressed patients were significantly more likely to relapse (64%) than were the nondepressed patients (19%). In one-third of the depressed patients who relapsed, depressive symptoms and the need to treat them were mentioned as part of the reason for the termination. Therefore, development of depression is a clinically important factor in the failure of the study treatments for these patients.

Further comparisons between the depressed and nondepressed patient groups with regard to baseline symptomatology revealed that when there were differences between the groups, depressed patients had less florid psychotic symptomatology as measured by grandiosity, uncooperativeness, and excitement on the Brief Psychiatric Rating Scale, but not greater despondency of mood. In addition, depressed patients exhibited more somatic symptoms as measured by the HDS at baseline. With regard to computerized tomography scan, medical and neurological examinations, clinical laboratory tests, psychiatric evaluations, and objective cognitive tests which included the Guild Memory Scale (Crook, Gilbert, & Ferris, 1980). Patients with a Hamilton Depression Scale score greater than 18 were excluded. The patients selected had Global Deterioration Scale scores of 2-4 (Reisberg, Ferris, de Leon, & Crook, in press).

Procedure

This was an open study designed to verify the safety and tolerance of combined choline/Piracetam treatment, and to obtain preliminary evidence as to possible efficacy. Patients received 9 g/d of choline chloride and 4.8 g/d of Piracetam for a period of 7 days. A short cognitive test battery (Buschke task, First-Last Names, facial recognition, Digit Symbol Substitution Test and tapping speed) and behavioral rating scales (IPSC-E psychiatrist's scale and MS-E self-rated mood scale) were administered at baseline and following the treatment period. Plasma and red blood cell (RBC) choline levels were also determined for 10 of the 15 subjects.

Results and Discussion

No side effects were reported. For the entire group, most cognitive measures showed small, nonsignificant improvements. Some subjects showed no changes, but none were worse. Since the study psychiatrist independently rated four patients as clinically improved, the cognitive measures for these patients were analyzed separately. The results for the Buschke Selective Reminding Task are shown in Figure 1. Each patient showed marked improvement in memory storage and retrieval. These "responders" were all subjects with moderate rather than very mild cognitive impairment. We have not previously observed such marked clinical improvements with choline treatment alone (Ferris et al., 1979; Ferris et al., 1981) or Piracetam treatment alone (Reisberg et al., 1981).

The results for the blood choline assays are shown in Figure 2. Of the 10 subjects for whom data were available, all showed marked increases

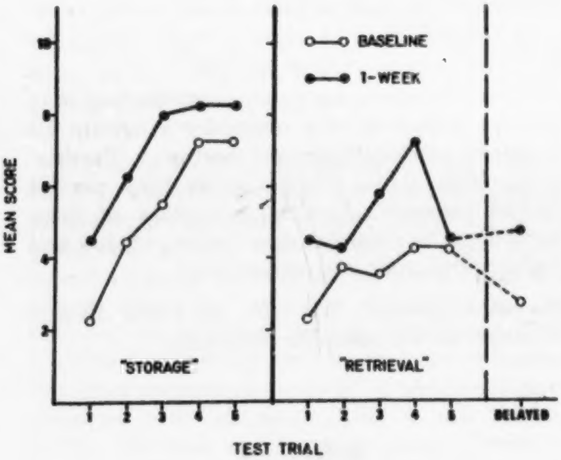


FIGURE 1. Mean scores for "storage" and "retrieval" on the Buschke Selective Reminding Task for the treatment "responders" ($N=4$) before and after treatment for 1 week with choline + Piracetam.

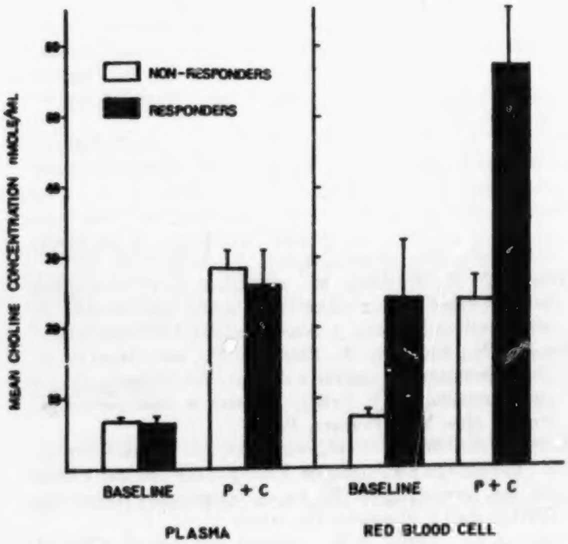


FIGURE 2. Mean (± SEM) plasma and red blood cell choline concentrations for the responders ($N=3$) and nonresponders ($N=7$), before and after 1 week of treatment with choline + Piracetam.

in both plasma and RBC choline levels during treatment. However, the responders showed much higher RBC choline levels than the nonresponders, both at baseline and during treatment (p's $< .025$). The plasma choline levels for the two groups were quite similar.

These interesting but preliminary findings suggest the possibility of a responder subgroup for combined choline/Piracetam treatment. Furthermore, high RBC choline levels may predict clinical response. Further evaluation of these possibilities by means of dose-finding studies and double-blind trials is recommended.

Acknowledgment: We wish to thank Denise Hernaize for her valuable assistance.

References

Bartus, R. T., Dean, R. L., Sherman, K., and Friedman, E. Enhancement of aged rodents retention via pharmacological modulation of choline availability. *Neurosci. Abstr.*, 6:112, 1980.

Crook, T., Gilbert, J. G., and Ferris, S. H. Operationalizing memory impairment for elderly persons: The Guild Memory Test. *Psychol. Rep.*, 47:1315-1318, 1980.

Ferris, S. H. CNS stimulants and metabolic enhancers in the treatment of senile dementia. In: Crook, T., and Gershon, S. (eds.), *Strategies for the Development of an Effective Treatment for Senile Dementia.* New Canaan, Conn.: Mark Powley Associates, 1981.

Ferris, S. H., de Leon, M. J., Wolf, A. P., et al. Positron emission tomography in the study of aging and senile dementia. *Neurobiol. Aging,* 1:127-131, 1980.

Ferris, S.H., Sathananthan, G., Reisberg, G., and Gershon, S. Long-term choline treatment of memory-impaired elderly patients. *Science,* 205:1039-1040, 1979.

Gibson, G. E., Shimada, M., and Blass, J. P. Alterations in acetylcholine synthesis and cyclic nucleotides in mild cerebral hypoxia. *J. Neurochem.*, 31:757-760, 1978.

Pomara, N., Reisberg, B., Ferris, S. H., and Gershon, S. Drug treatment of cognitive decline. In: Maletta, G. J., and Pirozollo, F. J. (eds.), *Advances in Neurogerontology.* Vol. 2. New York:Praeger, 1981.

Reisberg, B., Ferris, S. H., de Leon, M. J., and Crook, T. The Global Deterioration Scale (GDS): An instrument for the assessment of Primary Degenerative Dementia (PDD). *Am. J. Psychiatry.* (In press)

Reisberg, G., Ferris, S.H., Schneck, M., et al. Clinical cognitive effects of Piracetam. Proceedings of the 3d World Congress of Biological Psychiatry, Stockholm, June 28-July 3, 1981.

Smith, C. B., Goochee, C., Rapoport, S. I., and Sokoloff, L. Effects of aging on local rates of cerebral glucose utilization in the rat. *Brain,* 103:351-365.

Sokoloff, L. Effects of normal aging on cerebral circulation and energy metabolism. In: Hoffmeister, F., and Muller, C. (eds.), *Brain Function in Old Age, Bayer Symposium VII.* Berlin: Springer-Verlag, 1979.

Woelk, H. Effects of piracetam on the incorporation of ^{32}P into the phospholipids of neurons and glial cells isolated from rabbit cerebral cortex. *Pharmakopsychiat. Neuropsychopharmakol.*, 12:251-256, 1979.

life history characteristics, depressed patients were more likely to have a history of antidepressant and/or stimulant use, have been hospitalized for psychiatric illness in the past more often, and have had the truth about their illness told to family and friends.

The combination of the measures of somatic symptoms, grandiosity, prior use of stimulants, and the veracity of the explanation of the patient's hospitalization accounted for 19% of the variance in the prediction of depression status. Using the jackknife procedure (Mosteller & Tukey, 1977), a technique for replication which provides a more reliable estimate, 13% of the variance in depression status was accounted for. Despite the shrinkage, this is still significant. Thus, these data are able to provide some clues for prospective identification of those schizophrenic patients who will develop depressive symptomatology.

It is clear that depressive symptomatology in schizophrenic patients is a real problem and that more research is needed to better understand the phenomenon. The relationship of depression and relapse highlights the more pressing need for research into treatments for these symptoms.

References

Goplerud, E., and Depue, R. A. The diagnostic ambiguity of postpsychotic depression. *Schizophr. Bull.*, 4:477-480, 1978.

McGlashan, T. H., and Carpenter, W.T., Jr. Postpsychotic depression in schizophrenia. *Arch. Gen. Psychiatry*, 33:231-241, 1976.

Mosteller, F., and Tukey, J. W. Data analysis and regression. Reading, Mass.:Addison-Wesley Publishing Co., 1977.

Rifkin, A., Quitkin, F., and Klein, D. F. Akinesia: A poorly recognized drug-induced extrapyramidal disorder. *Arch. Gen. Psychiatry*, 32:672-674, 1975.

Roth, S. The seemingly ubiquitous depression following acute schizophrenic episodes, a neglected area of clinical discussion. *Am. J. Psychiatry*, 127:91-98, 1970.

Schooler, N. R., Levine, J., Severe, J. B., Brauzer, B., DiMascio, A., Klerman, G. L., and Tuason, V. B. Prevention of relapse in schizophrenia: An evaluation of fluphenazine decanoate. *Arch. Gen. Psychiatry*, 37:16-24, 1980.

Stern, M. J., Pillsbury, J. A., and Sonnenberg, S. M. Postpsychotic depression in schizophrenics. *Compr. Psychiatry*, 13:591-598, 1972.

Plasma Levels of Thiothixene by Radioreceptor Assay and Clinical Outcome[1]

Theodore van Putten, M.D.,[2] Philip R.A. May, M.D.,[2] Stephen R. Marder, M.D.,[2] and Jeffrey N. Wilkins, M.D.[2]

If plasma levels of antipsychotic drug were to relate to clinical outcome, the pharmacotherapy of schizophrenia might become less of a frontier profession. So far, research on the relationship between plasma levels of antipsychotic drugs and clinical outcome has been disappointing. On balance, few relationships have been found. This could be due to design deficiencies such as flexible dosage or contamination by other treatments or to problems with the assay (May & van Putten, 1978). The new radioreceptor assay (Creese & Snyder, 1977) appears simple to perform, sensitive, and suitable for routine clinical use.

The obvious question is whether the radioreceptor assay is clinically useful: specifically, does the assay correlate with clinical outcome or side effects?

Method

Thirty-four newly admitted schizophrenic patients who had not taken antipsychotic medication for at least 2 weeks (the majority not for several months) were treated with a fixed dose of thiothixene for 4 weeks. In general, these patients were admitted voluntarily (92%); in young middle age (mean age 32.7 years, SD 9.9); never married (50%); with a chronic disorder (mean duration of 5.2 years, SD 5.6).

Treatment

A fixed thiothixene dosage was given daily for 4 weeks at bedtime (0.44 mg/kg or 0.2 mg/lb). If there had been a serious toxic reaction to the first dose, the dosage was fixed at a lower level. Antiparkinson drugs were given if extrapyramidal side effects were troublesome.

---

[1] This research was supported by the Veterans Administration Medical Research Service.

[2] Veterans Administration Medical Center, Brentwood and UCLA School of Medicine, Los Angeles, CA 90024.

Address correspondence to Dr. van Putten at: VA Medical Center Brentwood, 11301 Wilshire Blvd., Los Angeles, CA 90073.

Thiothixene Assay

Thiothixene and its active metabolites were measured in plasma by Creese and Snyder's radioreceptor technique in which the added drug competes with [^{3}H]-spiperone for binding to dopamine receptors in calf caudate membranes (Lader, 1980).

Dopamine receptor-blocking activity of drug in the plasma samples was expressed as neuroleptic units (n.u.). One n.u. is defined as the amount of displacement of tritiated spiperone produced by 1 nmole of haloperidol.

The lower limit of sensitivity is 15 n.u.

Outcome Measures

Clinical outcome was measured before and after treatment on the Brief Psychiatric Rating Scale (BPRS) (completed by the psychiatrist) and by a Clinical Global Improvement Scale (CGI) and the Nurses' Observation Scale for Inpatient Evaluation (NOSIE) taking change in total score from baseline to the end of treatment as the criterion. The raters were blind to the plasma measurements.

Results

Relation to Outcome

Figure 1 shows the relationship between the nurses' global improvement ratings and plasma level. Improvement occurred over the entire range of recorded plasma levels, but the chances of substantial improvement appear greater above 40 n.u. If the sample is dichotomized to compare (very much + much improved) vs. (minimally improved + no change) with 40 n.u. as the criterion, chi square = 6.05, $p < .01$. The results with physician's global improvement ratings showed a similar trend, but the chi-square missed statistical significance.

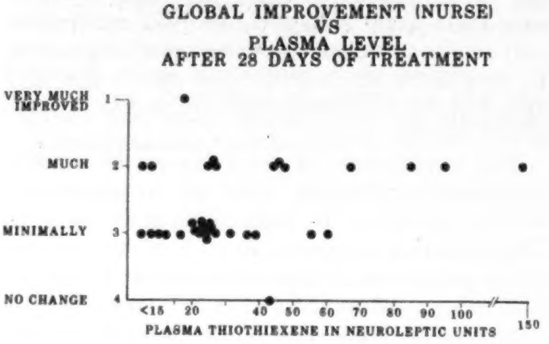


FIGURE 1

Figures 2 and 3 show the relationship between the NOSIE and BPRS change scores and plasma level. The trend is the same: improvement occurs over the entire recorded range of plasma levels, but the chances of substantial improvement appear greater above 40 n.u. It is clear, however, that many patients improved at lower neuroleptic levels; the relationship is far from substantial.

Correlations between plasma levels and outcome (both at 28 days) appear in the Table. Correlations for the doctor's CGI and NOSIE were significant at the .025 level.

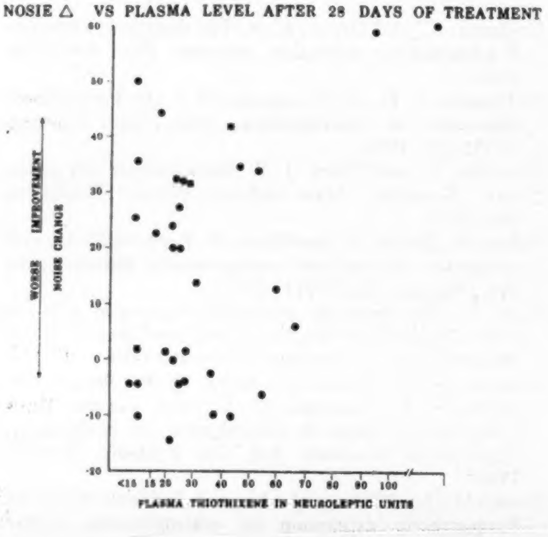


FIGURE 2

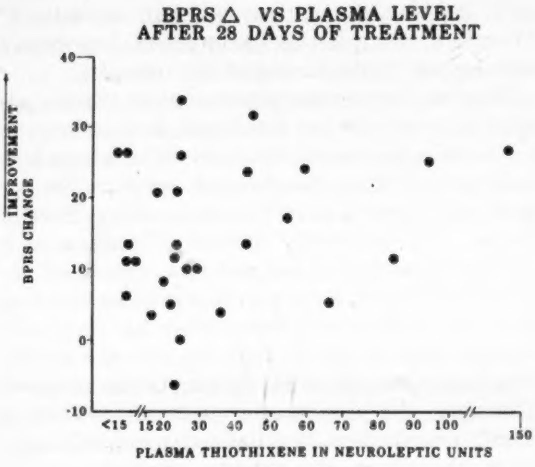


FIGURE 3

Relation to Side Effects

There was no consistent relationship between side effects after 4 weeks of treatment and plasma level. Some of the highest drowsiness ratings occurred in those with very low plasma levels. Similarly, there was no consistent relationship between akathisia or akinesia and plasma level.

Dosage and Outcome

There was no relationship between dosage (either mg or mg/kg) and any of the four outcome measures.

Discussion

The findings indicate that improvement is more likely at higher plasma levels (>40 n.u.) of thiothixene. Many, however, improved at very low plasma levels. Indeed, two of the six who improved at plasma levels < 15 n.u., had an illness which, in the past, responded only to an antipsychotic drug.

The data do not support the notion of a "therapeutic window" in that higher plasma levels were not associated with side effects or clinical deterioration (although at extreme plasma levels this must of course be so). In fact, an additional four patients who improved markedly only on very high doses (60, 120, 120, and 160 mg of thiothixene) had high plasma levels (65, 78, 170, and 140 n.u., respectively). Again, higher plasma levels appear associated with improvement, as long as the patient can tolerate them!

In 11 of 20 nonresponders, dosage could not be increased because of akathisia, drowsiness, or akinesia, either singly or in combinations. A plasma level of thiothixene may be particularly useful in the nonresponder with troublesome side effects. If such a nonresponder has a low plasma level (<40 n.u.), it would seem prudent to switch to another antipsychotic drug.

Table

Correlations (*r*) Between 28-Day Plasma Levels of Thiothixene and Outcome

	CGI Nurse	CGI Doctor	NOSIE	BPRS
r	.260	.358	.363	.289
p	n.s.	.025	.025	.05

References

Creese, I., and Snyder, S.H. A simple and sensitive radioreceptor assay for antischizophrenic drugs in blood. *Nature,* 270:180-182, 1977.

Lader, S.R. A radioreceptor assay for neuroleptic drugs in plasma. *J. Immunoassay,* 1:57-75, 1980.

May, P.R.A., and van Putten, T. Plasma and saliva levels of chlorpromazine in schizophrenia: A critical review of the literature. *Arch. Gen. Psychiatry,* 35:1081-1087, 1978.

The Effects of Psychotropic Drugs on Informed Consent[1]

Barbara Stanley, Ph.D.,[2] Michael Stanley, Ph.D.,[2] Eric Peselow, M.D.,[3] Adam Wolkin, M.D.,[3] Steven Deutsch, M.D.,[3] Laura Platt, M.S.W.,[3] Julie Speicher, M.D.,[3] Lynn Golash,[3] and Michael Kaufman, M.D.[4]

Acutely psychotic patients are frequent candidates for research projects which attempt to find more efficacious pharmacologic treatments for their conditions. These patients are often the only appropriate group for the final stage of testing the treatments. However, there is a good deal of concern about the abilities of hospitalized psychiatric patients to give consent. This concern is reflected by their status as a vulnerable population in the proposed regulations for the institutionalized mentally disabled (*Federal Register*, 1978). This classification deems them as needy of special protection. While there are many different opinions about the extent of their vulnerability, there are little empirical data which confirm the need for this proposed special protection.

Earlier research investigating this issue found that severely ill psychiatric patients perform as wellin the consent process as hospitalized medical patients (Stanley, Stanley, Schwartz, 1980; Stanley, Stanley, Lautin, Kane, & Schwartz, 1981). These findings indicated that it was important to look more closely at consent with the mentally ill.

Issues such as the differential effects of diagnosis, mood, and length of hospitalization on competency are in need of investigation. Further, there remains a question about the effect of psychotropic medication on patients' competency. Some have argued that patients would alter their opinions about participation in research or become more competent following stabilization on psychotropic drugs. On the other hand, it has also been argued that a consent obtained under the influence of psychotropic drugs can never be valid because the patient is "mind-controlled." Therefore, this question has practical importance with respect to the timing of the consent.

Does an investigator obtain consent while a patient is acutely ill, or should he first attempt to bring the symptoms under control with standard treatments, obtain the consent, washout the patient, and then conduct the experiment? This, of course, is procedurally difficult. However, if it can be demonstrated that patients make more rational decisions about research participation when they are medicated, then the procedural difficulties might be justified for the sake of a significant improvement in the quality of the consent. Therefore, the present study was undertaken to determine whether hospitalized psychiatric patients' abilities to give consent, change over the course of treatment—prior to a drug regimen and after stabilization on psychotropic medication.

In this preliminary study, the following questions were addressed: 1) do severely ill psychiatric patients alter their opinions with respect to their willingness to participate in a series of research projects with varying risk/benefit ratios prior to drug treatment and after becoming stabilized? 2) does comprehension of consent information increase following drug treatment? 3) does rationality or reasoning about their decision to participate or not participate improve after drug treatment? and 4) for those patients who changed their minds, did they become more reasonable in their decisions?

Method

In order to assess the effects of psychotropic medication on ability to give valid consent, a series of four hypothetical vignettes were administered to psychiatric patients prior to drug treatment and following treatment. Two of the vignettes were alternate forms of one high-risk/low-benefit vignette and one low-risk/high-benefit vignette. The other two vignettes were both administered twice. Patients' competency to give consent was assessed on four separate dimensions which represent common notions of competency (Sullivan, 1974; Friedman, 1975; Roth, Meisel, & Lidz, 1977): evidencing a choice;

---

[1] This research was supported in part by USPHS Grant MH-34001.

[2] Psychiatry, Ethics, and Law Program, Psychiatry Department, Wayne State University School of Medicine, Detroit, MI 48206.

[3] New York University School of Medicine, New York, NY 10016.

[4] Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114.

reaching a reasonable decision; comprehending the consent information; and reasoning in a rational manner about the decision.

In order to determine whether the patients' psychiatric conditions improved, a psychiatrist independently assessed the patients on admission and again at the time of the second competency interview. The Brief Psychiatric Rating Scale (BPRS) was utilized for the psychopathology assessments.

The sample was comprised of 39 psychiatric inpatients on a locked unit at Bellevue Psychiatric Hospital. All were interviewed within 72 hours after admission and again just prior to discharge. In most cases, patients were discharged within a day after the final assessment. When patients were not immediately discharged, it was usually as a result of disposition problems. Twenty-seven patients received psychotropic medication and 12 patients were unmedicated and served as a comparison group to control for the effects of hospitalization.

Table 1 shows the diagnostic categories into which the medicated patients fell. All but one—the personality disorder—fell into the range of very severe psychiatric illness. Table 2 shows that the medications these patients were taking at the time of discharge were the standard psychotropic drugs. The length of time patients were medicated coincides with the length of hospitalization ($\overline{X}$ = 27 days; *SD* = 12.6).

All medicated patients were judged by the treating psychiatrist to be stabilized on medication by the final competency assessment.

Table 1

Diagnosis

(*N* = 27)	Percent	*N*
Schizophrenic Disorder	48.2	13
Psychotic Disorder	33.3	9
Affective Disorder	14.8	4
Personality Disorder	03.7	1

Table 2

Medication on Discharge
(*N*-22)

	N
Prolixin Decanoate (12.5-75 mg)	5
Trilafon (16-48 mg)	4
Mellaril (300 mg)	2
Stelazine (10-40 mg)	2
Lithium (1,200-1,800 mg) and Trilafon (8-48 mg)	2
Haldol (2.5-30 mg) and Lithium (900-2,100 mg)	2
Haldol (5 mg) and Elavil (25 mg)	1
Lithium (900 mg) and Thorazine (200 mg)	1
Haldol (15 mg)	1
Lithium (900 mg)	1
Thorazine (1,000 mg)	1

Table 3

Patient Responses Prior to and Following Drug Treatment
(*N* = 27)

	Time 1-Time 2 Yes-Yes %	Time 1-Time 2 No-No %	Time 1-Time 2 Yes-No %	Time 1-Time 2 No-Yes %
High Risk/Low Benefit Studies*	14.8	37.0	25.9	22.3
	51.8		48.2	
Low Risk/High Benefit Studies*	51.8	14.8	18.5	14.8
	66.7		33.4	
Moderate Risk/High Benefit	3333	33.3	11.1	22.3
	66.6		33.4	

*Alternate forms

Results

To determine the effect of drugs on decisions about research participation, patients' responses to the hypothetical studies were analyzed. Responses prior to drug treatment and following treatment were compared. The percentage of patients who did not alter their opinions and those who did are presented in Table 3.

For the high-risk/low-benefit studies, about 15% of the patients agreed to participate both before and after treatment, while 37% refused both times. In this case, refusal would be the reasonable decision, because of the unfavorable risk/benefit ratio. Twenty-six percent changed from agreeing to refusing and about an equal percentage (22%) changed in the opposite direction from a reasonable or "good" decision to a poor choice. A statistical test of the difference in proportions for the four possible comparisons shows no significant differences among the proportions (HR/LB Study – $z = .39$, $N = 27$, NS). Thus, for the first study, patients do not become more or less reasonable in their decisions as a result of treatment.

This was also true for the other three vignettes (LR/HB Study $z = .27$, $N = 27$, NS; HR/HB Study $z = .14$, $N = 18$, NS; MR/HB Study $z = .85$, $N = 18$, NS). There was no significant directional change following any treatment. When patients change their minds, about an equal percentage moves in either direction. It is particularly striking to note about the last three vignettes that two-thirds of the patients do not change their minds at all. This suggests that drug treatment does not alter patients' decisions about research.

In comparing the drug-treated group with the group of patients who received no medication during their hospitalization, no significant differences emerged in willingness to participate in hypothetical studies. (Final Interview - HR/LB Study $x^2 = <1$, $N = 39$, NS; LR/HB Study $x^2 = <1$, $N = 39$, NS; HR/HB Study $x^2 = <1$, $N = 27$; MR/HB Study $x^2 = <1$, $N = 27$, NS).

Differences in comprehension of the consent information prior to and following drug treatment were also examined. Comprehension did not improve significantly ($t = 1.81$, $df = 17$,NS). An additional analysis of the patients' stated reasons for participation or refusal, revealed that the quality of reasoning about the consent decisions showed no significant improvement following treatment ($t = 1.57$, $df = 17$, NS). These findings are noteworthy because psychopathology decreased significantly (Initial BPRS scores $\overline{X} = 43.5$, S.D. $= 9.1$; final BPRS scores $\overline{X} = 38.3$, $SD = 7.9$; $t = 3.52$, $N = 27$, $p < .01$). Thus, although patients' conditions improved, their competency did not. This is consistent with previous findings which suggest that psychopathology does not correlate with ability to give consent (Stanley et al., 1981).

In conclusion, these preliminary results seem to indicate that the quality of consent does not improve following drug treatment. These data do not lend support to the notion that patients should be stabilized on standard drugs prior to enlisting them as subjects. Additional data are now being collected to determine whether these preliminary results will remain the same with a large sample.

References

Friedman, P.R. Legal regulation of applied behavioral analysis in mental institutions and prisons. *Ariz. Law Rev.*, 17: 39-104, 1975.

Roth, L.H., Meisel, A., and Lidz, C.W. Tests of competency o consent to treatment. *Am. J. Psychiatry*, 134:279-284, 1977.

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Research Involving Those Institutionalized as Mentally Infirm.* DHEW Publ. No. (OS) 78-0006, 1978.

Stanley, B., Stanley, M., Lautin, A., Kane, J., and Schwartz, N. Preliminary findings on psychiatric patients as research participants: A population at risk? *Am. J. Psychiatry*, 138: 669-671, 1981.

Stanley, B., Stanley, M., Schwartz, N., Lautin, A., and Kane, J. The ability of the mentally ill to evaluate research risks. *IRCS Med. Sci.*, 8:657-658, 1980.

Sullivan, M. The involuntarily confined mental patient and informed consent to psychiatric treatment. *Loyola Univ. Law J.*, 5:578-609, 1974.

Research Use of the Early Clinical Drug Evaluation Unit Data Bank

John E. Overall, Ph.D.,[1] and Howard M. Rhoades, M.A.[1]

The purpose of this brief report is to indicate one way in which the research potential of the Biometrics Laboratory Early Clinical Drug Evaluation Unit (ECDEU) data bank has been used for general methodological investigations. The Biometrics Laboratory at George Washington University provided a statistical data-analysis service for investigators in the ECDEU and New Clinical Drug Evaluation Unit (NCDEU) programs for almost a decade. During that time, a valuable data bank consisting of rating scales and other descriptive information on large numbers of patients was acquired. As far as the present report is concerned, it is important to emphasize that the data bank pertains specifically to patients who were subjects in clinical psychopharmacology research.

A problem in dealing with a data bank of this magnitude is that different studies use different rating scales and have differing protocols. In order to effectively manage this amount of data, an extraction was made so that each subject would have comparable data in a standard format. Patients included in this extraction were required to have at least the demographic information, a pretest rating on the Brief Psychiatric Rating Scale (BPRS), and a rating on the BPRS that fell 6 to 12 weeks after the onset of the clinical trial. The data to be presented refer to those patients and to studies that included a minimum sample size of at least six per group. Studies in which the BPRS was not used and studies with very small sample sizes were not included.

The first question that was asked of the derived data file concerned how many different drug treatment *populations* are represented. For this purpose a "drug treatment population" was defined as the population from which subjects for a particular study were drawn, and two studies were considered to involve the same drug treatment population if the mean symptom profiles for patients in the studies were similar. A multidimensional scaling of mean pretreatment BPRS profiles revealed two major clusters, one including studies of antipsychotic drugs and the other including studies of antidepressant/antianxiety drugs.

The fact that the data bank consists of two major treatment populations does not imply that individual patients within those treatment populations are phenomenologically homogeneous. An iterative profile analysis method was used to define BPRS profile patterns that are maximally representative of four phenomenological subtypes of depressive disorders within the one treatment population and maximally representative of four phenomenological subtypes of thinking disorder psychoses within the other treatment population. Depressive disorders are characterized as anxious, hostile, retarded, or agitated; and thinking disorder psychoses are characterized as florid, withdrawn-disorganized, hostile-suspicious, or agitation-excitement types. Although this typology of major psychiatric disorders is not new, its refinement to be maximally representative of patients in the ECDEU data bank is considered pertinent to further clinical psychopharmacology research.

Classification functions, which are simple weighted combinations of BPRS symptom ratings (scored 0 to 6), can be used to assign individuals among the eight phenomenological types. The weighting coefficients derived from the ECDEU data bank are presented in the Table. To classify an individual patient, one simply calculates the eight different weighted sums of his/her BPRS symptom ratings and assigns the individual to the group for which the weighted sum is greatest. This is one of several ways that phenomenological classification can be objectively achieved from analysis of BPRS profiles. It is a very simple matter to write a computer program that will calculate the weighted sums, given the classification function coefficients presented in the Table.

Given the ability to assign individual patients among the eight phenomenological types, several issues related to clinical drug trials were investigated. The percentages of good response to placebo were examined across 6 controlled trials of presumed antidepressant drugs and 17 placebo-controlled trials of presumed antipsychotic drugs.

---

[1] The University of Texas Medical School, Houston, TX 77025.

Table

Classification Functions for Eight Phenomenological Types

Phenomenological Type	BPRS Symptom																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Constant
Anxious Depression	.264	.640	.294	-.156	.333	.629	-.146	.290	2.012	-.057	-.142	-.297	-.506	.193	-.251	.086	-.377	-.045	-8.755
Retarded Depression	.302	.592	.490	-.405	.188	.513	-.006	.444	1.874	.101	-.260	-.360	.929	-.111	-.279	.241	-.425	.091	-9.631
Agitated Depression	.270	.465	-.058	-.381	.549	.835	-.354	.220	1.886	-.208	-.142	-.336	-.201	-.151	-.016	.029	1.723	-.123	-11.153
Hostile Depression	.117	.628	.134	-.369	.722	.766	-.142	-.012	1.558	2.156	-.158	-.367	.089	-.399	-.211	-.065	-.242	-.026	-11.386
Florid Thinking Disorder	.023	.191	.495	.555	-.071	.453	.170	.244	-.351	-.048	.139	.451	-.013	-.625	1.256	.523	-.056	-.241	-8.590
Withdrawn-Disorganized	-.102	.331	1.136	.142	-.198	.251	.378	.302	-.107	-.221	-.140	-.180	.262	-.424	-.350	1.044	-.346	.418	-7.344
Agitated Excitement	.228	.673	.005	.160	.016	.656	.250	.466	-.023	.573	.209	-.198	-.407	-.138	.677	.098	1.361	-.310	-9.375
Hostile Suspiciousness	.296	.740	.521	.058	-.075	.458	.102	.055	.237	.732	1.105	-.410	.145	.064	.664	.459	-.282	-.391	-9.503

The placebo response rate for anxious and hostile depression subtypes was approximately two-thirds, whereas the placebo response rates for retarded and agitated depressions was only about one-third. Across a larger pool of studies, the response rate for all four depressive subtypes to active medications was approximately two-thirds. Although the placebo patients were not concurrent controls in most of the same studies from which the drug-treated patients came, the pattern of response across depressive subtypes does seem to suggest that it may be more difficult to show a true treatment effect in the anxious and hostile subtypes of depressive disorder because of the good placebo response of such patients.

The same comparisons of response rates were made for placebo and active drug groups in the pool of antipsychotic drug trials from the ECDEU data bank. Placebo response rates ranged from 6 to 29% for the four thinking disorder syndromes. The response rates for florid thinking disorder, agitation-excitement, and hostile-suspiciousness syndromes were two to four times greater in the active medication pool than in the placebo pool. By way of contrast, the response rate for the withdrawn-disorganized type was approximately 9% in both the placebo and active drug pools. Again, the placebo patients were not concurrent controls for most of the active medication patients in the pooled data; however, comparison of response rates across phenomenological subtypes suggests that withdrawn-disorganized thinking disorder may not be a good type of patient for demonstrating clinical efficacy of antipsychotic medications because of the low rate of favorable response to both drug and placebo.

Many other and perhaps more interesting uses can be made of the ECDEU data bank. The main intent of this brief report is to emphasize the advantage that can derive from large accumulations of similar data from many small clinical trials. Individual trials usually do not involve sample sizes adequate to examine many issues of both methododological and clinical importance. Centralized facilities that provide statistical support services are in a particularly strategic position to develop meaningfully large data banks in a variety of research domains, as the ECDEU data bank exemplifies in clinical psychopharmacology.

Diagnostic and Statistical Manual-III and the Children's Psychiatric Rating Scale[1]

Betty Pfefferbaum, M.D.,[2] and John E. Overall, Ph.D.[2]

The purpose of this investigation was to identify primary dimensions of manifest psychopathology that distinguish among different emotional and behavioral disorders of childhood and to identify the Diagnostic and Statistical Manual-III (DSM-III) diagnoses for which each of the primary dimensions is particularly relevant. The Children's Psychiatric Rating Scale (CPRS) provides for assessment of a broad range of symptoms and behaviors related to childhood psychopathology (Guy, 1976). It consists of 63 symptom and behavior constructs which are rated on seven-point scales of severity. It was used in this investigation because it preceded the development of DSM-III and provides a description of the major emotional and behavioral components of childhood diagnoses using terms other than the specific criteria listed in DSM-III. The methodology of factor analysis was used to identify clusters of correlated symptom and behavior variables that define major dimensions of difference among diagnostic groups in the CPRS measurement space.

Five child and adolescent psychiatrists were asked to provide descriptions of what they considered, from their clinical experience, to be typical patients belonging to each of 18 DSM-III diagnostic categories. The descriptions were recorded as ratings of symptom severity on the 63 scales of the CPRS. The psychiatrists were asked to describe levels of severity for all associated symptoms as well as for primary target symptoms of each disorder.

A cluster-oriented multiple-group method of factor analysis was used to identify subsets of variables that tend to represent independent aspects of the symptom domain. Seven independent dimensions were identified. The factors were

---

[1] This research was supported in part by USPHS Grant MH-32457.

[2] Department of Psychiatry, The University of Texas Medical School, Houston, TX 77025.

then rotated to an oblique simple structure in which each CPRS variable tended to relate clearly to one and only one of the seven references axes (Overall, 1974). The seven factors were interpreted as representing behavioral problems, depression, thought disturbance, psychomotor excitation, psychomotor retardation, nervousness/tension, and organicity.

A single CPRS profile to represent each of the 18 diagnostic concepts was calculated by averaging across the five raters. A transposed (Q-type) factor analysis of the 18 diagnostic profiles resulted in identification of six distinct clusters which are presented in Table 1. This analysis provided a basis for grouping together the DSM-III diagnoses that tend to share predominant features of the total symptom and behavior profile pattern, while disregarding specific distinctions that contribute little to the overall differences in symptom profile patterns. The diagnosis oppositional disorder did not clearly relate to only one cluster but related to the cluster including the conduct disorders and the cluster including the anxiety disorders. It was, therefore, not included in any one cluster.

Table 1

Cluster	DSM-III Diagnosis and Code
I	Conduct Disorder, Undersocialized, Aggressive (312.00) Conduct Disorder, Undersocialized, Nonaggressive (312.10) Conduct Disorder, Socialized, Aggressive (312.23) Conduct Disorder, Socialized, Nonaggressive, (312.21)
II	Infantile Autism (299.0x) Childhood Onset Pervasive Development Disorder (299.9x) Schizophrenic Disorder (undifferentiated) (295.9x)
III	Separation Anxiety Disorder (309.21) Overanxious Disorder (313.00) Identity Disorder (313.82) Anorexia Nervosa (307.10)
IV	Attention Deficit Disorder with Hyperactivity (314.01) Attention Deficit Disorder without Hyperactivity (314.00)
V	Avoidant Disorder (313.21) Schizoid Disorder (313.22) Elective Mutism (313.23)
VI	Major Depression (296.2x)
	[Oppositional Disorder (313.81)]

The empirical clustering of symptom rating scale profiles produced a classification of disorders that generally corresponds to the major diagnostic groupings in DSM-III. The diagnostic clusters share enough of the total range of symptom manifestations to have highly similar factor score profiles and can be considered on empirical grounds to represent the major syndromes of childhood psychopathology. From the point of view of treatment evaluation, the clusters of specific diagnoses share enough common symptomatology to be evaluated along the same major dimensions.

The one or two discrepancies between the DSM-III classification of childhood diagnoses and the empirical grouping based on similarities of CPRS symptom and behavior rating profiles highlight the distinction between underlying dynamics and descriptions of behavior. For example, the diagnosis avoidant disorder is classified with the anxiety syndromes in DSM-III. The overt behavioral manifestations, however, primarily involve diminished social interaction. Elective mutism represents an extreme example of such behavioral manifestations. The CPRS profile places avoidant disorder with elective mutism and schizoid disorder in recognition of the manifest social withdrawal rather than with the anxiety disorders, even though anxiety may indeed by the underlying basis for the manifest behavior. Regardless of the DSM-III classification, it is apparent that the manifest psychopathology associated with avoidant disorder was considered by these psychiatrists to be represented in rating scale terms along the same primary dimensions that are useful in characterizing other forms of social and behavioral withdrawal. Another interesting difference between the DSM-III classification and this one is that anorexia nervosa and identity disorders are included in the category of anxiety disorders in this grouping. In all other respects the empirical classification based on complete CPRS profile patterns appears consistent with the DSM-III grouping of specific diagnoses into broader categories.

Based on examination of the mean factor score profiles for diagnostic groups in each of the six major clusters, as well as on clinical experience with the syndromes, specific factors are proposed as relevant for evaluation of psychopathology and measurement of treatment response in different diagnostic groups. These are presented in Table 2. For some clusters, one or two factors appear more relevant than the others and are indicated by an asterisk.

Table 2

Cluster	DSM-III Diagnosis and Code
I:	Conduct Disorders
	Behavioral Problems*
	Psychomotor Excitation
II:	Childhood Psychoses
	Behavioral Problems
	Thought Disturbance*
	Psychomotor Excitation
	Psychomotor Retardation
	Nervous/Tension
	Organicity*
III:	Anxiety Disorders
	Behavioral Problems
	Depression
	Psychomotor Excitation
	Nervous/Tension
IV:	Attention Deficit Disorders
	Behavioral Problems*
	Depression
	Psychomotor Excitation*
	Nervous/Tension
V:	Avoidant Disorders
	Depression
	Psychomotor Retardation*
	Nervous/Tension
VI:	Depression
	Behavioral Problems
	Depression*
	Psychomotor Excitation
	Psychomotor Retardation
	Nervous/Tension

*Greater relevance

The purpose of the cluster analysis was not to encourage use of the rating scale for diagnostic purposes. Results from the cluster analysis provide a guide to the CPRS symptom factors that are relevant for evaluation of levels of severity and treatment response in various DSM-III diagnostic groups. One can expect to measure significant improvement only on those major dimensions of psychopathology that are relevant to the particular diagnostic entities being treated.

In summary, factor analysis of the CPRS has been used to identify clinically meaningful factors and cluster analysis to identify six major clusters of DSM-III diagnostic groups. Examination of the results has led to an identification of the factors that are most relevant for characterizing the patients in each of these six diagnostic clusters. It is suggested that a modification of the CPRS based on this factor analysis could facilitate investigating and documenting psychopathology and treatment response in a more efficient manner.

Acknowledgment: The authors with to thank the psychiatrists who provided data for this study: Patricia M. Butler, M.D., Thomas A. Hamlin, M.D., Sarah E. Howell, M.D., and Rita Patton, M.D.

References

Guy, W. *ECDEU Assessment Manual for Psychopharmacology, Revised, 1976.* DHEW Publication No. (ADM) 76-338, 1976.

Overall, J.E. Marker variable factor analysis: A regional principal axes solution. *Multivariate Behav. Res.*, 9: 149-164, 1974.

Haloperidol in Autistic Children: Effects on Learning, Behavior, and Abnormal Involuntary Movements[1]

Magda Campbell, M.D.,[2] Lowell T. Anderson, Ph.D.,[2] Ira L. Cohen, Ph.D.,[2] Richard Perry, M.D.,[2] Arthur M. Small, M.D.,[2] Wayne H. Green, M.D.,[2] Lillian Anderson, R.N.,[2] and William H. McCandless, Jr., M.A.[2]

The efficacy of haloperidol as one treatment modality for young autistic children has been supported by the results of our two recently published studies (Campbell, Anderson, & Meier, 1978; Cohen, Campbell, & Posner, 1980). Both trials were double-blind and placebo-controlled, and patients were randomly assigned to treatments.

However, the following questions remained unanswered: 1) how does haloperidol facilitate learning—by directly affecting attentional mechanisms or by reducing withdrawal and stereotypies? 2) what are the long-term therapeutic effects of haloperidol? and 3) what are the possible long-term untoward effects, specifically the effects on neuroleptic-induced abnormal movements?

To answer these questions, a double-blind, placebo-controlled trial of haloperidol in 40 autistic children who met the Diagnostic and Statistical Manual-III (DSM-III) criteria was conducted. A total of 33 subjects ages 2.3 to 7.9 years (mean, 4.7 years) have thus far completed the study.

The children were maintained for 2 weeks on placebo for baseline evaluations. Those suitable were randomly assigned to one of two treatment sequences: haloperidol-placebo-haloperidol or placebo-haloperidol-placebo. Each treatment period lasted 4 weeks.

Discrimination learning, behavioral symptoms, and untoward effects were rated. The ratings of the two child psychiatrists using the Children's Psychiatric Rating Scale (CPRS), Clinical Global Impressions (CGI), Abnormal Involuntary Movement Scale (AIMS), and the Abbreviated Dyskinesia Rating Scale (Simpson, Lee, Zoubok, & Gardos, 1979) were videotaped. The results videotaped were as follows.

The optimal doses of haloperidol ranged from 0.5 mg/day to 3.0 mg/day (mean, 1.12 mg/day). At these doses, serum levels of haloperidol ranged from ND* or 1.30 to 8.30 ng/ml (collaborative study with Drs. Robert Rubin and Russell Poland, Torrance, California).

On these doses, haloperidol was found to be significantly superior to placebo in reducing behavioral symptoms on the CGI and the CPRS; specifically, stereotypies, withdrawal, hyperactivity, abnormal object relations, and fidgetiness were lower on drug ($p < .001$) (Figure 1). The placebo scores were significantly higher than haloperidol scores on the Conners' Parent Teacher Questionnaire (PTQ) ($p < .01$). The Timed Behavioral Rating Sheet revealed that the effects on stereotypies were a function of the structure of the rating conditions; in the unstructured rating, mean stereotypy scores remained high across treatment, while in the structured situation stereotypies decreased on haloperidol relative to placebo.

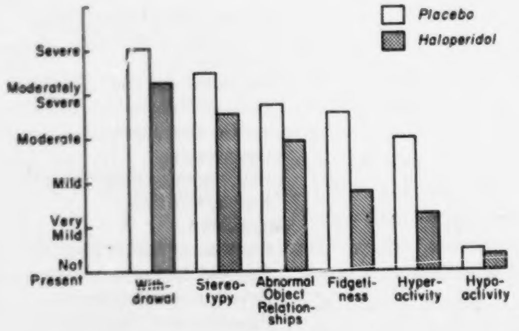


FIGURE 1. Comparison of 33 autistic children receiving placebo vs. haloperidol in terms of their average scores on the Children's Psychiatric Rating Scale. There was a significant difference between groups ($p < .001$) as determined by a matched-pairs signed ranks test, on all items except hypoactivity: children receiving haloperidol were rated to have less severe behavioral symptoms.

---

[1] This study was supported in part by USPHS Grant MH-32212 from the National Institute of Mental Health. The authors wish to thank McNeil Pharmaceuticals for supplying haloperidol and matching placebo tablets.

[2] Department of Psychiatry, New York University Medical Center, New York, NY 10016.

***ND = < .05 ng/ml.**

Administration of haloperidol at these doses not only resulted in reduction of behavioral symptoms, but also facilitated learning in the laboratory situation. There, a computer-controlled operant conditioning apparatus was used to present stimuli, record responses, present reinforcers according to a specified schedule, and record durations of stereotypic behavior; motor activity levels were also recorded from pressure sensors mounted under carpeting.

Children were required to learn that reinforcement was available if the lever was pressed during the presentation of an auditory-visual stimulus pattern (S+) and was not available when the stimulus pattern was off (S−). Discrimination indices were computed for each child and the mean across children plotted as a function of sessions and treatments.

The results indicate that children receiving haloperidol learned the discrimination while those on placebo did not (Figure 2). This was by virtue of the haloperidol group displaying fewer responses when the auditory-visual stimulus pattern was off (S−). Children who acquired the discrimination on haloperidol retained it when placed on placebo. Children shifted from placebo to haloperidol showed continued improvements in performance and decelerations in inappropriate responding which were comparable to the children who acquired the discrimination on haloperidol. Developmental level, *per se,* did not interact with drug to determine performance.

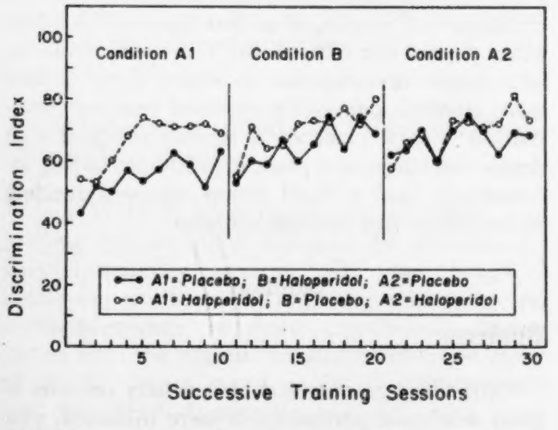


FIGURE 2. Discrimination learning in 22 autistic children during two treatment sequences.

There was no significant effect of medication on stereotypies between the two groups in the laboratory; this suggests that reduction in this symptom is not responsible for the improvement in learning.

The second part of the study was an investigation of long-term effects of haloperidol. If the child responded well to haloperidol during the 12-week trial, he was placed on this drug for an additional 6 months. Children were randomly assigned to one of the two conditions: 5 days of haloperidol and 2 days of placebo (discontinuous treatment), or haloperidol every day of the week (continuous treatment). Every 6 months, haloperidol was discontinued and the child was placed on placebo for 4 weeks. Behavioral ratings on the CPRS and CGI, and ratings on the AIMS and abridged Simpson Scale (Simpson et al., 1979) with videotaping were done at fixed intervals. At the present time, 22 children have been on haloperidol for 6 months, and 11 children for 1 year or more, on doses ranging from 0.5 to 3.0 mg/d.

As for behavioral symptoms, their reduction was maintained at the 6-month followup rating. One week after the discontinuation of haloperidol, ratings of fidgetiness, hyperactivity, stereotypies, withdrawal, and abnormal object relations on the CPRS as well as CGI ratings showed significant increases ($p<.05$, Matched-Pairs Signed Ranks Test).

As for movements, to date four children developed drug-related abnormal movements in this prospective study, as shown in the Table.

In summary, in young children diagnosed as having infantile autism according to DSM-III criteria (axis I), haloperidol, at conservative doses of 0.5 to 3.0 mg/day, yields both clinically and statistically decreases of behavioral symptoms and facilitates learning in our discrimination tasks. This occurs with a bioavailability of ND* or 1.30 to 8.30 ng/ml in serum. On the same dosage, in about 12% of these patients studied prospectively, haloperidol yields worsening of preexisting voluntary abnormal movements or involuntary abnormal movements *de novo;* this occurs while the patient is on drug maintenance (from 3 to 11 months), or as a withdrawal phenomenon. These data were obtained under careful clinical monitoring; drug compliance was excellent.

*ND = <.05 ng/ml

Table

Abnormal Movements Related to Neuroleptic Administration in Four Autistic Children

	Patient No.			
	1	2	3	4
Sex	F	F	F	F
Chronological age* (years/months)	4/2	4/6	3/2	5/2
Haloperidol dosage (mg/day)	1.5	0.5–1.0	3.0	0.5
Treatment schedule**: haloperidol/placebo, in days per week	5/2	5/2	7/0	7/0
Duration of drug administration in months†	3	11	6	6
Onset of movements	On haloperidol	On haloperidol	During withdrawal	On haloperidol
Movements: *de novo* or change in severity or topography of preexisting stereotypies	Preexisting	Preexisting	*de novo*	*de novo*
Duration of movements in months	9	3	< 1	2
Cessation of movements	On placebo§	On haloperidol	On placebo	On placebo

*At the time of enrollment into study.

**5/2 = discontinuous schedule (5 days a week on haloperidol, 2 days on placebo); 7/0 = continuous schedule (7 days a week on haloperidol).

†Prior to onset or change in movements.

§ Decrease only.

References

Campbell, M. Anderson, L.T., Meier, M., et al. A comparison of haloperidol and behavior therapy and their interaction in autistic children. *J. Am. Acad. Child Psychiatry,* 17(4):640-655, 1978.

Cohen, I.L., Campbell, M., Posner, D., et al. Behavioral effects of haloperidol in young autistic children. An objective analysis using a within-subjects reversal design. *J. Am. Acad. Child Psychiatry,* 19(4):655-677, 1980.

Simpson, G.M., Lee, J.H., Zoubok, B., and Gardos, G. A rating scale for tardive dyskinesia. *Psychopharmacology (Berlin),* 64(2):171-179, 1979.

A Controlled Study of Methylphenidate in Combination with Academic Instruction

Rachel Gittelman, Ph.D.[1]

The issue whether stimulants are effective in altering children's learning deficits has been, and continues to be, the subject of much controversy (Dykman, 1980). Gittelman-Klein and Klein (1976) compared methylphenidate with a placebo in 61 children of average intelligence who had significant reading lags and no behavior problems. Methylphenidate was found to improve performance on many psychometric tests, but did not affect performance on standardized reading tests. The pattern of results indicated that performance on tasks which require speed of mental processing was improved by the drug, whereas performance on untimed, complex verbal tasks was not. In a further report (Gittelman, 1980), none of the patient characteristics investigated predicted drug effect, as defined by significant improvement in reading performance.

The results of Gittelman-Klein and Klein (1976) might be interpreted to indicate that attention and learning capacity had been enhanced by methylphenidate, but that, in the absence of concurrent special remedial efforts, the children were unable to profit from their better attentional capacity. These results prompted the investigation of the hypothesis that methylphenidate *in combination* with a program of reading instruction would be superior to reading remediation alone in children with reading disorders uncomplicated by other psychiatric difficulties. This study was part of a larger investigation in which three groups were studied: one group received reading remediation with a placebo; a second received academic tutoring and a placebo (without reading instruction); and a third group received reading remediation and methylphenidate.

Method

Subjects

Only children referred by teachers because of poor academic performance were included, provided they were not judged to have current behavior disorders. All children received reading remediation which which emphasized the teaching of phonic decoding and encoding skills. In addition, children were randomly assigned to either placebo or methylphenidate, and treated in double-blind fashion.

---

[1] New York State Psychiatric Institute New York, NY 10032.

Results

At the end of the 18-week period, the children were receiving an average of 44.19 mg/d of methylphenidate. The range of daily dosage was from 10 to 60 mg. The children's weight ranged from 24.5 to 78.8 kg, and the mean daily dose was 1.19 mg/kg at the end of treatment (range = .41 to 2.23 mg/kg).

Methylphenidate Effects on Reading Achievement

The scores of the Wide Range Achievement Test (WRAT) and Gray Oral at the end of treatment were not significantly different between the two groups.

On a phonetic reading test, significantly superior performance for the methylphenidate-treated children as compared to the placebo group was found on one of the reading tasks. Trends were found on the Reading Age ($p < .10$) and on the reading of Graded Phonically Complex Words ($p < .06$) in favor of the methylphenidate-treated children. Of the four reading tests of the Stanford Achievement Tests, the Language subtest showed a significant advantage for the methylphenidate group ($p < .02$).

Methylphenidate Effects on Academic Tasks Other Than Reading

The WRAT grade levels of arithmetic and spelling did not differ between the placebo and methylphenidate groups. On the Stanford Achievement Test, the children who were on methylphenidate obtained significantly higher scores than the placebo-treated children on three of the four math measures: Math Computation ($p < .04$), Math Application ($p < .005$), and Total Math ($p < .0003$). In addition, the drug-treated group performed significantly better than the placebo group on the Social Studies subtest of the Stanford Achievement Test ($p < .005$).

Long-Term Effects of Methylphenidate Treatment

The long-term effects of the 4 months of treatment with methylphenidate were examined 2 and 8 months after treatment termination. One of the children received medication or tutoring during these intervals. The two treatment groups obtained indistinguishable scores at both followup points.

Discussion

The inference may be drawn that, among children who receive individual reading assistance consisting of phonetic remediation, the addition of methylphenidate in the doses used induces significant advantages in academic tasks other than reading. The failure to find long-term advantages for the methylphenidate-treated children, when drug effects had been obtained during treatment, suggests that stimulants may not enhance learning. Rather, they may be viewed as improving performance. In contrast with other reports (Swanson & Kinsbourne, 1976), no evidence for state-dependent learning was obtained. Our results indicate that, even at relatively high doses, performance can be significantly improved by methylphenidate. High dosage does not compromise learning (Sprague & Sleator, 1977); whether more drug effects would have been obtained with less medication cannot be addressed.

References

Gittelman, R. Indication for the use of stimulant treatment in learning disorders. *J. Acad. Child Psychiatry*, 19:623-636, 1980.

Gittelman-Klein, R., and Klein, D.F. Methylphenidate effects in learning disabilities. *Arch. Gen. Psychiatry*, 33:655-664, 1976.

Sprague, R.L., and Sleator, E.K. Methylphenidate in hyperkinetic children: Differences in dose effects on learning and social behavior. *Science*, 198:1274-1276, 1977.

Methylphenidate in Adults with Minimal Brain Dysfunction Symptomatology

Jeffrey A. Mattes, M.D.,[1] Lane Boswell, B.A., [2] and Herman Oliver, M.D.[2]

The fate of children with minimal brain dysfunction (MBD) is uncertain. Until recently, it was believed that children outgrow the symptoms of MBD around the time of puberty (Eisenberg, 1966). Recent studies, however, indicate that the outcome of children with MBD is not universally positive. Family (Cantwell, 1975) and followup (Weiss, Minde, Werry, et al., 1971) studies suggest that hyperactive children are at risk for behavioral difficulties, including alcoholism and sociopathy, past puberty; though the symptom of hyperactivity may decrease, distractibility, impulsivity, excitability, low self-esteem, poor academic achievement, and interpersonal difficulties may continue into later life. There are also preliminary data suggesting that stimulant medication may be effective in adult conditions possibly related to childhood MBD (Wood, Reimherr, Wender, & Johnson, 1976; Wender, Reimherr, & Wood, 1981). However, these studies did not include a control group, and so were not able to determine the specificity of drug effect.

The objectives of this study were to evaluate whether methylphenidate (Ritalin), a standard treatment for childhood MBD, is effective in adults with symptoms considered related to MBD, and to evaluate the specificity of drug response. The overall goal was to determine if MBD is a specific diagnostic entity in adulthood with a specific treatment, stimulant medication.

Method

All patients applying to an adult psychiatric outpatient clinic (approximately 3,000 patients during the course of this study) were screened by questionnaires and (for eligible patients) interviewed to determine eligibility. Two groups of patients were identified:

1) an experimental patient group with adult symptoms of MBD (restlessness, poor concentration, emotional lability, and impulsivity) and retrospective diagnoses of childhood MBD (more specifically, MBD with hyperactive symtomatology), and
2) a control group with similar adult symptoms but with no childhood histories of MBD (this controlled for the possibility that methylphenidate is helpful for certain adult symptoms regardless of childhood history).

It was assumed that the control group would manifest adult MBD-like symptomatology as a result of anxiety or depression; however, severe depressives (major depressive episodes of greater than mild severity), schizophrenics, and manic depressives were excluded. All patients were entered into a double-blind, crossover design, and given 3-week trials of methylphenidate (up to 60 mg/day; the actual mean dosage was 48 mg/d) and placebo.

Baseline evaluation included ratings by patients, psychiatrists, and significant others, on MBD-related and other symptomatology. In addition, old school records were obtained, and parents were asked to retrospectively rate the patient's childhood MBD symptomatology. Evaluation of drug effect included ratings by patients, psychiatrists, and significant others.

Results

Final results, with an *N* of 63 (approximately 30 in each group) are as follows:

The Diagnostic and Statistical Manual-III (DSM-III) diagnoses of the two groups did not differ significantly except, as expected, that the experimental group much more frequently met the criteria for attention deficit disorder, residual type. The most common diagnoses were major depressive disorder (mild in severity; $N = 19$), alcohol abuse ($N = 17$), drug abuse ($N = 16$), borderline personality disorder ($N = 16$), generalized anxiety disorder ($N = 7$), and antisocial personality disorder ($N = 5$).

A number of baseline measures differentiated the two groups. The experimental group (with childhood hyperactivity) began drinking heavily at an earlier age (if they drank heavily), had histories of more drug abuse, had missed more time from work, had more conflicts with others, had more childhood antisocial symptoms, and did worse on the aphasia test and the tactual perception test. These differences were in the expected direction and indicate that we were successful in identifying relatively distinct groups.

---

[1] Bronx VA Medical Center, Bronx, NY 10468.

[2] Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 11004.

Unfortunately, however, the groups did not differ in response to medication (the principal analyses were 4-way analyses of variance: Drug x Group x Order x Sex). There was no evidence of overall benefit from methylphenidate in either group, and no tendency for the experimental group to respond better than the control group.

Attempts to identify predictors of drug response were generally unsuccessful. Correlations between the baseline measures and improvement on methylphenidate were, for the most part, nonsignificant; of the few significant correlations with greater improvement, some were in the expected direction (e.g., more drug abuse and more childhood vandalism), but others were in the opposite-than-expected direction (e.g., less temper outbursts and less retrospective parent-rated childhood hyperactivity). Analyses comparing "Improvers" on methylphenidate vs. "Non-Improvers" were also generally unsuccessful in identifying predictors of drug response. In particular, retrospective parent ratings of childhood hyperactivity, reported by Wender et al. (1981), to predict stimulant responsiveness did not predict response in our sample. History of drug abuse (polydrug) was the best predictor of positive methylphenidate response.

Despite these generally negative results, we were impressed that a few patients (about 10 in the total sample) did appear to obtain clinically meaningful benefit from the methylphenidate (but not from placebo); these patients were as likely to come from the control group as from the experimental group. For these patients methylphenidate was recommended clinically following this study, and several of these patients followed this recommendation and continued to benefit from methylphenidate (periodic trials off medication confirmed this benefit). The response to methylphenidate in some of these cases was as dramatic as in the case histories reported by Wood et al. (1976) and Wender et al. (1981).

Discussion

This study failed to find evidence of methylphenidate response among adults with symptomatology suggestive of MBD. No baseline measure, including history of childhood MBD, predicted methylphenidate response. The clinical evidence of response in certain patients was not evident statistically, and is therefore basically anecdotal. It appears that further work should be done to identify predictors of stimulant response among adults with MBD symptomatology.

References

Cantwell, D.P. Familial-genetic research with hyperactive children. In: Cantwell, D.P. (ed.). *The Hyperactive Child.* New York: Spectrum Publications, 1975, pp. 93-105.

Eisenberg, L. The management of the hyperactive child. *Develop. Med. Child. Neurol.* 8(10):593-598,1966.

Weiss, B., Minde, K., Werry, J.S., Douglas, V., et al. Studies on the hyperactive child, VII. Five year follow-up. *Arch. Gen. Psychiatry*, 24(5):409-414, 1971.

Wender, P.H., Reimherr, F.W., and Wood D.R. Attention deficit disorder in adults. *Arch. Gen. Psychiatry*, 38(4):49-456, 1981.

Wood, D.R., Reimherr, F.W., Wender, P.H., and Johnson, G.E. Diagnosis and treatment of Minimal Brain Dysfunction in adults. *Arch. Gen. Psychiatry*, 33(12):1453-1460, 1976.

Cumulative Index

Psychopharmacology Bulletin, 1981

A. Index of Contents

Vol. 17, No. 1, January 1981

Page

Research Reorganization within the National Institute of Mental Health 1
International News 2
Publication Announcements 3
Evaluation of Drug Efficacy in Dementia: A Computerized Cognitive Assessment System—*Roland J. Branconnier, Donald DeVitt, and Jonathan O. Cole* 4

Eighteenth Annual Meeting of the ACNP—Abridged Proceedings—

Neuroendocrine Studies of Depressive Disorders—

Vasopressin Function in Depression and Mania—*Philip W. Gold, Frederick K. Goodwin, Robert M. Post, and Gary L. Robertson* 7
Neuroendocrinology of Depression—A Discussion—*Gregory M. Brown, Eva Grof, and Paul Grof* 10

Serotonin: Twenty-Five Years Later—

Monoamine Theories of Sleep: The Role of Serotonin—A Review—*Peter J. Morgane* 13
Studies on the Role of Serotonin in Avoidance Learning—*Sven-Ove Ögren* 17
Changes in 5-Hydroxytryptamine and its Metabolites in Neuropsychiatric Disorders—*Merton Sandler* 19

Investigational Antidepressant Drugs: Implications for Future Research and Treatment of the Affective Illnesses—

Novel Antidepressants: A Clinical Trial of Mianserin—*Patrick J. McGrath, Frederick J. Quitkin, Jonathan W. Stewart, Michael Liebowitz, Abby Fyer, Sharon Davies, and Donald F. Klein* 21
Clinical Trials with New Bicyclic and Tetracyclic Compounds: Zimelidine and Maprotiline—*James L. Claghorn and Roy J. Mathew* 23
Crossover Study of Zimelidine and Desipramine in Depression: Evidence for Amine Specificity—*William Z. Potter, Helene M. Calil, Irl Extein, Giovanni Muscettola, and Frederick K. Goodwin* 26
Methadone and Morphine in Depression—*Irl Extein, David Pickar, Mark S. Gold, Philip W. Gold, A.L.C. Pottash, Donald S. Sweeney, Richard J. Ross, Robert Rebard, David Martin, and Frederick K. Goodwin* 29
Second Generation Antidepressants: A Clinical Pharmacotherapeutic Research Strategy—*Baron Shopsin* 33

Page

Behavioral Interventions and Pharmacological Treatments in Schizophrenia: Differential Indications and Strategies for Future Research—

Natural and Therapeutic Environmental Indicators of Maintenance Dosage Requirements—*Gerard E. Hogarty* . . . 36

Assessment of Drug Scheduling—

Use of Currently Available Data Sources to Assess Drug Scheduling—*Charles W. Gorodetzky* . . . 38
Guidelines for Scheduling Drugs Under the Controlled Substances Act—*Ronald Kartzinel* . . . 40
Discussion of Presentation by Dr. Kartzinel—*Richard Dorsey* . . . 42
Impact of Drug Scheduling on Utilization—*John M. Holt* . . . 43

Aspects of Tardive Dyskinesia—

Animal Models of Tardive Dyskinesia—*Arnold B. Davidson* . . . 45
Preliminary Findings with Regard to Risk Factors in the Development of Tardive Dyskinesia—*John Kane, Frederick Struve, Margaret Woerner, and Paul Weinhold* . . . 46
Dopaminergic and GABAergic Aspects of Tardive Dyskinesia—*Daniel E. Casey, Jes Gerlach, Gerhard Magelund, and Torben Rosted Christensen* . . . 49

Supersensitivity and the Dependent State—

The Relationship Between the Acute Behavioral Effects of Narcotic Antagonists and the Narcotic-Dependent State—*Rita J. Valentino, Seymore Herling, and James H. Woods* . . . 51
Supersensitivity to the Behavioral Effects of Opiate Antagonists—*Roger D. Spealman, Roger T. Kelleher, William H. Morse, and Steven R. Goldberg* . . . 54
A Reformulation of the Dual-Action Model of Opioid Dependence: Opioid-Specific Neuronal Kindling—*Julian E. Villarreal and Antonio Castro* . . . 56

Neurochemical Correlates of Aggressive Behavior—

Drug Regimens Facilitating Aggression: Behavior, Amine, and Receptor Alterations—*Burr Eichelman* . . . 58
Pharmacological Evidence for Catecholamine Involvement in Animal Aggression—*Klaus A. Miczek* . . . 60
Discussion of Paper by Dr. Klaus Miczek—*William T. McKinney, Jr.* . . . 62
Cerebrospinal Fluid Amine Metabolites and Cyclic Nucleotides in Human Aggression—*Gerald L. Brown, Frederick K. Goodwin, James C. Ballenger, and Peter F. Goyer* . . . 63

The Psychobiology of Depression: Report of the National Institute of Mental Health Collaborative Study—Biological Component—

Introduction—Overview of the Study—*Stephen H. Koslow and Steven Secunda* . . . 65
Diagnostic Assessments and Relationships to Outcome—*Jack Croughan, James Kocsis, and Alan Ramsey* . . . 68
Behavioral Aspects and Relationships to Outcome—*Martin M. Katz, Robert Shulman, and Eli Robins* . . . 69
Pretreatment Amine Neurotransmitter System Interrelationships in Depression—*Charles L. Bowden, D. Eugene Redmond, Alan Swann, and James W. Maas* . . . 70
Unexpected Neuroendocrine-Transmitter Relationships—*Peter E. Stokes, Alan Frazer, and Regina Casper* . . . 72

Schizoaffective Disease and Atypical Psychosis—

The Pharmacological Treatment of Schizoaffective Disorder-Depressed: A Review of the Literature—*Duane G. Spiker* . . . 75
Genetic Nature of Schizoaffective Disorder—*Diane K. Wagener* . . . 79

L-Tryptophan in Psychiatry and Neurology—

Daytime Effects of L-Tryptophan—*Cheryl L. Spinweber* . . . 81

Psychopharmacology of Opiate Agonist-Antagonist Drugs—

Structure Activity and Receptor Binding of Antagonist Analgesics—*John William Lewis and Michael John Rance* . . . 83

Page
Clinical Pharmacology of Mixed Agonist-Antagonist Drugs—*Donald R. Jasinski* 85

Poster Session—

Plasma and CSF MHPG in Normals—*David C. Jimerson, James C. Ballenger, C. Raymond Lake, Robert M. Post, Frederick K. Goodwin, and Irwin J. Kopin* 86

Annual NCDEU Meeting (1980)—Abridged Proceedings—

Biological Strategies in Clinical Psychopharmacology Research—

The Dexamethasone Suppression Test in the Identification of Subtypes of Depression Differentially Responsive to Antidepressants—*Walter Armin Brown, Richard J. Haier, and C. Brandon Qualls* 88
Possible Pathophysiological Mechanisms in Subtypes of Unipolar Depressive Disorders Based on Differences in Urinary MHPG Levels—*Joseph J. Schildkraut, Paul J. Orsulak, Alan F. Schatzberg, Jonathan O. Cole, and Alan H. Rosenbaum* 90
Repeated Antidepressant Treatments Induce a Long-Lasting Dopamine Autoreceptor Subsensitivity: Is Daily Treatment Necessary for Clinical Efficacy?—*Seymour M. Antelman and Louis A. Chiodo* 92

Psychiatric Symptom and Cognitive Test Measures as Aids in Differential Diagnosis of Geriatric Patients—

DSM-III Differential Diagnosis in the Elderly—*Andrew E. Skodol and Robert L. Spitzer* 94
Psychiatric Symptoms in the Elderly—*Allen Raskin and Donald S. Rae* 96
The Relationship Between Psychiatric Assessments and Cognitive Test Measures in Mild to Moderately Cognitively Impaired Elderly—*Barry Reisberg, Steven H. Ferris, Michael K. Schneck, Mony de Leon, Thomas H. Crook, and Samuel Gershon* 99

Monoamine Oxidase and Monoamine Oxidase Inhibitors—

Nongenetic Factors Affecting Human Platelet Monoamine Oxidase—*Arnold J. Friedhoff and Jeanette C. Miller* 101
Platelet Monoamine Oxidase in an Aged General Population and Elderly Chronic Schizophrenics—*T. Peter Bridge, Dilip V. Jeste, C. David Wise, Steven G. Potkin, Bruce H. Phelps, and Richard Jed Wyatt* 103
Effects of Phenelzine and Amitriptyline on Depression—*Eugene S. Paykel, Peter R. Rowan, and Robert R. Parker* 104
The Benefits and Risks of Combining an MAO Inhibitor and a Tricyclic Antidepressant—*Kerrin White* 106

Childhood Depression and Hyperkinesis—

Hyperactives as Young Adults: Past and Current Antisocial Behavior (Stealing, Drug Abuse) and Moral Development—*Lily Hechtman, Gabrielle Weiss, and Terrye Perlman* 107

Free Communications—Session A—

Discrimination of Functionally Heterogeneous Receptor Subpopulations: Antipsychotic and Antidopaminergic Properties of Metaclopramide—*John Rotrosen, Michael Stanley, Andrew Lautin, David Wazer, and Samuel Gershon* 110
Plasma Levels of Chlorpromazine and Clinical Response—*Theodore van Putten, Philip R. A. May, and Donald J. Jenden* 113
The Effects of a Drug Holiday on Relapse and Tardive Dyskinesia in Chronic Schizophrenics—*Solomon C. Goldberg, Ram S. Shenoy, Anne Sadler, Robert Hamer, and Beverly Ross* 116
Effects of Gradual Decrease and Discontinuation of Neuroleptics on Clinical Condition and Tardive Dyskinesia—*Marc H. Branchey, Laure B. Branchey, and Mary A. Richardson* 118
Long-Term Changes in AIMS Ratings and Their Relation to Medication History—*James M. Smith, Mary P. Burke, and Cheung O. Moon* 120
Analysis of Single-and Double-Blind Procedure, Maintenance of Placebo Effects, and Drug-Induced Dyskinesia with Mentally Retarded Patients—A Brief Report—*Stephen E. Breuning, Donald G. Ferguson, and Salvatore Cullari* 122

Page

Effects of Lithium Carbonate and Haloperidol on Cognition in Aggressive, Hospitalized School Age Children—*Jane E. Platt, Magda Campbell, and Ira L. Cohen* 123

Molindone Hydrochloride in the Treatment of Aggressive, Hospitalized Children—*Lawrence L. Greenhill, Joseph E. Barmack, David Spalten, Mary Anderson, and Frieda Halpern* 125

The Effects of Lecithin on Memory in Patients with Senile Dementia of the Alzheimer's Type—*George A. Vroulis, Robert C. Smith, Samuel Brinkman, Joseph Schoolar, and Jack Gordon* 127

A Double-Blind, Placebo-Controlled Study of Piracetam in Elderly Psychiatric Patients—*Guy Chouinard, Lawrencs Annable, Andree Ross-Chouinard, Mireille Olivier, and Francine Fontaine* 129

The Therapeutic Profile of Mianserin in Mild Elderly Depressives—*Roland J. Branconnier, Jonathan O. Cole, and Sasan Ghazvinian* 129

Free Communications—Session B—

Predictors of Adolescent Height and Weight in Hyperkinetic Boys Treated with Methylphenidate—*Jan Loney, Mary Anne Whaley-Klahn, Laura Boles Ponto, and Kenneth Adney* 132

Public Judgments on the Importance of Valium Information—*Seymour Fisher and Bruce Mansbridge* 134

Clinical Trial of Halazepam and Clorazepate: Considerations of a Single Bedtime Dose—*Neal L. Cohen, Murray Alpert, and Arnold J. Friedhoff* 134

Evaluation of a Training Program in Using the Research Diagnostic Criteria—*Arthur Rifkin, Gerard Reardon, Samuel Siris, and Jean Endicott* 135

Efficacy of Desipramine in Mildly Depressed Patients: A Double-Blind, Placebo-Controlled Trial—*Jonathan W. Stewart, Frederic Quitkin, Michael R. Liebowitz, Patrick J. McGrath, and Donald F. Klein* 136

Factors which Affect Antidepressant Drug Response in a Multicenter Controlled Trial—*James N. Logue and Barry A. Sachais* 138

Clinical Efficacy of the New Antidepressant Bupropion (Wellbutrin®)—*Angelos E. Halaris, Warren Stern, and Nancy Harto-Truax* 140

Lithium and Imipramine in the Prophylaxis of Unipolar and Bipolar II Depression: A Prospective, Placebo-Controlled Comparison—*Frederic M. Quitkin, John M. Kane, Arthur Rifkin, Jorge R. Ramos-Lorenzi, Kishore Saraf, Alfreda Howard, and Donald F. Klein* 142

Prophylactic Lithium with and without Imipramine for Bipolar I Patients: A Double-Blind Study—*John M. Kane, Frederic M. Quitkin, Arthur Rifkin, Jorge R. Ramos-Lorenzi, Kishore Saraf, Alfreda Howard, and Donald F. Klein* 144

Cumulative Index—Psychopharmacology Bulletin—1980 146

Psychopharmacology—A Recurring Bibliography—

Subject Section S-1

Author Section A-57

Vol. 17, No. 2, April 1981

Page

Meeting Announcements 1
Book Reviews 2
Letter to the Editor 8

Adverse Drug Reactions—

Lithium, Leukocytosis, and Leukemia: The Probable Influence of Biologic Plausibility on Clinical Concern—*Paul Leber* 10

Research Center Reports—

Current Research Activities in India—*V.N. Bagadia* 14
Neuropsychopharmacology Research in Psychiatry at Yale University—*Malcolm Bowers, Jr., Michael Stitelman, and Jane Halbing Stitelman* 17

Brief Reports—

Hydergine as a Treatment for Organic Brain Syndrome in Late Life—*Lissy F. Jarvik* 40

Articles—

On the Clinical Response-Serum Level Relationship for Antidepressants I: Amitriptyline—*John E. Dutt* 42
Department of Health and Human Services (DHHS) Regulations Affecting Psychopharmacology Research—*Natalie Reatig* 56
The Nature of Missing Data in a Psychiatric Data Inventory—*Joseph Galdi and Roland Bonato* 66

American Psychological Association Meeting—1980

Recent Perspectives on Placebo Effectiveness—

The Placebo Response in Pain Control—*Frederick J. Evans* 72
Physiological Substrates of Placebo Analgesia—*Newton C. Gordon and Jon D. Levine* 76
Motivational Factors in Placebo Responsivity—*Frederick X. Gibbons and Stefan E. Hormuth* ...

Ethical Issues in Research with Animals—

Experimental Psychology, Animal Rights, Welfare, and Ethics—*Michael W. Fox* 80
Regulating Psychological Experimentation with Animals in the United Kingdom—*Derek E. Blackman* 84
The Use of Animals for Experimentation in the United States—*Jeri A. Sechzer* 88
The Scientist's Concern for Animal Welfare—*Perri M. Adams* 91

Electroencephalography in Drug Research—Scientific Symposium—1980—

Workshop 1: EEG in Clinical Pharmacology—

The Significance of Quantitative Pharmaco-Electroencephalography in Establishing Dose-Time Relations and its Impact on Clinical Pharmacology: Critical Review and Perspectives—*M. Fink* 94
Quantitative Pharmaco-Electroencephalography to Determine Central Nervous System Efficacy or Toxicity of Drugs—*T. M. Itil, D. M. Shapiro, and K. Z. Itil* 94
Evidence for the Potentiating Effect of Two Different Psychotropic Compounds (Cloxazolam and Noveril) by Means of Pharmaco-Electroencephalography and Polarity Profiles—*R. Vollmer, M. Matejcek, K. Knor, and K. Jellinger* 95
Dose-Response Relationships Between Three Benzodiazepines Based on the Vigilosomnogram—*K. Fichte, H. Ott, J. Kugler, and A. Doenicke* 95
Drug-Induced EEG Changes and the Clinical Effects of Zimelidine—*M. Saito, S. Kita, and Y. Kagono* 96
Paradoxical Sleep in Rats as a Pharmacological Test Model—*H. Kleinlogel* 96
Relations Between Pharmacodynamics and Kinetics: EEG and Psychometric Studies with OX 373 and Nomifensine—*B. Saletu, J. Grunberger, K. Taeuber, and V. Nitsche* 97

Page

Performance Tests and Pharmaco-EEG with 1.4-and 1.5-Benzodiazepines—*W. Sitting, M. Badian, and W. Rupp* 97

Lateral Cerebral Differences in Psychotropic Drug Effects—*M. Fink and P. Irwin* 98

Workshop 2: EEG as an Instrument for the Detection and Characterization of Drug Effects on the CNS: Animal and Human Studies—

The Importance of Quantitative EEG in Animals for the Development of Drugs: Critical Review and Perspectives—*G. Stille* 98

The Significance of Quantitative Pharmaco-EEG in the Detection and Classification of Psychotropic Drugs for Humans: Critical Review and Perspectives—*T. M. Itil* 99

The Effect of Clonazepam on the Rabbit's EEG—*H. Petsche, H. Pockberger, P. Rappelsberger, and I. B. Müller-Paschinger* 99

SELAVCO: A New Method to Determine Event-Related Potentials—*T. Gasser, J. Möcks, and R. Verleger* 100

Occurrence Time and Scalp Location of Components of Evoked and Spontaneous EEG Potential Fields—*D. Lehmann and W. Skrandies* 100

Correlated EEG and Evoked Potential Maps with Deoxyglucose Positron Emission Tomography in Schizophrenia—*M.S. Buchsbaum, R. Coppola, and D. Ingvar* 100

Reliability Studies with Quantified EEG Parameters—*G.K. Schenk, W. Filler, W. Ranft, D. Zerbin, D. Dokk, J. Haverkorn, E. Lemke, and R. Windelschmidt* 101

Interpretation of Correlations Between EEG-Power-Spectra and Psychological Performance Variables—*H. Ott, K. Fichte, W.M. Herrmann, and R.J. McDonald* 101

Discrimination Function with EEG and Psychoexperimental Variables for Objective Classification of Psychotropic Substances into a Five-Drug Class System—*W.M. Herrmann, H. Ott, K. Fichte, and St. Kubicki* 102

Critical Flicker—Fusion Frequency, EEG, and Psychoactive Drugs—*M. Fink and P. Irwin* 103

EEG Reactivity to Verbal Material and Quality of Learning—*M. Koukkou, H. Beck, and D. Lehmann* 103

Workshop 3: Effects with Nonclassical Psychotropics—

The Action of Lithium on the EEG of Normal Subjects and Manic-Depressive Patients: Results and Hypotheses—*D. Bente, W. Scheuler, G. Ulrich, and B. Müller-Oerlinghausen* 104

EEG Sleep Patterns and Profiles, and their Modification by Sleep Drugs in Volunteers and Sleep-Disturbed Patients: Critical Review and Perspectives—*St. Kubicki, W.M. Herrmann, H. Ott, and L. Holler* 104

An Appraisal of Age-Related Changes in the Human EEG: Derived Hypotheses and Implications for Drug Research in the Light of Experimental Evidence—*M. Matejcek* 105

EEG Profile of Mepindolol Sulfate as Compared to Diazepam and Placebo—*H. Kunkel and H. Mock* 106

Beta Blockers and EEG: A Quantitative Study with Mepindolol and Propanolol in Normal Subjects—*D. Bente, B. Berzewski, and W.H. Herrmann* 107

Opiates, Opiate Antagonists, Endorphins, and the Somatosensory-Evoked Potentials—*M.S. Buchsbaum, G.C. Davis, D. Nabor, and D. Rey* 107

EEG Spectral Analysis of Met-5-Enkephalin Effects on the Rabbit Brain—*G. Rosadini, F. Ferrillo, V. Montano, and G. Rodriguez* 108

EEG Changes During Long-Term Lithium Treatment of 6 to 10 Years—*R. Kocher and M. Gastpar* 108

First Effects of Yohimbine on EEG, Quantified by Fourier Spectral Analysis—*P. Etevenon, B. Pidoux, Y. Lecrubier, P. Peron-Magnan, and G. Verdeaux* 108

Psychopharmacology—A Recurring Bibliography—

Subject Section S-1

Author Section A-71

Vol. 17, No. 3, July 1981

Page

Foundations' Fund Prize for Research in Psychiatry 1
Meeting Announcements 2
Book Reviews 3
Book Announcements 5

Adverse Drug Reactions—

Sudden Death as a Risk of Neuroleptic Treatment: (A Continuing Controversy)—*Paul Leber* 6

Brief Report—

A Synopsis of the Status of the New Antidepressant—*Robert F. Prien* 10

Report from a WHO Collaborative Reference Center for the Study of Psychotropic Drugs—

Current Psychopharmacological Research Activities of the WHO Center in Italy—*C.L. Cazzullo* 12

Nineteenth Annual Meeting of the ACNP—Abridged Proceedings—

Bioequivalency of Psychotropic Agents—

Suitable Analytical Methods for Bioequivalence of Antipsychotic Drugs—*Kamal K. Midha, John K. Cooper, Edward M. Hawes, John W. Hubbard, Richard M.H. Roscoe, H. Umesha Shetty, and Pollen K.F. Yeung* 15
CNS Effects of Clonidine in Normal Volunteers—*Max Fink and Peter Irwin* 16
What Is So Different About Bioequivalency of Psychotropic Drugs?—*Louis A. Gottschalk* 17

Sleep and Neuroendocrine Abnormalities in Affective Disorders: New Findings—

EEG Studies of Sleep and the Dexamethasone Suppression Test in the Diagnosis of Depression—*Michael Feinberg, J. Christian Gillin, Bernard J. Carroll, John F. Greden, and Athanasios P. Zis* 20
Sleep EEG and Dexamethasone Suppression Testing Findings in Unipolar Depressions—*A. John Rush, Howard P. Roffwarg, Donna E. Giles, and C Richard Parker* 22

Neuropsychopharmacology of Clonidine—Preclinical Aspects—

Studies on Clonidine in Animal Tests for Antianxiety Activity—*Jerry Sepinwall and Leonard Cook* 24

Platelet Monoamine Oxidase Activity in Schizophrenia—

Effect of Neuroleptic Drugs on Platelet Monoamine Oxidase Activity—*Herbert Y. Meltzer, Herbert Jackman, Ramesh C. Arora, Suman Sahai, and Marybeth Duncavage* 26
Effects of Oxygen, pH, and Toluene on the Activity of Platelet MAO Obtained from Healthy and Chronic Schizophrenic Individuals—*Wolfgang H. Vogel, Mina T. Gentile, Wade H. Berrettini, Kenneth J. Weiss, and Thomas C. Benfield* 28

Neurochemical Modulation of Sensory Motor Reflexes—

Some Recent Observations on the Organization of the Mammalian Spinal Cord—*M. David Egger* 31
Neurochemical Modulation of the Acoustic Startel Reflex—*Michael Davis* 33
Pharmacologic Studies of the Hoffman Reflex Recovery Curve in Humans—*John Metz and Herbert Y. Meltzer* 34
Neurophysiologic Testing from the Laboratory to the Clinic—*Charles Shagass* 35

Biological and/or Genetic Factors in Alcoholism—

Biological Risk Factor Assessment in Lithium Treatment of Alcoholism—*John L. Sullivan, Paula D. Sullivan, Jonathan Davidson, Allan A. Maltbie, Steve Mahorney, Ronald J. Taska, and Jesse O. Cavenar* 37
Path Analysis of Multifactorial Segregation Distributions: Current Work and Future Directions—*John Rice, Theodore Reich, and C.R. Cloninger* 40

Page

Phenolsulfotransferase—

Evidence for Multiple Forms of Human Phenolsulfotransferase—*Glen Rein, Vivette Glover, and Merton Sandler* 43
Sulfoconjugation of Monoamines in Human Platelets—*Giovanni B. Picotti, Andrea M. Cesura, Rolf Kettler, and Mosé Da Prada* 45
Human Platelet Phenolsulfotransferase (PST)—*Godfried M.J. van Kempen and Ed J.M. Pennings* 46
Characterization of Human Brain Phenosulfotransferase—*Jerome A. Roth, A. Jennifer Rivett, and Kevin J. Renskers* 48
Phenolsulfotransferase: Purification and Characterization of the Rat Brain Enzyme—*Anna Baranczyk-Kuzma, Ronald T. Borchardt, Charles S. Schasteen, and Carol L. Pinnick* 50
Clinical Studies on Platelet Phenolsulfotransferase—*Merton Sandler, Vivette Glover, Susan M. Bonham Carter, Julia Littlewood, and Glen Rein* 51

Neurochemistry of Brainstem Functions—

Thirst Induced by Angiotensin II Analyzed Pharmacologically—*M. Ian Phillips, Arturo Camacho, and Colin Sumners* 53
Neurochemistry of Motivated Behavior—*Matthew J. Wayner and Frank C. Barone* 56
Brain Catecholamine Projections: Their Function in Control of Spontaneous and Drug-Induced Changes in Feeding Behavior, Appetite, and Body Weight—*Sarah Fryer Leibowitz* 59
Neurochemistry of Thermoregulation—*Robert D. Myers* 62
Monoaminergic and Peptidergic Control of Gonadotropin Secretion—*Samuel M. McCann* . . 66
Multifactorial and Multitransmitter Basis of Behaviors, and Their Cholinergic Concomitants—*Alexander Karczmar* 68

Endorphins and Enkephalins—

Studies Related to the Metabolic Processing of Endogenous Opioids—*Jack D. Barchas, Sue Sullivan, Huda Akil, Michael Boarder, Eckard Weber, and William C. Hewlett* 70
Potentiation by Leucine Enkephalin of Narcotic Effects in vitro and in vivo—*Akira E. Takemori, Jeffry L. Vaught, Takafumi Kitano, and Alice A. Larson* 73
Endorphins in Shock and Spinal Injury: Therapeutic Role for Opiate Antagonists—*John W. Holaday and Alan I. Faden* 74
Cerebrospinal Fluid Endorphins in Psychiatric Patients—*David Pickar, Dieter Naber, Robert M. Post, Daniel P. van Kammen, James Ballenger, Robert M. Cohen, David Rubinow, Robert N. Waters, Frederick K. Goodwin, and William E. Bunney, Jr.* 76

Genetics of Affective Disorders: New Data and Methods—

The Iowa 500: Family Studies of Bipolar and Unipolar Affective Disorders—*George Winokur, Ming T. Tsuang, and Raymond R. Crowe* 78
Dextroamphetamine and Arecoline as Pharmacogenetic Probes in Normals and Remitted Bipolar Patients—*John I. Nurnberger, Elliot S. Gershon, Natraj Sitaram, J. Christian Gillin, Gregory Brown, Michael Ebert, Philip Gold, David Jimerson, and Linda Kessler* 80
The Behavioral and Mood Response to d-Amphetamine: Some Possible Physiological Correlates—*Uriel Halbreich, Gregory M. Asnis, Donald Ross, and Jean Endicott* 83
Platelet Monoamine Oxidase Activity and Lithium Transport in Families of Bipolar Patients—*Ghanshyam N. Pandey, Elizabeth Dorus, Rita Shaughnessy, and John M. Davis* 85

Drug Treatment and Family Intervention During the Aftercare Treatment of Schizophrenics—

The Effects of Family Therapy on Treatment Compliance in Schizophrenia—*John S. Strang, Ian R. H. Falloon, Howard B. Moss, Javad Razani, and Jeffrey L. Boyd* 87
Keeping the Patient Well: Drug and Social Treatments of Schizophrenic Patients—*Ruth Berkowitz, Liz Kuipers, and Julian Leff* 89

Pharmacotherapy of Anxiety and Depression—

Pharmacotherapy of Anxiety and Depression: Rationale and Study Design—*Ronald S. Lipman, Lino Covi, Robert W. Downing, Seymour Fisher, Richard J. Kahn, Douglas M. McNair,*

Page

Karl Rickels, and Virginia K. Smith ... 91

Description of Sample, Comparison of Anxious and Depressed Groups, and Attrition Rates—*Robert W. Downing, Karl Rickels, Douglas M. McNair, Ronald S. Lipman, Richard J. Kahn, Seymour Fisher, Lino Covi, and Virginia K. Smith* ... 94

Effects of Psychotropic Agents on High Anxiety Subjects—*Richard J. Kahn, Douglas M. McNair, Lino Covi, Robert W. Downing, Seymour Fisher, Ronald S. Lipman, Karl Rickels, and Virginia K. Smith* ... 97

Effects of Psychotropic Agents on Primary Depression—*Lino Covi, Karl Rickels, Ronald S. Lipman, Douglas M. McNair, Virginia K. Smith, Robert Downing, Richard Kahn, and Seymour Fisher* ... 100

Teaching Clinical Psychopharmacology—

Teaching Psychopharmacology to Medical Students—*James S. Eaton, Jr.* ... 103

Methods for Evaluating Effects of Opioid Peptides in Laboratory Animals—

Analgesic Testing of Opioid Peptides—*Robert C. A. Frederickson, Edward L. Smithwick, Robert Shuman, and Paul D. Gesellchen* ... 106

Multiple Opiate Receptors and in vitro Methodology for Opioid Peptides—*Kwen-Jen Chang* ... 108

Chronobiology in Psychiatry—

Chronopsychopharmacology—*Ross J. Baldessarini, Alexander Campbell, Joseph Madsen, Michael Herschel, Seth Finkelstein, James M. Smith, Ronald Majocha, and George Arana* ... 112

Studies of Cortisol Diurnal Rhythm and Cortisol Response to d-Amphetamine in Depressive Patients—*Uriel Halbreich, Edward J. Sachar, Gregory M. Asnis, R. Swami Nathan, and Frieda Halpern* ... 114

Neuropsychopharmacology of Clonidine—Clinial Studies—

Neurochemical Studies of Tourette's Syndrome and the Effects of Clonidine—*Donald J. Cohen, J. Gerald Young, Jill Detlor, James F. Leckman, Diane Harcherik, and Bennett A. Shaywitz* ... 116

Pharmaco-EEG and Bioequivalence—A Practical Methodology for Psychoactive Drugs—*Max Fink* ... 120

Clonidine Treatment of Panic Disorder—*Michael R. Liebowitz, Abby J. Fyer, Patrick McGrath, and Donald F. Klein* ... 122

Response to Clonidine in Korsakoff's Disease: Significance and Implications for Future Research—*William J. McEntee, Robert G. Mair, Robert J. Zatorre, and Philip J. Langlais* ... 123

Clonidine: Effects on Mood, Anxiety, and Pain—*Thomas W. Uhde, Robert M. Post, Larry Siever, Monte S. Buchsbaum, David C. Jimerson, Edward K. Silberman, Dennis Murphy, and William E. Bunney, Jr.* ... 125

Clonidine Versus Methadone for Opiate Detoxification—*Arnold M. Washton and Richard B. Resnick* ... 127

The Cholinergic System in Neuropsychiatry—

Tolerance to Cholinergic Agents—*Roger W. Russell* ... 128

Cholinergic Supersensitivity in Affect Disorder Patients: Behavioral and Neuroendocrine Observations—*David S. Janowsky, Samuel C. Risch, Lewis L. Judd, Leighton Y. Huey, and Donal C. Parker* ... 129

Cholinergic-Endogenous Opioid Mechanisms in Mood and Cognition in Man—*Samuel C. Risch, David S. Janowsky, Ned H. Kalin, Robert M. Cohen, and Dennis L. Murphy* ... 132

Methods for Assessing the Abuse Potential of Psychotropic Drugs in Humans—

Abuse Liability: Testing in Humans—*Donald R. Jasinski* ... 137

Human Self-Administration of Sedative and Stimulant Drugs—*Roland R. Griffiths and George E. Bigelow* ... 138

Geriatric Neuropsychopharmacology—

Cholinomimetics and the Treatment of Memory Disorders—*Kenneth L. Davis, Richard C. Mohs, Bonnie M. Davis, Michael Levy, Gordon S. Rosenberg, Thomas B. Horvath, Alison Ross,*

Page

and Allen Rothpearl 141

Neuropeptides, Psychopathology, and Behavior—

Studies Related to the Clinical Use of Opioid Agonists and Antagonists—*Jack D. Barchas, Philip A. Berger, Stanley J. Watson, Huda Akil, Steven Maier, and John Madden, IV* 142
Similarities and Differences in the Effects of Centrally Administered Neurotensin and Neuroleptics—*Charles B. Nemeroff, Arthur J. Prange, Jr., Daniel Luttinger, Daniel E. Hernandez, Richard A. King, and Susan K. Burgess* 145
Neuroleptic-Like Activity of Des-Tyrosine-γEndolphin (β-LPH$_{62-77}$): Possible Mediation by an Active Metabolite, β-LPH$_{66-77}$—*Norman W. Pedigo, Hans Schoemaker, Paul Ragan, Eric S. Berens, Nicholas C. Ling, and Henry I. Yamamura* 147

Impact of Perinatal Environment of Neural Function—

The Sympathetic Nervous System as a Model for Studying Drug-Induced Alterations of Nerve Development—*Theodore A. Slotkin, Jorge Bartolome, Randy Deskin, Christopher Lau, Elliott Mills, and Peter G. Smith* 151

MAO Inhibitors, New Biochemical and Clinical Findings—

Phenelzine Plasma Levels, Pharmacokinetics, and Clinical Outcome—*Donald S. Robinson, Alexander Nies, John Corcella, and Thomas B. Cooper* 154
Tranylcypromine—*Kerrin L. White* 157
Phenelzine and Imipramine in Atypical Depression—*Michael R. Liebowitz, Frederick M. Quitkin, Jonathan W. Stewart, Patrick J. McGrath, Wilma Harrison, David Schwartz, Judith Rabkin, Elaine Tricamo, and Donald F. Klein* 159

Conditioned Drug Effects: Implications for Neuropsychopharmacology—

Conditioned Behavioral and Biochemical Effects of Amphetamine, Apomorphine, Haloperidol, and Droperidol—*Stanley R. Schiff, Wagner H. Bridger, Nansie S. Sharpless, and Carol Barboni* 162
Context-Dependent Cocaine Sensitization: Role of Vasopressin—*Robert M. Post, Nancy R. Contel, and Philip W. Gold* 164
Conditional Drug Responses and Drug Tolerance—*Shepard Siegel* 166

Clinical Psychoneuroendocrinology: An Update—

Prolactin Secretion: An Update—*Herbert Y. Meltzer, D.A. Busch, Alan Robertson, Betty Jo Tricou, and Victor S. Fang* 168
Thyrotropin (TSH) Response to Thyrotropin-Releasing Hormone (TRH) in Psychiatric Patients—*Peter T. Loosen* 171

Patient Package Inserts: Dogma and Data—

Preliminary Findings on the Effects of a Patient Package Insert for Valium—*Bruce Mansbridge and Seymour Fisher* 173

Poster Sessions—

Effect of Duration of Lithium Therapy of Various Psychiatric Patients on Red Blood Cell/Plasma Choline Ratio—*Edward F. Domino, Abdul Riaz, Ernst Rodin, Sandra Demetriou, Benjamin Mathews, and Sandra Tait* 174
Fluphenazine Pharmacokinetics and Therapeutic Response—*Maurice W. Dysken, Javaid I. Javaid, Sidney S. Chang, Agha Shahid, Regina Casper, and John M. Davis* 176
Relationship of TRH Test and Dexamethasone Suppression Test Abnormalities in Unipolar Depression—*Irl Extein, A.L.C. Pottash, Mark S. Gold, and Frederick K. Goodwin* ... 177
A Double-Blind, Placebo-Controlled Study of Zimelidine in Depression—*Anastase Georgotas* 178
A Double-Blind, Controlled Trial of Lithium Carbonate in Primary Anorexia Nervosa—*Howard A. Gross, Michael H. Ebert, Solomon C. Goldberg, Vivian B. Faden, Linda E. Nee, and Walter H. Kaye* 179
8-Hydroxy-2-(Dl-n-Propylamino)Tetralin: Central 5-HT-Receptor Stimulating Activity—*Stephan Hjorth, Arvid Carlsson, Per Lindberg, Domingo Sanchez, Håkan Wikström, Lars-Erik*

Page

Arvidsson, Uli Hacksel, and J. Lars G. Nilsson 180

Effects of Methylphenidate on Interpersonal Perceptions—*David S. Janowsky, Paul L. Clopton, Leighton Huey, and Lewis L. Judd* 183

Independent Regulation of Haloperidol-Induced Behavioral Supersensitivity and Biochemical Tolerance—*Emanuel Meller, Arnold J. Friedhoff, and Eitan Friedman* 187

Stress Effects on β-Endorphin and Opioid Activity in Human Plasma: Relationships to Psychophysiological and Psychological Variables—*Dieter Naber, Monika Bullinger, Ted Zahn, Jeannette L. Johnson, Paiivi Huhtaniemi, David Pickar, Martin R. Cohen, and William E. Bunney, Jr* 187

Evaluation of Saliva Samples for Pharmacokinetic Studies and Steady-State Levels of Tricyclic Antidepressants—*N. Narasimhachari and Robert O. Friedel* 190

Amphetamine Increases Prolactin but Neither Growth Hormone nor Beta-Endorphin Immunoreactivity in Schizophrenic Patients—*S. Charles Schulz, Daniel P. van Kammen, Alan D. Rogol, Michael Ebert, David Pickar, Martin R. Cohen, and Dieter Naber* 193

Carcinogenicity of Hydantoins: Data, Hypotheses, and Public Reviews—*Barrett Scoville and Billy G. White* 195

Repeated Administration of Drugs Known to Inhibit the Activity of Serotonergic Neurons Potentiates the Prolactin-Releasing Effect of Serotonin Agonists—*Miljana Simonovic, Victor S. Fang, and Herbert Y. Meltzer* 198

Pharmacological Treatment of Delusional Depressives—*Duane G. Spiker, Israel Hanin, June E. Cofsky, John F. Neil, and Denise Sorisio* 201

Hydergine Treatment and Brain Functioning (CNV Rebound) in Alzheimer's Patients: Preliminary Findings—*Joseph J. Tecce, Mary Beth Boehner, Lynn Cattanach, Roland Branconnier, and Jonathan O. Cole* 202

1-Desamino-D-Arginine Vasopressin (DDAVP) in Cognitively Impaired Patients—*Jared R. Tinklenberg, Adolf Pfefferbaum, and Philip A. Berger* 206

Platelet Monoamine Oxidase (MAO) and Clinical Variables in Schizophrenia: Interrelationships with Spinal Fluid Norepinephrine (NE) and Dopamine-beta-hydroxylase (DBH)—*Daniel P. van Kammen, Kenneth L. Malas, David E. Sternberg, Dennis L. Murphy, Pauline Lerner, C. Raymond Lake, Lynne A. Dalton, and William E. Bunney, Jr.* 207

Psychopharmacology—A Recurring Bibliography—

Subject Section S-1

Author Section A-55

Vol. 17, No. 4, October 1981

Page

Meeting Announcement 1
Book Review 1
Adverse Drug Reactions—More on Lithium-Related Leukemia 5
Availability of Psychotropic Compounds 6
Report from a Mental Health Research Center—
  Western Psychiatric Institute and Clinic—*David J. Kupfer* 9
Review—
  Electroconvulsive Therapy Update—*Joyce G. Small and Iver F. Small* 29
Articles—
  Structural Correlates of the Aging Process in the Brain—*Kenneth R. Brizzee* 43
  Maintenance Treatment of Unipolar Depression—*Eric D. Peselow, David L. Dunner, Ronald R. Fieve, Gary Gulbenkian, Stephen I. Deutsch, and Michael Kaufmann* 53
The Bureau of Drugs' Symposium on the Development of Psychopharmacologic Drugs for the
  Cognitively and Emotionally Impaired Elderly: Background and Aims—*Paul Leber* 57
  Pharmacology and Aging—*Robert N. Butler* 58
  Some Ethical and Legal Considerations—*Robert Schwartz* 64
  Problems in Assessing Response to Treatment in the Elderly by Physical and Social Function—*Margaret W. Linn and Bernard S. Linn* 74
  The Evaluation of Ward Behavior Rating Scales for Psychogeriatric Use—*Gilbert Honigfeld* 82
  The Assessment of Behavioral Changes in Geriatric Patients—*J. Richard Wittenborn* 96
  Special Considerations in the Assessment of Psychopathology in the Elderly—*Allen Raskin* 104
  The Conduct of Clinical Trials in the Impaired Elderly—*Samuel Gershon* 108
Psychopharmacology—A Recurring Bibliography—
  Subject Section S-1
  Author Section A-59

B. Author Index

Adams, Perrie M.
Vol. 17, No. 2, 1981, p. 91
Adney, Kenneth
Vol. 17, No. 1, 1981, p. 132
Akil, Huda
Vol. 17, No. 3, 1981, pp. 70, 142
Alpert, Murray
Vol. 17, No. 1, 1981, p. 134
Anderson, Mary
Vol. 17, No. 1, 1981, p. 125
Annable, Lawrence
Vol. 17, No. 1, 1981, p. 129
Antelman, Seymour M.
Vol. 17, No. 1, 1981, p. 92
Arana, George
Vol. 17, No. 3, 1981, p. 112
Arora, Ramesh C.
Vol. 17, No. 3, 1981, p. 26
Arvidsson, Lars-Erik
Vol. 17, No. 3, 1981, p. 180
Asnis, Gregory M.
Vol. 17, No. 3, 1981, pp. 83, 114

Badian, M.
Vol. 17, No. 2, 1981, p. 97
Bagadia, V. N.
Vol. 17, No. 2, 1981, p. 14
Baldessarini, Ross J.
Vol. 17, No. 3, 1981, p. 112
Ballenger, James C.
Vol. 17, No. 1, 1981, pp. 63, 86
Vol. 17, No. 3, 1981, p. 76
Baranczyk-Kuzma, Anna
Vol. 17, No. 3, 1981, p. 50
Barboni, Carol
Vol. 17, No. 3, 1981, p. 162
Barchas, Jack D.
Vol. 17, No. 3, 1981, pp. 70, 142
Barmack, Joseph E.
Vol. 17, No. 1, 1981, p. 125
Barone, Frank C.
Vol. 17, No. 3, 1981, p. 56
Bartholome, Jorge
Vol. 17, No. 3, 1981, p. 151
Beck, H.
Vol. 17, No. 2, 1981, p. 103
Benfield, Thomas C.
Vol. 17, No. 3, 1981, p. 28
Bente, D.
Vol. 17, No. 2, 1981, pp. 104, 107
Berens, Eric S.
Vol. 17, No. 3, 1981, p. 147
Berger, Philip A.
Vol. 17, No. 3, 1981, pp. 142, 206
Berkowitz, Ruth
Vol. 17, No. 3, 1981, p. 89
Berrettini, Wade H.
Vol. 17, No. 3, 1981, p. 28
Berzewski, B.
Vol. 17, No. 2, 1981, p. 107
Bigelow, George E.
Vol. 17, No. 3, 1981, p. 138
Blackman, D. E.
Vol. 17, No. 2, 1981, p. 84
Boarder, Michael
Vol. 17, No. 3, 1981, p. 70
Bonato, Roland R.
Vol. 17, No. 2, 1981, p. 66
Boehner, Mary Beth
Vol. 17, No. 3, 1981, p. 202
Bonham-Carter, Susan M.
Vol. 17, No. 3, 1981, p. 51
Borchardt, Ronald T.
Vol. 17, No. 3, 1981, p. 50
Bowden, Charles L.
Vol. 17, No. 1, 1981, p. 70
Bowers, Malcolm, Jr.
Vol. 17, No. 2, 1981, p. 17
Boyd, Jeffrey L.
Vol. 17, No. 3, 1981, p. 87
Branchey, Laure B.
Vol. 17, No. 1, 1981, p. 118
Branchey, Marc H.
Vol. 17, No. 1, 1981, p. 118
Branconnier, Roland J.
Vol. 17, No. 1, 1981, pp. 4, 129
Vol. 17, No. 3, 1981, p. 202
Breuning, Stephen E.
Vol. 17, No. 1, 1981, p. 122
Bridge, T. Peter
Vol. 17, No. 1, 1981, p. 103
Bridger, Wagner H.
Vol. 17, No. 3, 1981, p. 162
Brinkman, Samuel
Vol. 17, No. 1, 1981, p. 127
Brizzee, Kenneth R

Vol. 17, No. 4, 1981, p. 43
Brown, Gerald L.
Vol. 17, No. 1, 1981, p. 63
Brown, Gregory M.
Vol. 17, No. 1, 1981, p. 10
Vol. 17, No. 3, 1981, p. 80
Brown, Walter Armin
Vol. 17, No. 1, 1981, p. 88
Buchsbaum, M. S.
Vol. 17, No. 2, 1981, pp. 100, 107
Vol. 17, No. 3, 1981, p. 125
Bullinger, Monika
Vol. 17, No. 3, 1981, p. 187
Bunney, William E., Jr.
Vol. 17, No. 3, 1981, pp. 76, 125, 187, 207
Burgess, Susan K.
Vol. 17, No. 3, 1981, p. 145
Burke, Mary P.
Vol. 17, No. 1, 1981, p. 120
Busch, D.A.
Vol. 17, No. 3, 1981, p. 168
Butler, Robert N.
Vol. 17, No. 4, 1981, p. 58

Calil, Helene M.
Vol. 17, No. 1, 1981, p. 26
Camacho, Arturo
Vol. 17, No. 3, 1981, p. 53
Campbell, Alexander
Vol. 17, No. 3, 1981, p. 112
Campbell, Magda
Vol. 17, No. 1, 1981, p. 123
Carlsson, Arvid
Vol. 17, No. 3, 1981, p. 180
Carroll, Bernard J.
Vol. 17, No. 3, 1981, p. 20
Casey, Daniel E.
Vol. 17, No. 1, 1981, p. 49
Casper, Regina
Vol. 17, No. 1, 1981, p. 72
Vol. 17, No. 3, 1981, p. 176
Castro, Antonio
Vol. 17, No. 1, 1981, p. 56
Cattanach, Lynn
Vol. 17, No. 3, 1981, p. 202
Cavenar, Jesse O.
Vol. 17, No. 3, 1981, p. 37
Cazzulo, C.L.
Vol. 17, No. 3, 1981, p. 12
Cesura, Andrea
Vol. 17, No. 3, 1981, p. 45
Chang, Kwen-Jen
Vol. 17, No. 3, 1981, p. 108
Chang, Sidney S.
Vol. 17, No. 3, 1981, p. 176
Chiodo, Louis A.
Vol. 17, No. 1, 1981, p. 92
Chounard, Guy
Vol. 17, No. 1, 1981, p. 129
Christensen, Torben Rosted
Vol. 17, No. 1, 1981, p. 49
Claghorn, James L.
Vol. 17, No. 1, 1981, p. 23
Cloninger, C.R.
Vol. 17, No. 3, 1981, p. 40
Clopton, Paul L.
Vol. 17, No. 1, 1981, p. 183
Cofsky, Jane E.
Vol. 17, No. 3, 1981, p. 201
Cohen, Donald J.
Vol. 17, No. 3, 1981, p. 116
Cohen, Ira L.
Vol. 17, No. 1, 1981, p. 123
Cohen, Martin R.
Vol. 17, No. 3, 1981, pp. 187, 193
Cohen, Neal L.
Vol. 17, No. 1, 1981, p. 134
Cohen, Robert M.
Vol. 17, No. 3, 1981, pp. 76, 132
Cole, Jonathan O.
Vol. 17, No. 1, 1981, pp. 4, 90, 129
Vol. 17, No. 3, 1981, p. 202
Contel, Nancy R.
Vol. 17, No. 3, 1981, p. 164
Cook, Leonard
Vol. 17, No. 3, 1981, p. 24
Cooper, John K.
Vol. 17, No. 3, 1981, p. 15
Cooper, Thomas B.
Vol. 17, No. 3, 1981, p. 154
Coppola, R.
Vol. 17, No. 2, 1981, p. 100
Corcella, John
Vol. 17, No. 3, 1981, p. 154
Covi, Lino
Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Crook, Thomas H.
Vol. 17, No. 1, 1981, p. 99
Croughan, Jack
Vol. 17, No. 1, 1981, p. 68
Crowe, Raymond R.
Vol. 17, No. 3, 1981, p. 78

Cullari, Salvatore
  Vol. 17, No. 1, 1981, p. 122

Dalton, Lynne A.
  Vol. 17, No. 3, 1981, p. 207
Davidson, Arnold B.
  Vol. 17, No. 1, 1981, p. 45
Davidson, Jonathan
  Vol. 17, No. 3, 1981, p. 37
Davies, Sharon
  Vol. 17, No. 1, 1981, p. 21
Davis, Bonnie M.
  Vol. 17, No. 3, 1981, p. 141
Davis, G.C.
  Vol. 17, No. 2, 1981, p. 107
Davis, John M.
  Vol. 17, No. 3, 1981, pp. 85, 176
Davis, Kenneth L.
  Vol. 17, No. 3, 1981, p. 141
Davis, Michael
  Vol. 17, No. 3, 1981, p. 33
de Leon, Mony
  Vol. 17, No. 1, 1981, p. 99
Demetriou, Sandra
  Vol. 17, No. 3, 1981, p. 174
Deskin, Randy
  Vol. 17, No. 3, 1981, p. 151
Detlor, Jill
  Vol. 17, No. 3, 1981, p. 116
Deutsch, Stephen I.
  Vol. 17, No. 4, 1981, p.53
DeVitt, Donald
  Vol. 17, No. 1, 1981, p. 4
Doenicke, A.
  Vol. 17, No. 2, 1981, p. 95
Dokk, D.
  Vol. 17, No. 2, 1981, p. 101
Domino, Edward F.
  Vol. 17, No. 3, 1981, p. 174
Dorsey, Richard
  Vol. 17, No. 1, 1981, p. 42
Dorus, Elizabeth
  Vol. 17, No. 3, 1981, p. 85
Downing, Robert W.
  Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Duncavage, Marybeth
  Vol. 17, No. 3, 1981, p. 26
Dunner, David L.
  Vol. 17,No. 4, 1981, p. 53
Dutt, John E.
  Vol. 17, No. 2, 1981, p. 42
Dysken, Maurice W.
  Vol. 17, No. 3, 1981, p. 176

Eaton, James S., Jr.
  Vol. 17, No. 3, 1981, p. 103
Ebert, Michael
  Vol. 17, No. 3, 1981, pp. 80, 179, 193
Egger, M. David
  Vol. 17, No. 3, 1981, p. 31
Eichelman, Burr
  Vol. 17, No. 1, 1981, p. 58
Endicott, Jean
  Vol. 17, No. 1, 1981, p. 135
  Vol. 17, No. 3, 1981, p. 83
Etevenon, P.
  Vol. 17, No. 2, 1981, p. 108
Evans, Frederick J.
  Vol. 17, No. 2, 1981, p. 72
Extein, Irl
  Vol. 17, No. 1, 1981, pp. 26, 29
  Vol. 17, No. 3, 1981, p. 177

Faden, Alan I.
  Vol. 17, No. 3, 1981, p. 74
Faden, Vivian B.
  Vol. 17, No. 3, 1981, p. 179
Falloon, Ian R.H.
  Vol. 17, No. 3, 1981, p. 87
Fang, Victor S.
  Vol. 17, No. 3, 1981, p. 168, 198
Feinberg, Michael
  Vol. 17, No. 3, 1981, p. 20
Ferguson; Donald G.
  Vol. 17, No. 1, 1981, p. 122
Ferrillo, F.
  Vol. 17, No. 2, 1981, p. 108
Ferris, Steven H.
  Vol. 17, No. 1, 1981, p. 99
Fichte, K.
  Vol. 17, No. 2, 1981, pp. 95, 101, 102
Fieve, Ronald R.
  Vol. 17, No. 4, 1981, p. 53
Filler, W.
  Vol. 17, No. 2, 1981, p. 101
Fink, Max
  Vol. 17, No. 2, 1981, pp. 94, 98, 103
  Vol. 17, No. 3, 1981, pp. 16, 120
Finkelstein, Seth
  Vol. 17, No. 3, 1981, p. 112
Fisher, Seymour
  Vol. 17, No. 1, 1981, p. 134

Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100, 173
Fontaine, Francine
Vol. 17, No. 1, 1981, p. 129
Fox, Michael W.
Vol. 17, No. 2, 1981, p. 80
Frazer, Alan
Vol. 17, No. 1, 1981, p. 72
Frederickson, Robert C.A.
Vol. 17, No. 3, 1981, p. 106
Friedel, Robert O.
Vol. 17, No. 3, 1981, p. 190
Friedhoff, Arnold J.
Vol. 17, No. 1, 1981, pp. 101, 134
Vol. 17, No. 3, 1981, p. 187
Friedman, Eitan
Vol. 17, No. 3, 1981, p. 187
Fyer, Abby
Vol. 17, No. 1, 1981, p. 21
Vol. 17, No. 3, 1981, p. 122

Galdi, Joe
Vol. 17, No. 2, 1981, p. 66
Gasser, T.
Vol. 17, No. 2, 1981, p. 100
Gastpar, M.
Vol. 17, No. 2, 1981, p. 108
Gentile, Nina T.
Vol. 17, No. 3, 1981, p. 28
Georgotas, Anastase
Vol. 17, No. 3, 1981, p. 178
Gerlach, Jes
Vol. 17, No. 1, 1981, p. 49
Gershon, Elliot S.
Vol. 17, No. 3, 1981, p. 80
Gershon, Samuel
Vol. 17, No. 1, 1981, pp. 99, 110
Vol. 17, No. 4, 1981, p. 108
Gesellchen, Paul D.
Vol. 17, No. 3, 1981, p. 106
Ghazvinian, Sasan
Vol. 17, No. 1, 1981, p. 129
Gibbons, Frederick X.
Vol. 17, No. 2, 1981, p. 77
Giles, Donna E.
Vol. 17, No. 3, 1981, p. 22
Gillin, J. Christian
Vol. 17, No. 3, 1981, pp. 20, 80
Glover, Vivette
Vol. 17, No. 3, 1981, pp. 43, 51
Gold, Mark S.
Vol. 17, No. 1, 1981, p. 29
Vol. 17, No. 3, 1981, p. 177
Gold, Philip W.
Vol. 17, No. 1, 1981, pp. 7, 29
Vol. 17, No. 3, 1981, p. 80, 164, 177
Goldberg, Solomon C.
Vol. 17, No. 1, 1981, p. 116
Vol. 17, No. 3, 1981, p. 179
Goldberg Steven R.
Vol. 17, No. 1, 1981, p. 54
Goodwin, Frederick K.
Vol. 17, No. 1, 1981, pp. 7, 26, 29, 63, 86
Vol. 17, No. 3, 1981, pp. 76, 177
Gordon, Jack
Vol. 17, No. 1, 1981, p. 127
Gordon, Newton C.
Vol. 17, No. 2, 1981, p. 76
Gorodetzky, Charles W.
Vol. 17, No. 1, 1981, p. 38
Gottschalk, Louis A.
Vol. 17, No. 3, 1981, p. 17
Goyer, Peter F.
Vol. 17, No. 1, 1981, p. 63
Greden, John F.
Vol. 17, No. 3, 1981, p. 20
Greenhill, Lawrence L.
Vol. 17, No. 1, 1981, p. 125
Griffiths, Roland R.
Vol. 17, No. 3, 1981, p. 138
Grof, Eva
Vol. 17, No. 1, 1981, p. 10
Grof, Paul
Vol. 17, No. 1, 1981, p. 10
Gross, Howard A.
Vol. 17, No. 3, 1981, p. 179
Grünberger, J.
Vol. 17, No. 2, 1981, p. 97
Gulbenkian, Gary
Vol. 17, No. 4, 1981, p. 53

Hacksel, Uli
Vol. 17, No. 3, 1981, p. 180
Haier, Richard J.
Vol. 17, No. 1, 1981, p. 88
Halaris, Angelos E.
Vol. 17, No. 1, 1981, p. 140
Halbreich, Uriel
Vol. 17, No. 3, 1981, pp. 83, 114
Halpern, Frieda
Vol. 17, No. 1, 1981, p. 125
Vol. 17, No. 3, 1981, p. 114
Hamer, Robert,

  Vol. 17, No. 1, 1981, p. 116
Hanin, Israel
  Vol. 17, No. 3, 1981, p. 201
Harcherik, Diane
  Vol. 17, No. 3, 1981, p. 116
Harrison, Wilma
  Vol. 17, No. 3, 1981, p. 159
Harto-Truax, Nancy
  Vol. 17, No. 1, 1981, p. 140
Haverkorn, J.
  Vol. 17, No. 2, 1981, p. 101
Hawes, Edward M.
  Vol. 17, No. 3, 1981, p. 15
Hechtman, lily
  Vol. 17, No. 1, 1981, p. 107
Herling, Seymore
  Vol. 17, No. 1, 1981, p. 51
Hernandez, Daniel E.
  Vol. 17, No. 3, 1981, p. 145
Herrmann, W.M.
  Vol. 17, No. 2, 1981, pp. 101, 102, 104, 107
Herschel, Michael
  Vol. 17, No. 3, 1981, p. 112
Hewlett, William C.
  Vol. 17, No. 3, 1981, p. 70
Hjorth, Stephan
  Vol. 17, No. 3, 1981, p. 180
Hogarty, Gerard E.
  Vol. 17, No. 1, 1981, p. 36
Holaday, John W.
  Vol. 17, No. 3, 1981, p. 74
Höller, L.
  Vol. 17, No. 2, 1981, p. 104
Holt, John M.
  Vol. 17, No. 1, 1981, p. 43
Honigfeld, Gilbert
  Vol. 17, No. 4, 1981, p. 82
Hormuth, Stefan E.
  Vol. 17, No. 2, 1981, p. 77
Horvath, Thomas B.
  Vol. 17, No. 3, 1981, p. 141
Howard, Alfreda
  Vol. 17, No. 1, 1981, pp. 142, 144
Hubbard, John W.
  Vol. 17, No. 3, 1981, p. 15
Huey, Leighton Y.
  Vol. 17, No. 3, 1981, p. 129, 183
Huhtaniemi, Paiivi
  Vol. 17, No. 3, 1981, p. 187
Ingvar, D.
  Vol. 17, No. 2, 1981, p. 100
Irwin, P.
  Vol. 17, No. 2, 1981, pp. 98, 103
  Vol. 17, No. 3, 1981, p. 16
Itil, K.Z
  Vol. 17, No. 2, 1981, p. 94
Itil, T.M.
  Vol. 17, No. 2, 1981, pp. 94, 99
Jackman, Herbert
  Vol. 17, No. 3, 1981, p. 26
Janowsky, David S.
  Vol. 17, No. 3, 1981, pp. 129, 132, 183
Jarvik, Lizzy F.
  Vol. 17, No. 2, 1981, p. 40
Jasinski, Donald R.
  Vol. 17, No. 1, 1981, p. 85
  Vol. 17, No. 3, 1981, p. 137
Javaid, Javaid I.
  Vol. 17, No. 3, 1981, p. 176
Jellinger, K.
  Vol. 17, No. 2, 1981, p. 95
Jenden, Donald J.
  Vol. 17, No. 1, 1981, p. 113
Jeste, Dilip V.
  Vol. 17, No. 1, 1981, p. 103
Jimerson, David C.
  Vol. 17, No. 1, 1981, p. 86
  Vol. 17, No. 3, 1981, pp. 80, 125
Johnson, Jeanette L.
  Vol. 17, No. 3, 1981, p. 187
Judd, Lewis L.
  Vol. 17, No. 3, 1981, pp. 129, 183

Kagono, Y.
  Vol. 17, No. 2, 1981, p. 96
Kahn, Richard J.
  Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Kane, John
  Vol. 17, No. 1, 1981, pp. 46, 142, 144
Kanin, Ned H.
  Vol. 17, No. 3, 1981, p. 132
Karczmar, Alexander
  Vol. 17, No. 3, 1981, p. 68
Kartzinel, Ronald
  Vol. 17, No. 1, 1981, p. 40
Katz, Martin M.
  Vol. 17, No. 1, 1981, p. 69
Kaufmann, Michael
  Vol. 17, No. 4, 1981, p.53
Kaye, Walter H.

Vol. 17, No. 3, 1981, p. 179
Kelleher, Roger T.
Vol. 17, No. 1, 1981, p. 54
Kessler, Linda
Vol. 17, No. 3, 1981, p. 80
Kettler, Rolf
Vol. 17, No. 3, 1981, p. 45
King, Richard A.
Vol. 17, No. 3, 1981, p. 145
Kita, S.
Vol. 17, No. 2, 1981, p. 96
Kitano, Takafumi
Vol. 17, No. 3, 1981, p. 73
Klein, Donald F.
Vol. 17, No. 1, 1981, pp. 21, 136, 142, 144
Vol. 17, No. 3, 1981, pp. 122, 159
Kleinlogel, H.
Vol. 17, No. 2, 1981, p. 96
Knor, K.
Vol. 17, No. 2, 1981, p. 95
Kocher, R.
Vol. 17, No. 2, 1981, p. 108
Kocsis, James
Vol. 17, No. 1, 1981, p. 68
Kopin, Irwin J.
Vol. 17, No. 1, 1981, p. 86
Koslow, Stephen H.
Vol. 17, No. 1, 1981, p. 65
Koukkou, M.
Vol. 17, No. 2, 1981, p. 103
Kubicki, St.
Vol. 17, No. 2, 1981, pp. 102, 104
Kugler, J.
Vol. 17, No. 2, 1981, p. 95
Kuipers, Liz
Vol. 17, No. 3, 1981, p. 89
Künkel, H.
Vol. 17, No. 2, 1981, p. 106
Kupfer, David J.
Vol. 17, No. 4, 1981, p. 9

Lake, C. Raymond
Vol. 17, No. 1, 1981, p. 86
Vol. 17, No. 3, 1981, p. 207
Langlais, Phillip J.
Vol. 17, No. 3, 1981, p. 123
Larson, Alice A.
Vol. 17, No. 3, 1981, p. 73
Lau, Christopher
Vol. 17, No. 3, 1981, p. 151
Lautin, Andrew
Vol. 17, No. 1, 1981, p. 110
Leber, Paul
Vol. 17, No. 2, 1981, p. 10
Vol. 17, No. 3, 1981, p. 6
Vol. 17, No. 4, 1981, p. 57
Leckman, James F.
Vol. 17, No. 3, 1981, p. 116
Lecrubier, Y.
Vol. 17, No. 2, 1981, p. 108
Leff, Julian
Vol. 17, No. 3, 1981, p. 89
Lehmann, D.
Vol. 17, No. 2, 1981, pp. 100, 103
Leibowitz, Sarah Fryer
Vol. 17, No. 3, 1981, p. 59
Lemke, E.
Vol. 17, No. 2, 1981, p. 101
Lerner, Pauline
Vol. 17, No. 3, 1981, p. 207
Levine, Jon D.
Vol. 17, No. 2, 1981, p. 76
Levy, Michael
Vol. 17, No. 3, 1981, p. 141
Lewis, J.W.
Vol. 17, No. 1, 1981, p. 83
Liebowitz, Michael
Vol. 17, No. 1, 1981, pp. 21, 136
Vol. 17, No. 3, 1981, pp. 122, 159
Lindberg, Per
Vol. 17, No. 3, 1981, p. 180
Ling, Nicholas C.
Vol. 17, No. 3, 1981, p. 147
Linn, Bernard S.
Vol. 17, No. 4, 1981, p. 74
Linn, Margaret W.
Vol. 17, No. 4, 1981, p. 74
Lipman, Ronald S.
Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Littlewood, Julia
Vol. 17, No. 3, 1981, p. 51
Logue, James N.
Vol. 17, No. 1, 1981, p. 138
Loney, Jan
Vol. 17, No. 1, 1981, p. 132
Loosen, Peter T.
Vol. 17, No. 3, 1981, p. 171
Luttinger, Daniel
Vol. 17, No. 3, 1981, p. 145

Maas, James W.
Vol. 17, No. 1, 1981, p. 70
Madden, John, IV
Vol. 17, No. 3, 1981, p. 142
Madsen, Joseph
Vol. 17, No. 3, 1981, p. 112
Magelund, Gerhard
Vol. 17, No. 1, 1981, p. 49
Mahorney, Steve
Vol. 17, No. 3, 1981, p. 37
Maier, Steven
Vol. 17, No. 3, 1981, p. 142
Mair, Robert G.
Vol. 17, No. 3, 1981, p. 123
Majocha, Ronald
Vol. 17, No. 3, 1981, p. 112
Malas, Kenneth L.
Vol. 17, No. 3, 1981, p. 207
Maltbie, Arthur A.
Vol. 17, No. 3, 1981, p. 37
Mansbridge, Bruce
Vol. 17, No. 1, 1981, p. 134
Vol. 17, No. 3, 1981, p. 173
Martin, David
Vol. 17, No. 1, 1981, p. 29
Matejcek, M.
Vol. 17, No. 2, 1981, pp. 95, 105
Mathew, Roy J.
Vol. 17, No. 1, 1981, p. 23
Mathews, Benjamin
Vol. 17, No. 3, 1981, p. 174
May, Philip R.A.
Vol. 17, No. 1, 1981, p. 113
McCann, Samuel M.
Vol. 17, No. 3, 1981, p. 66
McDonald, R.J.
Vol. 17, No. 2, 1981, p. 101
McEntee, William J.
Vol. 17, No. 3, 1981, p. 123
McGrath, Patrick J.
Vol. 17, No. 1, 1981, pp. 21, 136
Vol. 17, No. 3, 1981, pp. 122, 159
McKinney, William T., Jr.
Vol. 17, No. 1, 1981, p. 62
McNair, Douglas M.
Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Meller, Emanuel
Vol. 17, No. 3, 1981, p. 187
Meltzer, Herbert Y.
Vol. 17, No. 3, 1981, pp. 26, 34, 168, 198
Metz, John
Vol. 17, No. 3, 1981, p. 34
Miczek, Klaus A.
Vol. 17, No. 1, 1981, p. 60
Midha, Kamel K.
Vol. 17, No. 3, 1981, p. 15
Miller, Jeanette C.
Vol. 17, No. 1, 1981, p. 101
Mills, Elliott
Vol. 17, No. 3, 1981, p. 151
Mock, H.
Vol. 17, No. 2, 1981, p. 106
Möcks, J.
Vol. 17, No. 2, 1981, p. 100
Mohs, Richard C.
Vol. 17, No. 3, 1981, p. 141
Montano, V.
Vol. 17, No. 2, 1981, p. 108
Moon, Cheung O.
Vol. 17, No. 1, 1981, p. 120
Morgane, Peter J.
Vol. 17, No. 1, 1981, p. 13
Morse, William H.
Vol. 17, No. 1, 1981, p. 54
Moss, Howard B.
Vol. 17, No. 3, 1981, p. 87
Müller-Oerlinghausen, B.
Vol. 17, No. 2, 1981, p. 104
Müller-Paschinger, I.B.
Vol. 17, No. 2, 1981, p. 99
Murphy, Dennis
Vol. 17, No. 3, 1981, pp. 125, 132, 207
Muscettola, Giovanni
Vol. 17, No. 1, 1981, p. 26
Myers, Robert D.
Vol. 17, No. 3, 1981, p. 62

Naber, Dieter
Vol. 17, No. 2, 1981, p. 107
Vol. 17, No. 3, 1981, pp. 76, 187, 193
Narasimhachari, N.
Vol. 17, No. 3, 1981, p. 190
Nathan, R. Swami
Vol. 17, No. 3, 1981, p. 114
Nee, Linda E.
Vol. 17, No. 3, 1981, p. 179
Neil, John F.
Vol. 17, No. 3, 1981, p. 201
Nemeroff, Charles B.
Vol. 17, No. 3, 1981, p. 145
Nies, Alexander
Vol. 17, No. 3, 1981, p. 154

Nilsson, J. Jars G.
  Vol. 17, No. 3, 1981. p. 180
Nitsche, V.
  Vol. 17, No. 2, 1981, p. 97
Nurnberger, John I.
  Vol. 17, No. 3, 1981, p. 80

Ogren, Sven-Ove
  Vol. 17, No. 1, 1981, p. 17
Olivier, Mireille
  Vol. 17, No. 1, 1981, p. 129
Orsulak, Paul J.
  Vol. 17, No. 1, 1981, p. 90
Ott, H.
  Vol. 17, No. 2, 1981, pp. 95, 102, 104

Pande, Ghanshyam N.
  Vol. 17, No. 3, 1981, p. 85
Parker, C. Richard
  Vol. 17, No. 3, 1981, p. 22
Parker, Donal C.
  Vol. 17, No. 3, 1981, p. 129
Parker, Robert R.
  Vol. 17, No. 1, 1981, p. 104
Paykel, Eugene S.
  Vol. 17, No. 1, 1981, p. 104
Pedigo, Norman W.
  Vol. 17, No. 3, 1981, p. 147
Pennings, Ed J.M.
  Vol. 17, No. 3, 1981, p. 46
Perlman, Terrye
  Vol. 17, No. 1, 1981, p. 107
Peron-Magnan, P.
  Vol. 17, No. 1, 1981, p. 108
Peselow, Eric D.
  Vol. 17, No. 4, 1981, p. 53
Petsche, H.
  Vol. 17, No. 2, 1981, p. 99
Pfefferbaum, Adolf
  Vol. 17, No. 3, 1981, p. 206
Phelps, Bruce H.
  Vol. 17, No. 1, 1981. p. 103
Phillips, M. Ian
  Vol. 17, No. 3, 1981, p. 53
Pickar, David
  Vol. 17 No. 1, 1981, p. 29
  Vol. 17 No. 3, 1981, pp. 76, 187, 193
Picotti, Giovanni B.
  Vol. 17, No. 3, 1981, p. 45
Pidoux, B.
  Vol. 17, No. 2, 1981, p. 108
Pinnick, Carol L.
  Vol. 17, No. 3, 1981, p. 50
Platt, Jane E.
  Vol. 17, No. 1, 1981, p. 123
Pockberger, H.
  Vol. 17, No. 2, 1981, p. 99
Ponto, Laura Boles
  Vol. 17, No. 1, 1981, p. 132
Post, Robert M.
  Vol. 17, No. 1, 1981, pp. 7, 86
  Vol. 17, No. 3, 1981, pp. 76, 125, 164
Potkin, Steven G.
  Vol. 17, No. 1, 1981, p. 103
Pottash, A.L.C.
  Vol. 17, No. 1, 1981, p. 29
  Vol. 17, No. 3, 1981, p. 177
Potter, William Z.
  Vol. 17, No. 1, 1981, p. 26
Prada, Mosé Da
  Vol. 17, No. 3, 1981, p. 45
Prakash, Rudra
  Vol. 17, No. 4, 1981, p. 5
Prange, Arthur J., Jr.
  Vol. 17, No. 3, 1981, p. 145
Prien, Robert F.
  Vol. 17, No. 3, 1981, p. 10

Qualls, C. Brandon
  Vol. 17, No. 1, 1981, p. 88
Quitkin, Frederick J.
  Vol. 17, No. 1, 1981 pp. 21, 136, 142, 144
  Vol. 17, No. 3, 1981, p. 159

Rabkin, Judith
  Vol. 17, No. 3, 1981, p. 159
Rae, Donald S.
  Vol. 17, No. 1, 1981, p. 96
Ragan, Paul
  Vol. 17, No. 3, 1981, p. 147
Ramos-Lorenzi, Jorge R.
  Vol. 17, No. 1, 1981, pp. 142, 144
Ramsey, Alan
  Vol. 17, No. 1, 1981, p. 68
Ranft, W.
  Vol. 17, No. 2, 1981, p. 101
Rappelsberger, P.
  Vol. 17, No. 2, 1981, p. 99
Raskin, Allen
  Vol. 17, No. 1, 1981, p. 96
  Vol. 17, No. 4, 1981, p. 104
Razani, Javad

Vol. 17, No. 3, 1981, p. 87
Reardon, Gerard
Vol. 17, No. 1, 1981, p. 135
Reatig, Natalie
Vol. 17, No. 2, 1981, p. 56
Rebard, Robert
Vol. 17, No. 1, 1981, p. 29
Redmond, D. Eugene
Vol. 17, No. 1, 1981, p. 70
Reich, Theodore
Vol. 17, No. 3, 1981, p. 40
Rein, Glen
Vol. 17, No. 3, 1981, pp. 43, 51
Reisberg, Barry
Vol. 17, No. 1, 1981, p. 99
Renskers, Kevin J.
Vol. 17, No. 3, 1981, p. 48
Resnick, Richard B.
Vol. 17, No. 3, 1981, p. 127
Rey, D.
Vol. 17, No. 2, 1981, p. 107
Riaz, Abdul
Vol. 17, No. 3, 1981, p. 174
Rice, John
Vol. 17, No. 3, 1981, p. 40
Richardson, Mary A.
Vol. 17, No. 1, 1981, p. 118
Rickels, Karl
Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Rifkin, Arthur
Vol. 17, No. 1, 1981, pp. 135, 142, 144
Risch, Samuel C.
Vol. 17, No. 3, 1981, pp. 129, 132
Rivett, Jennifer
Vol. 17, No. 3, 1981, p. 48
Robertson, Alan
Vol. 17, No. 3, 1981, p. 168
Robertson Gary L.
Vol. 17, No. 1, 1981, p. 7
Robins, Eli
Vol. 17, No. 1, 1981, p. 69
Robinson, Donald S.
Vol. 17, No. 3, 1981, p. 154
Rodin, Ernst
Vol. 17, No. 3, 1981, p. 174
Rodriguez, G.
Vol. 17, No. 2, 1981, p. 108
Roffwarg, Howard P.
Vol. 17, No. 3, 1981, p. 22
Rogol, Alan D.
Vol. 17, No. 3, 1981, p. 193
Rosadini, G.
Vol. 17, No. 2, 1981, p. 108
Roscoe, Richard M.H.
Vol. 17, No. 3, 1981, p. 15
Rosenbaum, Alan H.
Vol. 17, No. 1, 1981, p. 90
Rosenberg, Gordon S.
Vol. 17, No. 3, 1981, p. 141
Ross, Alison
Vol. 17, No. 3, 1981, p. 141
Ross, Beverly
Vol. 17, No. 1, 1981, p. 116
Ross, Donald
Vol. 17, No. 3, 1981, p. 83
Ross, Richard J.
Vol. 17, No. 1, 1981, pp. 29, 116
Ross-Chouinard, Andree
Vol. 17, No. 1, 1981, p. 129
Roth, Jerome A.
Vol. 17, No. 3, 1981, p. 48
Rothpearl, Allen
Vol. 17, No. 3, 1981, p. 141
Rotrosen, John
Vol. 17, No. 1, 1981, p. 110
Rowan, Peter R.
Vol. 17, No. 1, 1981, p. 104
Rubinow, David
Vol. 17, No. 3, 1981, p. 76
Rupp, W.
Vol. 17, No. 2, 1981, p. 97
Rush, A. John
Vol. 17, No. 3, 1981, p. 22
Russell, Roger W.
Vol. 17, No. 3, 1981, p. 128

Sachais, Barry A.
Vol. 17, No. 1, 1981, p. 138
Sachar, Edward J.
Vol. 17, No. 3, 1981, p. 114
Sadler, Anne
Vol. 17, No. 1, 1981, p. 116
Sahai, Suman
Vol. 17, No. 3, 1981, p. 26
Saito, M.
Vol. 17, No. 2, 1981, p. 96
Saletu, B.
Vol. 17, No. 2, 1981, p. 97
Sanchez, Domingo
Vol. 17, No. 3, 1981, p. 180
Sandler, Merton
Vol. 17, No. 1, 1981, p. 19

  Vol. 17, No. 3, 1981, p. 43, 51
Saraf, Kishore
  Vol. 17, No. 1, 1981, pp. 142, 144
Schasteen, Charles S.
  Vol. 17, No. 3, 1981, p. 50
Schatzberg, Alan F.
  Vol. 17, No. 1, 1981, p. 90
Schenck, G.K.
  Vol. 17, No. 2, 1981, p. 101
Scheuler, W.
  Vol. 17, No. 2, 1981, p. 104
Schiff, Stanley R.
  Vol. 17, No. 3, 1981, p. 162
Schildkraut, Joseph J.
  Vol. 17, No. 1, 1981, p. 90
Schneck, Michael K.
  Vol. 17, No. 1, 1981, p. 99
Schoemaker, Hans
  Vol. 17, No. 1, 1981, p. 147
Schoolar, Joseph
  Vol. 17, No. 1, 1981, p. 127
Schultz, S. Charles
  Vol. 17, No. 3, 1981, p. 193
Schwartz, David
  Vol. 17, No. 3, 1981, p. 159
Schwartz, Robert,
  Vol. 17, No. 4, 1981, p. 64
Scoville, Barrett
  Vol. 17, No. 3, 1981, p. 195
Sechzer, Jeri A.
  Vol. 17, No. 2, 1981, p. 88
Secunda, Steven
  Vol. 17, No. 1, 1981, p. 65
Sepinwall, Jerry
  Vol. 17, No. 3, 1981, p. 24
Sethi, Brij B.
  Vol. 17, No. 4, 1981, p. 5
Sethi, N.
  Vol. 17, No. 4, 1981, p. 5
Shagass, Charles
  Vol. 17, No. 3, 1981, p. 35
Shahid, Agha
  Vol. 17, No. 3, 1981, p. 176
Shapiro, D.M.
  Vol. 17, No. 2, 1981, p. 94
Sharpless, Nansie S.
  Vol. 17, No. 3, 1981, p. 162
Shaughnessy, Rita
  Vol. 17, No. 3, 1981, p. 85
Shaywitz, Bennett A.
  Vol. 17, No. 3, 1981, p. 116
Shenoy, Ram S.
  Vol. 17, No. 1, 1981, p. 116
Shetty, M. Umesha
  Vol. 17, No. 3, 1981, p. 15
Shopsin, Baron
  Vol. 17, No. 1, 1981, p. 33
Shulman, Robert
  Vol. 17, No. 1, 1981, p. 69
Shuman, Robert
  Vol. 17, No. 3, 1981 p. 106
Siegel, Shepard
  Vol. 17, No. 3, 1981, p. 166
Siever, Larry
  Vol. 17, No. 3, 1981, p. 125
Silberman, Edward K.
  Vol. 17, No. 3, 1981, p. 125
Simonovic, Miljana
  Vol. 17, No. 3, 1981, p. 198
Sirus, Samuel
  Vol. 17, No. 1, 1981, p. 135
Sitaram, Natraj
  Vol. 17, No. 3, 1981, p. 80
Sitting, W.
  Vol. 17, No. 2, 1981, p. 97
Skodol, Andrew E.
  Vol. 17, No. 1, 1981, p. 94
Skrandies, W.
  Vol. 17, No. 2, 1981, p. 100
Slotkin, Theodore A.
  Vol. 17, No. 3, 1981, p. 151
Small, Joyce G.
  Vol. 17, No. 4, 1981, p. 29
Small, Iver F.
  Vol. 17, No. 4, 1981, p. 29
Smith, James M.
  Vol. 17, No. 1, 1981, p. 120
  Vol. 17, No. 3, 1981, p. 112
Smith, Peter G.
  Vol. 17, No. 3, 1981, p. 151
Smith, Robert C.
  Vol. 17, No. 1, 1981, p. 127
Smith, Virginia K.
  Vol. 17, No. 3, 1981, pp. 91, 94, 97, 100
Smithwick, Edward L.
  Vol. 17, No. 3, 1981, p. 106
Sorisio, Denise
  Vol. 17, No. 3, 1981, p. 201
Spalten, David
  Vol. 17, No. 1, 1981, p. 125
Spealman, Roger D.
  Vol. 17, No. 1, 1981, p. 54

Spiker, Duane G.
Vol. 17, No. 1, 1981, p. 75
Vol. 17, No. 3, 1981, p. 201
Spinweber, Cheryl L.
Vol. 17, No. 1, 1981, p. 81
Spitzer, Robert L.
Vol. 17, No. 1, 1981, p. 94
Stanley, Michael
Vol. 17, No. 1, 1981, p. 110
Stern, Warren
Vol. 17, No. 1, 1981, p. 140
Sternberg, David E.
Vol. 17, No. 3, 1981, p. 207
Stewart, Jonathan W.
Vol. 17, No. 1, 1981, pp. 21, 136
Vol. 17, No. 3, 1981, p. 159
Stille, G.
Vol. 17, No. 2, 1981, p. 98
Stitelman, Jane Halbing
Vol. 17, No. 2, 1981, p. 17
Stitelman, Michael
Vol. 17, No. 2, 1981, p. 17
Stokes, Peter E.
Vol. 17, No. 1, 1981, p. 72
Strang, John S.
Vol. 17, No. 3, 1981, p. 87
Struve, Frederick
Vol. 17, No. 1, 1981, p. 46
Sullivan, John L.
Vol. 17, No. 3, 1981, p. 37
Sullivan, Paula D.
Vol. 17, No. 3, 1981, p. 37
Sullivan, Sue
Vol. 17, No. 3, 1981, p. 70
Sumners, Colin
Vol. 17, No. 3, 1981, p. 53
Swann, Alan
Vol. 17, No. 1, 1981, p. 70
Sweeney, Donald R.
Vol. 17, No. 1, 1981, p. 29

Taeuber, K.
Vol. 17, No. 2, 1981, p. 97
Tait, Sandra
Vol. 17, No. 3, 1981, p. 174
Takemori, Akira E.
Vol. 17, No. 3, 1981, p. 73
Taska, Ronald J.
Vol. 17, No. 3, 1981, p. 37
Tecce, Joseph J.
Vol. 17, No. 3, 1981, p. 202
Tinklenberg, Jared R.
Vol. 17, No. 3, 1981, p. 206
Tricamo, Elaine
Vol. 17, No. 3, 1981, p. 159
Tricou, Betty Jo
Vol. 17, No. 3, 1981, p. 168
Tsuang, Ming T.
Vol. 17, No. 3, 1981, p. 78

Uhde, Thomas W.
Vol. 17, No. 3, 1981, p. 125
Ulrich, G.
Vol. 17, No. 2, 1981, p. 104

Valentine, Rita J.
Vol. 17, No. 1, 1981, p. 51
van Kammen, Daniel P.
Vol. 17, No. 3, 1981, pp. 76, 193, 207
van Kempen, Godfried M.J.
Vol. 17, No. 3, 1981, p. 46
van Putten, Theodore
Vol. 17, No. 1, 1981, p. 113
Vaught, Jeffry L.
Vol. 17, No. 3, 1981, p. 73
Verdeaux, G.
Vol. 17, No. 2, 1981, p. 108
Verleger, R.
Vol. 17, No. 2, 1981, p. 100
Villarreal, Julian E.
Vol. 17, No. 1, 1981, p. 56
Vogel, Wolfgang H.
Vol. 17, No. 3, 1981, p. 28
Vollmer, R.
Vol. 17, No. 2, 1981, p. 95
Vroulis, George A.
Vol. 17, No. 1, 1981, p. 127

Wagener, Diane K.
Vol. 17, No. 1, 1981, p. 79
Washton, Arnold M.
Vol. 17, No. 3, 1981, p. 127
Waters, Robert N.
Vol. 17, No. 3, 1981, p. 76
Watson, Stanley J.
Vol. 17, No. 3, 1981, p. 142
Wayner, Matthew J.
Vol. 17, No. 3, 1981, p. 56
Wazer, David
Vol. 17, No. 1, 1981, p. 110
Weber, Eckard
Vol. 17, No. 3, 1981, p. 70

Weinhold, Paul
  Vol. 17, No. 1, 1981, p. 46
Weiss, Gabrielle
  Vol. 17, No. 1, 1981, p. 107
Weiss, Kenneth J.
  Vol. 17, No. 3, 1981, p. 28
Whaley-Klahn, Mary Anne
  Vol. 17, No. 1, 1981, p. 132
White, Billy G.
  Vol. 17, No. 3, 1981, p. 195
White, Kerrin
  Vol. 17, No. 1, 1981, p. 106
  Vol. 17, No. 3, 1981, p. 157
Wikstrom, Hakan
  Vol. 17, No. 3, 1981, p. 180
Windelschmidt, R.
  Vol. 17, No. 2, 1981, p. 101
Winokur, George
  Vol. 17, No. 3, 1981, p. 78
Wise, C. David
  Vol. 17, No. 1, 1981, p. 103
Wittenborn, J. Richard
  Vol. 17, No. 4, 1981, p. 96
Woerner, Margaret
  Vol. 17, No. 1, 1981, p. 46
Woods, James H.
  Vol. 17, No. 1, 1981, p. 51
Wyatt, Richard Jed
  Vol. 17, No. 1, 1981, p. 103

Yamamura, Henry I.
  Vol. 17, No. 3, 1981, p. 147
Yeung, Pollen K.F.
  Vol. 17, No. 3, 1981, p. 15
Young, J. Gerald
  Vol. 17, No. 3, 1981, p. 116

Zahn, Ted
  Vol. 17, No. 3, 1981, p. 187
Zatorre, Robert J.
  Vol. 17, No. 3, 1981, p. 123
Zerbin, D.
  Vol. 17, No. 3, 1981, p. 101
Zis, Athanasios P.
  Vol. 17, No. 3, 1981, p. 20

Psychopharmacology — A Recurring Bibliography

The bibliography below is offered to our readers to alert them to recent papers on psychopharmacology from the world literature. It was computer-generated by the Medical Literature Analysis and Retrieval System (MEDLARS) of the National Library of Medicine, National Institutes of Health, and represents papers which were entered into the system during the 3 months before the *Bulletin* went to press.

The subject headings from Index Medicus were selected by the WHO International Reference Center at the NIMH to reflect significant current interest of the international scientific community. Some nonrelevant citations may appear, and some relevant ones may be absent, but this is usual for machine-generated searches. Each subsequent issue of the *Bulletin* will provide such a bibliography, which contains two parts — a Subject Section and an Author Section.

Comments and suggestions are invited.

ISSN 0048-5764

SUBJECT SECTION

ACEPROMAZINE

Determination of blood pressure by indirect methods in dogs given acetylpromazine maleate. Coulter DB, et al. **Cornell Vet** 1981 Jan; 71(1):75–84

The metabolism of promazine and acetylpromazine in the horse. Dewey EA, et al. **Drug Metab Dispos** 1981 Jan–Feb;9(1):30–6

ACETYLCHOLINE

Acetylcholine-like activity in the fruit of the black nightshade (Solanaceae). de Melo AC, et al. **Acta Physiol Lat Am** 1978; 28(4–5):19–26

Correlation between cholinergic histamine release and quinuclidinyl-benzilate ([3H]-QNB) binding in mast cell membranes. Masini E, et al. **Agents Actions** 1981 Apr;11(1–2):55–9

Release of acetylcholine in the isolated heart. Löffelholz K. **Am J Physiol** 1981 Apr;240(4):H431–40 (101 ref.)

Electrophysiological effects of acetylcholine on rabbit cardiac Purkinje Fibers. Mubagwa K, et al. **Arch Int Pharmacodyn Ther** 1981 Feb; 249(2):326–7

Requirement for calcium ions in acetylcholine-stimulated phosphodiesteratic cleavage of phosphatidyl-myo-inositol 4,5-bisphosphate in rabbit iris smooth muscle. Akhtar RA, et al. **Biochem J** 1980 Dec 15;192(3):783–91

Reconstitution of acetylcholine receptor function using purified receptor protein. Wu WC, et al. **Biochemistry** 1981 Feb 17;20(4):694–701

Effects of cholinergic stimulation on levels and fatty acid composition of diacylglycerols in mouse pancreas. Banschbach MW, et al. **Biochim Biophys Acta** 1981 Jan 26;663(1):34–45

Cyclic nucleotides of canine antral smooth muscle. Effects of acetylcholine, catecholamines and gastrin. Baur S, et al. **Biochim Biophys Acta** 1981 Jan 7;672(1):1–6

Changes in acetylcholine in caudate nucleus tissue isolated in situ detected by gas chromatography mass spectrometry selected ion monitoring. Haug P, et al. **Biomed Mass Spectrom** 1980 Nov;7(11–12):533–6

A comparison of stereospecificity at central and peripheral 'muscarine-sensitive' acetylcholine receptors: observations with the enantiomeric forms of procyclidine and tricyclamol. Barlow RB, et al. **Br J Pharmacol** 1981 Feb;72(2):277–80

5-hydroxytryptamine controls ACh-receptor sensitivity of bullfrog sympathetic ganglion cells. Akasu T, et al. **Brain Res** 1981 Apr 27; 211(1):217–20

Acetylcholine induced modulation of hippocampal pyramidal neurons. Benardo LS, et al. **Brain Res** 1981 Apr 27;211(1):227–34

Ontogenetic development of high potassium- and acetylcholine-induced release of dopamine from striatal slices of the rat. Nomura Y, et al. **Brain Res** 1981 Apr;227(2):171–7

Maintenance and dissolution of acetylcholine receptor clusters in the embryonic muscle cell membrane. Orida N, et al. **Brain Res** 1981 Apr; 227(2):293–8

Evidence of the modulatory role of serotonin in acetylcholine release from striatal interneurons. Vizi ES, et al. **Brain Res** 1981 May 11; 212(1):89–99

Potentiation and inhibition of nicotinic effects on striated muscle by the tetramine disulfide benextramine. Benfey BG, et al. **Can J Physiol Pharmacol** 1980 Aug;58(8):984–8

Gastric inhibitory polypeptide stimulated secretion of somatostatinlike immunoreactivity from the stomach: inhibition by acetylcholine or vagal stimulation. McIntosh CH, et al. **Can J Physiol Pharmacol** 1981 May; 59(5):468–72

Selective inhibition of schistosome acetylcholinesterase by dansylated acetylcholine analogs. Dotson MJ, et al. **Comp Biochem Physiol [C]** 1981;68C(2):229–30

Effect of acetylcholine on calcium efflux from atrial myocardium. Prokopczuk A, et al. **Eur J Pharmacol** 1981 Mar 5;70(1):1–6

Conformational analysis of the reverse ester of acetylcholine, cholinergic potency, and cholinergic models. Reed KW, et al. **Gen Pharmacol** 1981; 12(3):177–85

Human fetal membranes: investigations on membrane potentials and membrane 24Na permeability in vitro and the possible involvement of acetylcholine. Welsch F. **Gynecol Obstet Invest** 1981;12(3):113–22

Control of glycogen synthesis in isolated rat hepatocytes by insulin, glucagon & acetylcholine. Beynen AC, et al. **Indian J Exp Biol** 1981 Jan;19(1):46–8

Effect of ovulation on the response of the rabbit oviduct to acetylcholine in vitro. Rajkumar K, et al. **Int J Fertil** 1981;26(1):57–60

Stabilization of acetylcholine receptor channels by lipids in cholate solution and during reconstitution in vesicles. Anholt R, et al. **J Biol Chem** 1981 May 10;256(9):4377–87

Acetyl coenzyme A and acetylcholine in slices of rat caudate nuclei incubated in the presence of metabolic inhibitors. Říčný J, et al. **J Biol Chem** 1981 May 25;256(10):4919–23

Acetylcholine receptor kinetics. Adams PR. **J Membr Biol** 1981 Feb 28; 58(3):161–74 (132 ref.)

Mechanisms for the effects of acetylcholine on sodium transport in frog skin. Cuthbert AW, et al. **J Membr Biol** 1981 Mar 15;59(1):65–75

Acetylcholine receptor-controlled ion flux in electroplax membrane vesicles: identification and characterization of membrane properties that affect ion flux measurements. Kim PS, et al. **J Membr Biol** 1981 Feb 28;58(3):203-11

Acetylcholine turnover and compartmentation in rat brain synaptosomes. Jope RS. **J Neurochem** 1981 May;36(5):1712-21

Simultaneous release of acetylcholine and ATP from stimulated cholinergic synaptosomes. Morel N, et al. **J Neurochem** 1981 May; 36(5):1766-73

The release of gamma-aminobutyric acid, glutamate, and acetylcholine from striatal slices: a mass fragmentographic study. Moroni F, et al. **J Neurochem** 1981 May;36(5):1691-9

Choline uptake and acetylcholine synthesis in synaptosomes: investigations using two different labeled variants of choline. Weiler MH, et al. **J Neurochem** 1981 May;36(5):1802-12

The effect of cold stress on the modulation of vascular adrenergic transmission by acetylcholine. Merrigan MD, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):142-7

The effect of phencyclidine on the turnover rate of acetylcholine in various regions of rat brain. Murray TF, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):733-7

Effects of acute and chronic administration of DDVP (dichlorvos) on distribution of brain acetylcholine in rats. Kobayashi H, et al. **J Toxicol Sci** 1980 Nov;5(4):311-9

Effect of progesterone therapy on the responses of the isolated rat stomach fundus strip preparations to 5-hydroxytryptamine and acetylcholine. Qayum A, et al. **JPMA** 1981 Apr;31(4):84-8

A further study on constrictor responses of dog coronary arterial strips to acetylcholine under potassium-contracture. Sakanashi M, et al. **Jpn Heart J** 1981 Mar;22(2):211-7

Cat heart acetylcholine: unilateral vagotomy studies with pyrolysis-mass fragmentography. Brown OM. **Life Sci** 1981 Feb 16;28(7):819-25

Action of colchicine on cholinergic and adrenergic mechanisms in guinea pig vas deferens. Takeyasu K, et al. **Life Sci** 1981 Feb 23; 28(8):851-60

The identification of an invertebrate acetylcholine receptor. Thomas WE, et al. **Life Sci** 1981 Mar 2;28(9):965-71 (42 ref.)

Piracetam diminishes hippocampal acetylcholine levels in rats. Wurtman RJ, et al. **Life Sci** 1981 Mar 9;28(10):1091-3

Does rigidity in structure of muscarinic agonists and antagonists reflect drug specificity? Fisher A, et al. **Monogr Neural Sci** 1980;7:41-54

Regulation of acetylcholine liberation from presynaptic nerve terminals. Rahamimoff R, et al. **Monogr Neural Sci** 1980;7:3-18

Multiple actions of beta-bungarotoxin on acetylcholine release at amphibian motor nerve terminals. Alderdice MT, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):126-30

Tetanus toxin and botulinum A toxin inhibit acetylcholine release from but not calcium uptake into brain tissue. Bigalke H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):143-8

Choline inhibits acetylcholine release via presynaptic muscarine receptors. Kilbinger H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):131-4

A comparison of the actions of acetylcholine and bradykinin on the guinea pig ileum. Roberts ML. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):267-70

Changes in the biochemical and biophysical parameters of cholinergic synaptic vesicles on transmitter release and during a subsequent period of rest. Giompres PE, et al. **Neuroscience** 1981;6(4):775-85

Ultrastructural localization of VIP-like immunoreactivity in large dense-core vesicles of 'cholinergic-type' nerve terminals in cat exocrine glands. Johansson O, et al. **Neuroscience** 1981;6(5):847-62

Factors affecting choline transport by the cat superior cervical ganglion during and following stimulation, and the relationship between choline uptake and acetylcholine synthesis. O'Regan S, et al. **Neuroscience** 1981; 6(3):511-20

The time course of the muscarinic response to ionophoretic acetylcholine application to the S-A node of the rabbit heart. Osterrieder W, et al. **Pfluegers Arch** 1981 Mar;389(3):283-91

Interactions between ionophores, Mg2+ and Ca2+ on acetylcholine formation and release in brain slices. Mantovani P, et al. **Pharmacol Res Commun** 1981 Feb;13(2):175-64

Saturable acetylcholine transport into purified cholinergic synaptic vesicles. Michaelson DM, et al. **Proc Natl Acad Sci USA** 1981 Apr; 78(4):2048-52

Catecholamines, acetylcholine and excitability of mechanoreceptors. Akoev GN. **Prog Neurobiol** 1980;15(4):269-94

Effects of lithium on behavioral reactivity: relation to increases in brain cholinergic activity. Russell RW, et al. **Psychopharmacology (Berlin)** 1981;73(2):120-5

Pirenzepine selectively inhibits gastric acid secretion: a comparative pharmacological study between pirenzepine and seven other antiacetylcholine drugs. Heathcote BV, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):15-26

Increase of evoked release of acetylcholine at the neuromuscular junction by a fraction from the venom of the eastern green mamba snake (Dendroaspis angusticeps). Harvey AL, et al. **Toxicon** 1981; 19(3):373-81

[Effect of social isolation on the transmitter sensitivity of striatal and hippocampal neurons of the rat] Oehler J, et al. **Acta Biol Med Ger** 1980;39(10):1089-93 (Eng. Abstr.) **(Ger)**

[Structure and conformation-activity relationships of cyclic acetylcholine analogues / 12th communication: Synthesis and cholinergic properties of stereoisomeric 3-acetoxythiacyclohexanes (author's transl)] Lambrecht G. **Arzneimittelforsch** 1981;31(4):634-40 (Eng. Abstr.) **(Ger)**

[Effect of acetylcholine and adrenaline on membrane currents in ventricular muscle (author's transl)] Ochi R. **Kokyu To Junkan** 1980 Oct;28(10):1103-9 **(Jpn)**

[Effect of adrenaline, noradrenaline and acetylcholine on rabbit and human uterine activity in vivo (author's transl)] Sakoda H. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Jun;32(6):697-705 (Eng. Abstr.) **(Jpn)**

[Activation of Na, K-ATPase from nerve cell microsomes by acetylcholine in a model system] Elaev NR. **Biokhimiia** 1980 Oct; 45(10):1749-54 (Eng. Abstr.) **(Rus)**

[Effect of cholinergic factors on the state of erythrocyte membrane proteins of animals] Savina LS, et al. **Biull Eksp Biol Med** 1981 Feb; 91(2):153-5 (Eng. Abstr.) **(Rus)**

[Acetylcholine-bradykinin: a new peptide-amine transmitter interaction (editorial)] Pirola CJ. **Medicina (B Aires)** 1980 Nov-Dec; 40(6 Pt 2):893-5 **(Spa)**

AFFECTIVE DISORDERS

Prophylactic effect of lithium against depression in cyclothymic patients: a life-table analysis. Peselow ED, et al. **Compr Psychiatry** 1981 May-Jun;22(3):257-64

Increased platelet monoamine oxidase activity in affective disorders. Reveley MA, et al. **Psychopharmacology (Berlin)** 1981;73(3):257-60

Methylphenidate in depression and states of apathy. Moore DP. **South Med J** 1981 Mar;74(3):347-8

AFFECTIVE DISORDERS, PSYCHOTIC

The antidepressant efficacy of zimelidine and maprotiline. Montgomery SA, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):219-24

Specific norepinephrine and serotonin uptake inhibitors in man: a crossover study with pharmacokinetic, biochemical, neuroendocrine and behavioral parameters. Potter WZ, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):152-65

Psychotropic drugs: lithium. Harris E. **Am J Nurs** 1981 Jul; 81(7):1311-5

Current concepts of lithium therapy [letter] Coppen A, et al. **Br J Hosp Med** 1981 Mar;25(3):309-10

Lithium updated. **Drug Ther Bull** 1981 Mar 13;19(6):21-4

Lithium response in the treatment of manic symptomatology. Channabasavanna SM, et al. **Indian J Med Res** 1980 Dec;72:908-9

Circadian rhythms of dopamine-beta-hydroxylase and c-AMP in plasma of controls and patients with affective disorders. Markianos M, et al. **J Neural Transm** 1981;50(2-4):149-55

Antidepressant efficacy of tranylcypromine isomers: a controlled study. Moises HW, et al. **J Neural Transm** 1981;50(2-4):185-92

Changes in blood plasma osmolality and states of mania. Baxter CF, et al. **Neurochem Res** 1981 Jan;6(1):47-53

Slow and rapid onset of manic episodes: implications for underlying biology. Post RM, et al. **Psychiatry Res** 1981 Apr;4(2):229-37

Vasopressin function in depression and mania [proceedings] Gold PW, et al. **Psychopharmacol Bull** 1981 Jan;17(1):7-9

Lithium and mania. Tosteson DC. **Sci Am** 1981 Apr; 244(4):164-6, 168, 171-2 et passim

[Modifications of cerebral amine metabolism in psychiatric illness] Linkowski P, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):559-73 (38 ref.) **(Fre)**

[Different effects of tricyclic (clomipramine and amitriptyline) and tetracyclic (maprotiline) antidepressors on the release of thyroid stimulating hormone, prolactin and growth hormone to thyrostimulating releasing hormone in patients with psychoaffective disorders (author's transl)] Schlienger JL, et al. **Acta Psychiatr Belg** 1980 Sep-Oct; 80(5):584-99 (Eng. Abstr.) **(Fre)**

[Pharmacokinetic study of delayed-action lithium in affective psychoses] Molcan J, et al. **Agressologie** 1980;21(A):11-4 (Eng. Abstr.) **(Ger)**

AGGRESSION

The septal forebrain and the inhibitory modulation of attack and defense in the rat. A review. Albert DJ, et al. **Behav Neural Biol** 1980 Dec; 30(4):357-88 (192 ref.)

Ergot drugs suppress plasma prolactin and lactation but not aggression in parturient mice. Mann M, et al. **Horm Behav** 1980 Dec; 14(4):[illegible]9-28

The psychopharmacology of aggression and social behavior. Symposium of the International Society for Research on Aggression. July 12, 1980, Groningen, The Netherlands. **Pharmacol Biochem Behav** 1981; 14 Suppl 1:1-124

6-hydroxydopamine and aggression in cats. Beleslin DB, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:29–32

The effects of antidepressants on aggressiveness induced by social deprivation in mice. Delini-Stula A, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:33–41

Drug effects on attack defense and escape in mice. Kršiak M, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:47–52

Involvement of the GABAergic system on shock-induced aggressive behavior in two strains of mice. Puglisi-Allegra S, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:13–8

Tryptophan deprivation: effects on mouse-killing and reactivity in the rat. Vergnes M, et al. **Pharmacol Biochem Behav** 1981; 14 Suppl 1:19–23

Subchronic treatment with the tricyclic antidepressant DMI increases isolation-induced fighting in rats. Willner P, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):475–9

Cerebrospinal fluid amine metabolites and cyclic nucleotides in human aggression [proceedings] Brown GL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):63–5

Drug regimens facilitating aggression: behavior, amine, and receptor alterations [proceedings] Eichelman B. **Psychopharmacol Bull** 1981 Jan; 17(1):58–60

Discussion of paper by Dr. Klaus Miczek [proceedings] McKinney WT Jr. **Psychopharmacol Bull** 1981 Jan;17(1):62–3

Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Miczek KA. **Psychopharmacol Bull** 1981 Jan; 17(1):60–2

Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children [proceedings] Platt JE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):123–5

Changes of response to dopaminergic drugs in rats submitted to REM-sleep deprivation. Tufik S. **Psychopharmacology (Berlin)** 1981; 72(3):257–60

Aggressive behavior of the rat induced by repeated administration of cadmium. Arito H, et al. **Toxicol Lett** 1981 Mar;7(6):457–61

[Psychotropic drugs and imprisonment in a psychiatric hospital for political reasons] Drucker H. **Acta Med Leg Soc (Liege)** 1980; 30(1):189–210 **(Fre)**

[The medical marking of the body. Or when the physician becomes the stigmatizer] Lenoir L, et al. **Acta Med Leg Soc (Liege)** 1980; 30(1):43–69 **(Fre)**

AMINO ACIDS

Determination of the N-terminal amino acids of ribosomal proteins after gel electrophoretical purification. Etzold G, et al. **Acta Biol Med Ger** 1980;39(11–12):1143–6

Rapid separation of amino acid phenylthiohydantoins by isocratic high-performance liquid chromatography. Tarr GE. **Anal Biochem** 1981 Feb;111(1):27–32

Amino acid transport, Na+/K+-ATPASE, and TAT induction in monolayer cultures of hepatocytes from developing rats. Bellemann P, et al. **Ann NY Acad Sci** 1980;349:385–6

Excitatory amino acid transmitters. Watkins JC, et al. **Annu Rev Pharmacol Toxicol** 1981;21:165–204 (294 ref.)

Plasma tryptophan and five other amino acids in depressed and normal subjects. DeMyer MK, et al. **Arch Gen Psychiatry** 1981 Jun; 38(6):642–6

Regulation of small RNAs in Escherichia coli. Alteration in the intracellular concentrations of small RNAs during amino acid and energy starvation. Pao CC, et al. **Biochim Biophys Acta** 1981 Mar 26; 653(1):1–8

The release of endogenous amino acids into the vitreous of the intact eye of the albino rat: effect of light, potassium, and ouabain. Coull BM, et al. **Brain Res** 1981 Apr 6;210(1–2):301–9

Regional release of [3H]adenosine derivatives from rat brain in vivo: effect of excitatory amino acids, opiate agonists, and benzodiazepines. Jhamandas K, et al. **Can J Physiol Pharmacol** 1980 Nov; 58(11):1262–78

The postexcitatory effects of acidic amino acids on spinal neurones. McLennan H, et al. **Can J Physiol Pharmacol** 1981 Mar; 59(3):239–43

Interaction between amino acid induced and K+-induced depolarization of primary afferents in the bullfrog spinal cord. Shefner SA, et al. **Can J Physiol Pharmacol** 1980 Nov;58(11):1286–94

Evidence that the depolarization of glial cells by inhibitory amino acids is caused by an efflux of K+ from neurones. Hösli L, et al. **Exp Brain Res** 1981;42(1):43–8

The radioautographical localization in the vertebrate retina of [3H]-(+ or −)-cis-aminocyclohexane carboxylic acid (ACHC); a selective inhibitor of neuronal GABA transport. Cunningham J, et al. **Exp Eye Res** 1981 Apr;32(4):445–50

Metabolic control for maintaining NAD in rats fed on tryptophan-limiting amino acid diets. Shibata K, et al. **J Nutr Sci Vitaminol (Tokyo)** 1980; 26(6):571–84

Plasma and erythrocyte concentrations of free amino acids in adult humans administered abuse doses of aspartame. Stegink LD, et al. **J Toxicol Environ Health** 1981 Feb;7(2):291–305

Inhibition of enkephalin-degrading enzymes from rat brain and of thermolysin by amino acid hydroxamates. Blumberg S, et al. **Life Sci** 1981 Jan 19;28(3):301–6

Pharmacological antagonists of excitant amino acid action. Evans RH, et al. **Life Sci** 1981 Mar 23;28(12):1303–8

Characteristics of synaptosomal tyrosine uptake in various brain regions: effect of other amino acids. Morre MC, et al. **Life Sci** 1981 Jan 5; 28(1):65–75

Adsorption of amino acid entantiomers by Na-montmorillonite. Friebele E, et al. **Orig Life** 1981 Mar–Jun;11(1–2):173–84

[Fragile site Xq27 and metabolism of monocarbons. Significant decrease of the frequency of chromosomal gaps by treatment in vitro and in vivo] Lejeune J, et al. **C R Acad Sci [D] (Paris)** 1981 Feb 16; 292(7):491–3 (Eng. Abstr.) **(Fre)**

[A comparative analysis of the proteins of wheat, rye and Triticale T275 and T294. III. Content of tryptophan and tyrosine in gliadines and glutenines and N-end amino acids of gliadine fraction (author's transl)] Górski A, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979; 34:311–6 (Eng. Abstr.) **(Pol)**

[Dansylated amino acid separation by polyacrylamide gel electrophoresis] Svinarchuk FP, et al. **Prikl Biokhim Mikrobiol** 1981 Jan–Feb; 17(1):144–50 (Eng. Abstr.) **(Rus)**

AMITRIPTYLINE

MAO inhibition and control of anxiety following amitriptyline therapy. A pilot study. Davidson J, et al. **Acta Psychiatr Scand** 1981 Feb; 63(2):147–52

A double-blind comparison of nomifensine and amitriptyline in the treatment of depression. Ong SB, et al. **Acta Psychiatr Scand** 1981 Mar; 63(3):198–207

Comparison of the cardiovascular effects of amitriptyline and zimelidine using thoracic impedance cardiography. Christie JE, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):385–92

Zimelidine and amitriptyline in the treatment of depressive illness in general practice. Loudon JB, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):454–63

A double blind comparison of zimelidine and amitriptyline in endogenous depression. Montgomery SA, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):314–27

Cardiovascular, sedative and anticholinergic effects of amitriptyline and zimelidine in young and elderly volunteers. Swift CG, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):425–32

Effect of alcohol consumption and cigarette smoking on antidepressant levels of depressed patients. Linnoila M, et al. **Am J Psychiatry** 1981 Jun;138(6):841–2

alpha 2-Adrenoreceptors in rat brain are decreased after long-term tricyclic antidepressant drug treatment. Smith CB, et al. **Brain Res** 1981 Apr 6;210(1–2):413–8

Cyclobenzaprine: a possible mechanism of action for its muscle relaxant effect. Commissiong JW, et al. **Can J Physiol Pharmacol** 1981 Jan; 59(1):37–44

Treatment of fibromyositis with fluphenazine and amitriptyline: a preliminary report. Connolly RG. **Del Med J** 1981 Apr;53(4):189–91

Cardiovascular effects of mianserin and amitriptyline in healthy volunteers. Wester HA, et al. **Int J Clin Pharmacol Ther Toxicol** 1980 Dec;18(12):513–7

Inhibition of riboflavin metabolism in rat tissues by chlorpromazine, imipramine, and amitriptyline. Pinto J, et al. **J Clin Invest** 1981 May; 67(5):1500–6

A double-blind study of dothiepin hydrochloride (Prothiaden) and amitriptyline in out-patients with masked depression. Dahl LE, et al. **J Int Med Res** 1981;9(2):103–7

A comparison of the therapeutic and cardiovascular effects of a single nightly dose of Prothiaden (dothiepin, dosulepin) and Lentizol (sustained-release amitriptyline) in depressed elderly patients. Khan AU. **J Int Med Res** 1981;9(2):108–12

Possible involvement of cyclic AMP and frontal cortex in amitriptyline mediated suppression of the hypotensive effect of clonidine. Greenberg S, et al. **Life Sci** 1980 Dec 22–29;27(25–26):2669–74

In defense of 'Limbitrol' [letter] Dudley RD Jr. **Minn Med** 1980 Oct; 63(10):713

Comparison of the antimuscarinic activity of mianserin and amitriptyline in the cat superior cervical ganglion. Kwok YH, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):161–4

Relationship between response to phenelzine and MAO inhibition in a clinical trial of phenelzine, amitriptyline and placebo. Raft D, et al. **Neuropsychobiology** 1981;7(3):122–6

Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors. Tang SW, et al. **Psychiatry Res** 1981 Apr;4(2):129–38

On the clinical response/serum level relationship for antidepressants I: Amitriptyline. Dutt JE. **Psychopharmacol Bull** 1981 Apr;17(2):42–55

Effects of phenelzine and amitriptyline on depression [proceedings] Paykel ES, et al. **Psychopharmacol Bull** 1981 Jan;17(1):104–6

The relationships between clinical response, psychophysiological variables and plasma levels of amitriptyline and diazepam in neurotic outpatients. Johnstone EC, et al. **Psychopharmacology (Berlin)** 1981;72(3):233–40

Medical therapies for mood disorders alter the blood–brain barrier. Preskorn SH, et al. **Science** 1981 Jul 24;213(4506):469–71

[Therapy of elderly depressive patients. Lofepramine and amitriptyline under double-blind conditions] Jessel HJ, et al. **ZFA (Stuttgart)** 1981 Apr 10;57(10):784–8 **(Ger)**

AMOBARBITAL

Habituation of the head–poke response: effects of an amphetamine–barbiturate mixture, PLG and fenfluramine. Koek W, et al. **Psychopharmacology (Berlin)** 1981;72(3):251–6

AMPHETAMINE

Investigations on the interaction between cyproheptadine and amphetamine. Cenajek D, et al. **Acta Physiol Pol** 1980;31(5):561–6

A primate analogue of amphetamine–induced behaviors in humans. Haber S, et al. **Biol Psychiatry** 1981 Feb;16(2):181–96

Effect of amphetamine on the metabolism and incorporation of [3H]–thymidine into DNA of developing rat brain. Béndek G, et al. **Dev Neurosci** 1981;4(1):55–65

Detection of amphetamine in bloodstains, semen, seminal stains, saliva, and saliva stains. Smith FP. **Forensic Sci Int** 1981 May–Jun; 17(3):225–8

Analysis of amphetamine effects on agonistic and affiliative behavior in squirrel monkeys (Saimiri sciureus). Miczek KA, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:103–7

An analysis of visual object reversal learning in the marmoset after amphetamine and haloperidol. Ridley RM, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):345–51

Computer analyzed EEG in amphetamine–responsive hyperactive children. McIntyre HB, et al. **Psychiatry Res** 1981 Apr;4(2):189–97

Habituation of the head–poke response: effects of an amphetamine–barbiturate mixture, PLG and fenfluramine. Koek W, et al. **Psychopharmacology (Berlin)** 1981;72(3):251–6

[The influence of trihexyphenidyl on the antiamphetaminic action of fluphenazine (author's transl)] Kleinrok Z, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979;34:341–5 (Eng. Abstr.) **(Pol)**

[The influence of atropine on the antiamphetaminic action of fluphenazine (author's transl)] Rechberger T, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979;34:333–9 (Eng. Abstr.) **(Pol)**

[Effect of certain pharamcologic preparations and different lighting setups on human work capacity] Bogatova RI, et al. **Kosm Biol Aviakosm Med** 1981 Jan–Feb;15(1):92–3 **(Rus)**

AMPHETAMINES

Recommendations for demand reduction of amphetamines. Streit F. **Chem Depend** 1980;4(1–2):135–43

Quantitation of biologically important primary amines as their isothiocyanate derivatives by gas chromatography using nitrogen detector and validation by selected ion monitoring. Narasimhachari N, et al. **Clin Chim Acta** 1981 Mar 5;110(2–3):235–43

Amphetamine radioimmunoassay––structure versus reactivity. Budd RD. **Clin Toxicol** 1981;18(3):299–316

A death due to 4–bromo–2,5–dimethoxyamphetamine. Winek CL, et al. **Clin Toxicol** 1981;18(3):267–71

Effects of the optical isomers of 2–amino–3–fluoro–1–phenylpropane (monofluoroamphetamine) hydrochloride on uptake and release of dopamine in rat striatum in vitro. Benderly A, et al. **Experientia** 1981 Mar 15;37(3):294–5

The effects of p–chloroamphetamine administration on locomotor activity and serotonin in neonatal and adult rats. Lucot JB, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):738–44

Estrogen potentiates the stereotypy induced by dopamine agonists in the rat. Chiodo LA, et al. **Life Sci** 1981 Feb 16;28(7):827–35

DOM and related 2,5–dimethoxy–4–alkylphenylisopropylamines: behavioral and serotonin receptor properties. Glennon RA, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):287–92

Effects of dorsolateral tegmental lesions on amphetamine– and lithium–induced taste aversions. Wellman PJ, et al. **Physiol Behav** 1981 Feb;26(2):341–4

The effect of altered dopaminergic activity on food intake in the rat: evidence for an optimal level of dopaminergic activity for behavior. Zigmond MJ, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):351–62

The metabolism of 3–methoxyamphetamine in dog, monkey and man. Midha KK, et al. **Xenobiotica** 1981 Feb;11(2):137–46

ANGER

The septal forebrain and the inhibitory modulation of attack and defense in the rat. A review. Albert DJ, et al. **Behav Neural Biol** 1980 Dec; 30(4):357–88 (192 ref.)

ANOREXIA NERVOSA

Schizophrenia and anorexia nervosa. Hsu LK, et al. **J Nerv Ment Dis** 1981 May;169(5):273–6

ANTIDEPRESSIVE AGENTS

Controlled cross–over study of a 5–HT uptake inhibiting and an NA uptake inhibiting antidepressant. Aberg A. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):244–55

Effects of antidepressants on cardiac function. Burgess CD. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):370–9

Some current problems related to the mode of action of antidepressant drugs. Carlsson A. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):63–6

Comparison of the cardiovascular effects of amitriptyline and zimelidine using thoracic impedance cardiography. Christie JE, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):385–92

The action of antidepressant drugs on 5–hydroxy–tryptamine uptake by platelets––relationship to therapeutic effect. Coppen A, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):236–43

Zimelidine to geriatric patients: a pharmacokinetic and clinical study. Dehlin O, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):410–24

Zimelidine vs maprotiline in depressed outpatients. A preliminary report. d'Elia G, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):225–35

Pre– and postsynaptic effects of zimelidine and norzimelidine on the serotoninergic system: single cell studies in the rat. de Montigny C, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):79–90

Safety data on zimelidine hydrochloride following an overdose. Georgotas A, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):257–61

Influence of depression and antidepressants on weight. Gottfries CG. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):353–6

Critical flicker fusion (CFF) test for sedative effect of antidepressants. Holmberg G. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):289–301

Depression: treatment compliance in general practice. Johnson DA. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):447–53

Beta–adrenergic stimulation and antidepressant activity. Lecrubier Y, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):173–8

Cardiovascular effects of zimelidine and other antidepressant in conscious rats. Lindbom LO, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):380–4

Zimelidine and amitriptyline in the treatment of depressive illness in general practice. Loudon JB, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):454–63

Effect of antidepressants, lithium and electroconvulsive treatment on rat serum prolactin levels. Meltzer HY, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):100–21

The antidepressant efficacy of zimelidine and maprotiline. Montgomery SA, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):219–24

A double blind comparison of zimelidine and amitriptyline in endogenous depression. Montgomery SA, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):314–27

Sedative/anxiolytic effects of antidepressants in animals. Ogren SO, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):277–88

Comparison of peripheral anticholinergic effects of antidepressants: dry mouth. Rafaelsen OJ, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):364–9

Central pre– and postsynaptic monoamine receptors in antidepressant therapy. Svensson TH, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):67–78

Cardiovascular, sedative and anticholinergic effects of amitriptyline and zimelidine in young and elderly volunteers. Swift CG, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):425–32

Zimelidine: comparison of different dosage regimes in general practice. Watson JM, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):464–70

Antidepressant drug therapy. DeGennaro M, et al. **Am J Nurs** 1981 Jul; 81(7):1304–10

Antidepressants: old drugs, new uses. Harris E. **Am J Nurs** 1981 Jul; 81(7):1308–9

Metabolism of zimelidine in rat, dog and man. Identification and synthesis of the principal metabolites. Lundström J, et al. **Arzneimittelforsch** 1981; 31(3):486–94

Determination of clovoxamine concentration in human plasma by electron capture gas chromatography. Hurst HE, et al. **Clin Chem** 1981 Jul; 27(7):1210–2

Effect of piribedil (ET–495) on plasma norepinephrine: relationship to antidepressant response. Reus VI, et al. **Commun Psychopharmacol** 1980; 4(3):207–13

The antidepressant effect of lithium. Arieli A, et al. **Curr Dev Psychopharmcol** 1981;6:165–90 (58 ref.)

Adverse effects of antidepressant drugs. Part 2: 'Second generation' antidepressants and rational decision making in antidepressant therapy.

Blackwell B. **Drugs** 1981 Apr;21(4):273–82 (120 ref.)
Classification, biochemistry of depression and the mode of action of antidepressant drugs. Okasha A. **Egypt J Psychiatry** 1979 Apr; 2(1):3–18
Effects of antidepressant drugs on different receptors in the brain. Hall H, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):393–407
Radioimmunoassay and pharmacokinetic profile of bupropion in the dog. Butz RF, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):602–10
Effects of acutely and chronically administered antidepressants on the clonidine-induced decrease in rat brain 3-methoxy-4-hydroxyphenylethylene-glycol sulphate content. Sugrue MF. **Life Sci** 1981 Jan 26;28(4):377–84
Acceleration of beta-receptor desensitization in combined administration of antidepressants and phenoxybenzamine. Crews FT, et al. **Nature** 1981 Apr 30;290(5809):787–9
Evaluation of the clinical efficacy of single daily doses of antidepressants. De Maio D, et al. **Prog Neuropsychopharmacol** 1980;4(6):607–12
The neuro- and cardiovascular pharmacology of RS-51324, a potential antidepressant. Wallach MB, et al. **Prog Neuropsychopharmacol** 1980; 4(6):569–84
Clinical efficacy of the new antidepressant bupropion (Wellbutrin) [proceedings] Halaris AE, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):140–2
Second generation antidepressants: a clinical pharmacotherapeutic research strategy [proceedings] Shopsin B. **Psychopharmacol Bull** 1981 Jan;17(1):33–5
The pharmacological treatment of schizoaffective disorder-depressed: a review of the literature [proceedings] Spiker DG. **Psychopharmacol Bull** 1981 Jan;17(1):75–8
[Different effects of tricyclic (clomipramine and amitriptyline) and tetracyclic (maprotiline) antidepressors on the release of thyroid stimulating hormone, prolactin and growth hormone to thyrostimulating releasing hormone in patients with psychoaffective disorders (author's transl)] Schlienger JL, et al. **Acta Psychiatr Belg** 1980 Sep–Oct; 80(5):584–99 (Eng. Abstr.) **(Fre)**
[Reflections on the classification of antidepressive agents] Simon P. **Prog Neuropsychopharmacol** 1980;4(4–5):503–5 (Eng. Abstr.) **(Fre)**
[Comparative evolution of prolactin plasma levels during antidepressant treatment (author's transl)] Vandel B, et al. **Therapie** 1981 Jan–Feb; 36(1):87–94 (Eng. Abstr.) **(Fre)**
[Pharmacological treatment of affective disorders (author's transl)] Beckmann H. **Nervenarzt** 1981 Mar;52(3):135–46 **(Ger)**
[Psychopathologic changes during 20 days of antidepressive or neuroleptic therapy] Woggon B. **Psychiatr Clin (Basel)** 1980;13(3–4):150–64 (Eng. Abstr.) **(Ger)**
[Psychotropic agents and the neuroendocrine system] Matussek N. **Verh Dtsch Ges Inn Med** 1980;86:100–6 **(Ger)**
[Effectiveness of treating early-onset malignant schizophrenia with psychotropic drugs and their combinations] Sobolev ES, et al. **Zh Nevropatol Psikhiatr** 1981;81(1):114–21 (Eng. Abstr.) **(Rus)**

ANXIETY

The treatment of phobic anxiety by zimelidine. Evans L, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):342–5
Anxiety and/or the depressive syndromes. Kline NS. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):271–6
A pilot study of the effect of the 5-HT-uptake inhibitor, zimelidine, on phobic anxiety. Koczkas S, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):328–41
Maternal psychological and physiologic correlates of fetal-newborn health status. Lederman E, et al. **Am J Obstet Gynecol** 1981 Apr 15; 139(8):956–8
Antianxiety, sedative hypnotics. Cooper Sa. **Clin Prevent Dent** 1981 Jan–Feb;3(1):25–6
Oxazepam in the treatment of anxiety associated with depression: results of treatment in 1600 cases (Studies in depression, VI). Bailey HR, et al. **Curr Med Res Opin** 1981;7(3):156–63
Tranquilizers not overprescribed for anxiety [news] Korcok M. **JAMA** 1981 Jul 3;246(1):14
Methods and methodological considerations in measuring anti-anxiety effects of tranquilizing drugs. Debus G, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):391–404
Responders and nonresponders to chlordiazepoxide and placebo: a discriminant function analysis. Downing RW, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):405–15
Preoperative anxiety and its management in orostomatology. Srivastava RP, et al. **Uttar Pradesh State Dent J** 1980 Oct;11(4):167–71

ANXIETY DISORDERS

MAO inhibition and control of anxiety following amitriptyline therapy. A pilot study. Davidson J, et al. **Acta Psychiatr Scand** 1981 Feb; 63(2):147–52
Catecholamines and monoamine oxidase activity in anxiety. Mathew RJ, et al. **Acta Psychiatr Scand** 1981 Mar;63(3):245–52
Antidepressants: old drugs, new uses. Harris E. **Am J Nurs** 1981 Jul; 81(7):1308–9
Clobazam and diazepam in anxiety. Rickels K, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):95–100
Relapse after short-term drug therapy in neurotic outpatients. Rickels K, et al. **Int Pharmacopsychiatry** 1980;15(3):186–92
Double-blind comparison of ketazolam and placebo using once-a-day dosing. Cohn JB, et al. **J Clin Pharmacol** 1980 Nov–Dec; 20(11–12):676–80
Double-blind clinical assessment of alprazolam, a new benzodiazepine derivative, in the treatment of moderate to severe anxiety. Greiss KC, et al. **J Clin Pharmacol** 1980 Nov–Dec;20(11–12):693–9
A comparison of prazepam, diazepam, lorazepam and placebo in anxious outpatients in non-psychiatric private practices. Zung WW, et al. **J Clin Psychiatry** 1981 Jul;42(7):280–4
Comparison of the therapeutic effect, tolerance and safety of ketazolam and diazepam administered for six months to out-patients with chronic anxiety neurosis. Fabre LF, et al. **J Int Med Res** 1981;9(3):191–8
New studies confirm MAO inhibitors' efficacy in treating severe anxiety [news] González ER. **JAMA** 1981 May 8;245(18):1799–801
[A double blind trial : oxprenolol/diazepam (author's transl)] Scharbach H. **Encephale** 1981;7(1):51–8 (Eng. Abstr.) **(Fre)**
[Treatment of chronic anxiety by behaviour therapy and with beta-blocking agents - an empirical study (author's transl)] Butollo W. **Psychother Psychosom Med Psychol** 1981 Mar;31(2):53–7 (Eng. Abstr.) **(Ger)**

APOMORPHINE

Resumption of prolactin secretion after dopaminergic inhibition: differential effects of dopamine and its agonists. Woolf PD. **Am J Physiol** 1981 Jun;240(6):E700–4
Avoidance learning and mechanism of the protective effect of apomorphine against hypoxia. Boismare F, et al. **Aviat Space Environ Med** 1981 May;52(5):299–303
hypobaric hypoxia: central catecholamine levels and cortical PO2 and avoidance response in rats treated with apomorphine. Saligaut C, et al. **Aviat Space Environ Med** 1981 Mar;52(3):166–70
The effects of chloral hydrate anesthesia on the metabolic response in the substantia nigra to apomorphine. Grome JJ, et al. **Brain Res** 1981 Jun 9;214(1):223–8
Effect of apomorphine hydrochloride administration on serum concentrations of prolactin and growth hormone in cattle. Gorewit RC. **Experientia** 1981 Feb 15;37(2):204–6
Estrogen potentiates the stereotypy induced by dopamine agonists in the rat. Chiodo LA, et al. **Life Sci** 1981 Feb 16;28(7):827–35
Blink rates and receptor supersensitivity. Karson CN, et al. **Neuropharmacology** 1981 Jan;20(1):91–3
Apomorphine-induced circling behaviour in hamsters following unilateral injection of scrapie gent in the striatum. Gorde JM, et al. **Neurosci Lett** 1981 Mar 10;22(2):201–4
Different effects of apomorphine on locomotor activity in C57BL/6 and DBA/2 mice. Sansone M, et al. **Pharmacol Biochem Behav** 1981 May; 14(5):741–3
Pharmacokinetic study of apomorphine-induced stereotypy in food deprived rats. Watanabe H, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):493–6
Use of the intracerebral injection technique to elucidate mechanisms of apomorphine climbing and its antagonism in the mouse. Costall B, et al. **Psychopharmacology (Berlin)** 1981;73(1):91–4
Repeated electroconvulsive shock prevents the sedative effect of small doses of apomorphine. Serra G, et al. **Psychopharmacology (Berlin)** 1981; 73(2):194–6
The effects of electroconvulsive shock on the discriminative stimulus properties of d-amphetamine and apomorphine: evidence for dopamine receptor alteration subsequent ECS. White DK, et al. **Psychopharmacology (Berlin)** 1981;73(3):211–4
[Evaluation of motor behavior in conditions of hyperprolactinemia] Rampello L, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):297–301 (Eng. Abstr.) **(Ita)**
[Diphasic action of apomorphine on motility in the rat. II. Time aspects of the effect of a single dose] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):381–6 (Eng. Abstr.) **(Ita)**
[Diphasic action of apomorphine on motility of the rat. I. Dose-effect relationship in exploratory and basal motility] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):374–80 (Eng. Abstr.) **(Ita)**

APPETITE

Cholecystokinin acts on the hypothalamic 'noradrenergic system' involved in feeding. McCaleb ML, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):47–9
[Effect of adrenergic beta-receptor blockers on the oxygen consumption or narcotized rats and the calorigenic action of adrenaline] Ankermann H. **Acta Biol Med Ger** 1980;39(11–12):1227–34 (Eng. Abstr.) **(Ger)**

AROMATIC AMINO ACID DECARBOXYLASES

New and highly sensitive assay for L-5-hydroxytryptophan decarboxylase activity by high-performance liquid chromatography-voltammetry. Rahman MK. et al. **J Chromatogr** 1980 Dec 12;221(2):265-70

The interaction of 2,3,4-trihydroxybenzylhydrazine with DOPA decarboxylase from pig kidney. Borri Voltattorni C, et al. **Life Sci** 1981 Jan 5;28(1):103-8

AROUSAL

Cardiovascular and sympathetic responses to PGF2 alpha injection into hypothalamic nuclei. Feuerstein G, et al. **Brain Res Bull** 1981 Mar; 6(3):203-7

Effect of methylphenidate on young adult's vigilance and event-related potentials. Coons HW, et al. **Electroencephalogr Clin Neurophysiol** 1981 Apr;51(4):373-87

ATTENTION

Effect of methylphenidate on young adult's vigilance and event-related potentials. Coons HW, et al. **Electroencephalogr Clin Neurophysiol** 1981 Apr;51(4):373-87

Residual attentional deficits in adolescents. Clampit MK. **J Learn Disabil** 1981 Apr;14(4):218-9

A simple system for control of the continuous performance test in psychopharmacological research. Aman MC, et al. **Prog Neuropsychopharmacol** 1980;4(6):621-6

Dopaminergic involvement in attention. A novel animal model. Katz RJ, et al. **Prog Neuropsychopharmacol** 1980;4(6):585-90

AUTISM

Serum serotonin, free tryptophan and plasma cyclic AMP levels in autistic children -with special reference to their relation to hyperkinesia. Hoshino Y, et al. **Fukushima J Med Sci** 1979;26(3-4):79-91

AUTISM, INFANTILE

Folic acid and B12 in autism and neuropsychiatric disturbances of childhood. Lowe TL, et al. **J Am Acad Child Psychiatry** 1981 Winter; 20(1):104-11

AVOIDANCE LEARNING

Avoidance learning and mechanism of the protective effect of apomorphine against hypoxia. Boismare F, et al. **Aviat Space Environ Med** 1981 May;52(5):299-303

hypobaric hypoxia: central catecholamine levels and cortical PO2 and avoidance response in rats treated with apomorphine. Saligaut C, et al. **Aviat Space Environ Med** 1981 Mar;52(3):166-70

Hippocampal lesion effects on conditioned taste aversion and pituitary-adrenal activity in rats. Smotherman WP, et al. **Behav Brain Res** 1981 Jan;2(1):33-48

Behavioral activity of met-enkephalin and ACTH4-10 and other peptides containing a phenylalanine and methionine residue. Rigter H, et al. **Biochem Biophys Res Commun** 1981 Jan 30;98(2):424-30

L-dopa enhances acquisition of an inhibitory avoidance response. Martinez JL Jr, et al. **Commun Psychopharmacol** 1980;4(3):215-8

Conditioned social aversion in the male Mongolian gerbil (Meriónes unguiculatus). Pettijohn TF. **J Comp Physiol Psychol** 1981 Apr; 95(2):228-39

Aversion to the reinforcer differentially affects conditioned reinforcement and instrumental responding. Wilson CL, et al. **J Exp Psychol [Anim Behav]** 1981 Apr;7(2):165-74

Effects of N-substituted analogs and metabolites of phencyclidine on avoidance behavior in the rat. Shannon HE, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):55-62

Adrenal steroids and extinction behavior: antagonism by progesterone, deoxycorticosterone and dexamethasone of a specific effect of corticosterone. Bohus B, et al. **Life Sci** 1981 Jan 26;28(4):433-40

Passive avoidance performance correlates with catecholamine turnover in discrete limbic brain regions. Kovács GL, et al. **Life Sci** 1981 Mar 9;28(10):1109-16

Retention of passive avoidance behavior in rats following alpha- and gamma-endorphin administration: effects of post-learning treatments. Kovács GL, et al. **Neurosci Lett** 1981 Feb 23;22(1):79-82

The effect of para-chlorophenylalanine and scopolamine on passive avoidance in chicks. Mattingly BA, et al. **Pharmacol Biochem Behav** 1981 May;14(5):669-76

Effects of chlorpromazine on escape and avoidance responses: a closer look. Spirduso WW, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):433-8

Septal lesions and avoidance behavior: genetic, neurochemical and behavioral considerations. Donovick PJ, et al. **Physiol Behav** 1981 Mar; 26(3):495-507

Effects of desglycinamide-lysine vasopressin on a conditioned taste aversion in rats. Vawter MP, et al. **Physiol Behav** 1980 Dec; 25(6):851-4

Effects of dorsolateral tegmental lesions on amphetamine- and lithium-induced taste aversions. Wellman PJ, et al. **Physiol Behav** 1981 Feb;26(2):341-4

Studies on the role of serotonin in avoidance learning [proceedings] Ogren SO. **Psychopharmacol Bull** 1981 Jan;17(1):17-9

Changes in action of tricyclic and tetracyclic antidepressants: desipramine and mianserin, on avoidance behavior in the course of the chronic treatment. Hano J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):265-8

Lesion of serotonergic neurons antagonizes clonidine induced suppression of avoidance behavior and locomotor activity in rats. Kostowski W, et al. **Psychopharmacology (Berlin)** 1981;73(3):261-4

[Hypobaric hypoxia effects on a conditioned avoidance response and on ADP, AMP dopamine and noradrenaline cerebral levels in rats treated or not with naftidrofuryl (author's transl)] Boismare F, et al. **J Pharmacol** 1981 Jan-Mar;12(1):51-7 (Eng. Abstr.) **(Fre)**

[1,6-Disubstituted 3-methylquinoxalin-2(1H)-ones. Effect on acquisition and modification of a conditioned avoidance response in the rat] Alamanni MC, et al. **Farmaco [Sci]** 1981 May;36(5):359-71 (Eng. Abstr.) **(Ita)**

[Formation and preservation of conditioned taste aversion in dogs] Vavilova NM, et al. **Zh Vyssh Nerv Deiat** 1981 Jan-Feb;31(1):171-2 **(Rus)**

BEHAVIOR

Specific norepinephrine and serotonin uptake inhibitors in man: a crossover study with pharmacokinetic, biochemical, neuroendocrine and behavioral parameters. Potter WZ, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):152-65

Effects of lithium carbonate on methylphenidate-induced mood, behavior, and cognitive processes. Huey LY, et al. **Psychopharmacology (Berlin)** 1981;73(2):161-4

EEG and behavioral effects of pirenzepine in normal volunteers. Fink M, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):39-46

BEHAVIOR, ANIMAL

Biochemical specificity of septal hyperreactivity: a behavioral discrimination. Chafetz MD, et al. **Behav Brain Res** 1981 May; 2(3):409-20

Behavioral supersensitivity to methamphetamine following chronic treatment with (—)-sulpiride in the rat. Montanaro N, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):401-6

Behavioral effects of opiates: a pharmacogenetic analysis. Oliverio A, et al. **Curr Dev Psychopharmcol** 1981;6:45-64 (78 ref.)

Behavioral and neurochemical effects of neonatal administration of monosodium L-glutamate in mice. Dawson R Jr, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):71-84

Role of monoamines in behavior of reserpinized rats given tranylcypromine stereoisomers. Smith DF. **J Neural Transm** 1981; 50(2-4):193-200

Unexpected differences between mazindol and its homologs on biochemical and behavioral responses. Heikkila RE, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):745-9

Prenatal exposure to imipramine alters early behavioral development and beta adrenergic receptors in rats. Jason KM, et al. **J Pharmacol Exp Ther** 1981 May;217(2):461-6

Neostriatal dopamine receptor loss and behavioral deficits in the senescent rat. Cubells JF, et al. **Life Sci** 1981 Mar 16;28(11):1215-8

Individual differences in effects of tricyclic antidepressants and anticholinergic drugs on operant behavior in the squirrel monkey. McKearney JW. **Life Sci** 1981 May 4;28(18):2049-54

Dorsal tegmental bundle destruction: effects on operant behavior, brain catecholamine levels, and behavioral suppression produced by adrenergic agonists. Morris MD, et al. **Life Sci** 1980 Dec 22-29; 27(25-26):2621-6

Neurotensin blocks certain amphetamine-induced behaviours. Ervin GN, et al. **Nature** 1981 May 7;291(5810):73-6

Nigral-derived muscimol circling—ipsiversive, contraversive or controversial? [letter] Starr MS, et al. **Nature** 1981 Apr 16; 290(5807):610

Differential electrophysiological and behavioral responses to optically active derivatives of phencyclidine. Marwaha J, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jan;315(3):203-9

The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Yamada K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):155-60

Phenytoin: plasma levels and behavioral changes associated with suppression of auditory evoked potentials in the cat. Faingold CL, et al. **Neuropharmacology** 1981 May;20(5):445-9

Behavioural, ECoG spectrum power and body temperature effects of BW 245C, a prostaglandin analogue after intraventricular microinjection in chicks. Rotiroti D, et al. **Neuropharmacology** 1981 May;20(5):517-20

Dopaminergic mediation of reward: evidence gained using a natural reinforcer in a behavioral contrast paradigm. Royall DR, et al. **Neurosci Lett** 1981 Jan 20;21(2):223–9

Influence of substance P on the behavioral changes induced by haloperidol in rats. Jolicoeur FB, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):103–7

DOM and related 2,5–dimethoxy–4–alkylphenylisopropylamines: behavioral and serotonin receptor properties. Glennon RA, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):287–92

Pharmaco–ethological analysis of social behaviour of isolated mice. Poshivalov VP. **Pharmacol Biochem Behav** 1981;14 Suppl 1:53–9

Tryptophan deprivation: effects on mouse–killing and reactivity in the rat. Vergnes M, et al. **Pharmacol Biochem Behav** 1981; 14 Suppl 1:19–23

Lack of specificity of an animal behavior model for hallucinogenic drug action. White FJ, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):339–43

Role of the pulvinar–lateral posterior nucleus complex in turning behavior. Motles E, et al. **Physiol Behav** 1980 Dec;25(6):921–9

Intracellular injection of t he catalytic subunit of cyclic AMP–dependent protein kinase simulates facilitation of transmitter release underlying behavioral sensitization in Aplysia. Castellucci VF, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7492–6

Drug regimens facilitating aggression: behavior, amine, and receptor alterations [proceedings] Eichelman B. **Psychopharmacol Bull** 1981 Jan; 17(1):58–60

Discussion of paper by Dr. Klaus Miczek [proceedings] McKinney WT Jr. **Psychopharmacol Bull** 1981 Jan;17(1):62–3

Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Miczek KA. **Psychopharmacol Bull** 1981 Jan; 17(1):60–2

Effects of single and long–term haloperidol administration on open field behavior of rats. Bernardi MM, et al. **Psychopharmacology (Berlin)** 1981; 73(2):171–5

Pharmacologic manipulations of brain catecholamines and the behavior of Callithrix jacchus (marmoset). Campos F, et al. **Psychopharmacology (Berlin)** 1981;73(3):252–6

Effects of chlorpromazine on food–maintained and observing behavior. Dearing ME, et al. **Psychopharmacology (Berlin)** 1981;73(3):281–5

Effects of neonatal 6–hydroxydopamine treatment on catecholamine levels and behavior during development and adulthood. Fobes JL, et al. **Psychopharmacology (Berlin)** 1981;73(1):27–30

Use of 6–hydroxydopamine to deplete brain catecholamines in the rhesus monkey: effects on urinary catecholamine metabolites and behavior. Kraemer GW, et al. **Psychopharmacology (Berlin)** 1981;73(1):1–11

Effect of 5,7–dihydroxytryptamine on serotonergic control of prolactin secretion and behavior in rats. Kuhn CM, et al. **Psychopharmacology (Berlin)** 1981;73(2):188–93

Behavioral and biochemical studies of the scopolamine–induced reversal of neuroleptic activity. Ondrusek MG, et al. **Psychopharmacology (Berlin)** 1981;73(1):17–22

Peripheral correlates of serotonergically–influenced behaviors in vervet monkeys (Cercopithecus aethiops sabaeus). Raleigh MJ, et al. **Psychopharmacology (Berlin)** 1981;72(3):241–6

Effects of lithium on behavioral reactivity: relation to increases in brain cholinergic activity. Russell RW, et al. **Psychopharmacology (Berlin)** 1981;73(2):120–5

Two distinct central serotonin receptors with different physiological functions. Peroutka SJ, et al. **Science** 1981 May 15;212(4496):827–9

[Evaluation of motor behavior in conditions of hyperprolactinemia] Rampello L, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):297–301 (Eng. Abstr.) **(Ita)**

[Diphasic action of apomorphine on motility of the rat. I. Dose–effect relationship in exploratory and basal motility] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):374–80 (Eng. Abstr.) **(Ita)**

[Diphasic action of apomorphine on motility in the rat. II. Time aspects of the effect of a single dose] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):381–6 (Eng. Abstr.) **(Ita)**

[Catecholamines in the brain structures of rats responding differently to the 'open field' test] Belova TI, et al. **Biull Eksp Biol Med** 1981 Feb; 91(2):136–8 (Eng. Abstr.) **(Rus)**

BENACTYZINE

[Certain biochemical and behavioral effects of morphine in rats following amyzil administration] Bandman AL, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):185–8 (Eng. Abstr.) **(Rus)**

BENZAZEPINES

Facilitation of Neuromuscular transmission by calcium antagonists, diltiazem, nifedipine and verapamil, in the dog. Sato T, et al. **Arch Int Pharmacodyn Ther** 1981 Feb;249(2):235–46

Inhibitory action of calcium antagonists on ATP–dependent calcium uptake by the renal cortical microsomes. Dan T, et al. **Jpn J Pharmacol** 1980 Dec;30(6):913–7

[Effects of diltiazem on hemodynamics and His bundle electrogram in the anesthetized dog (author's transl)] Nagao T, et al. **Nippon Yakurigaku Zasshi** 1981 Feb;77(2):195–203 (Eng. Abstr.)**(Jpn)**

BENZODIAZEPINE TRANQUILIZERS

The benzodiazepine––GABA––chloride ionophore receptor complex: common site of minor tranquilizer action. Paul SM, et al. **Biol Psychiatry** 1981 Mar;16(3):213–29

Quantitative analysis of CM 6912 (ethyl loflazepate) and its metabolites in plasma and urine by chemical ionization gas chromatography mass spectrometry. Application to pharmacokinetic studies in man. Cautreels W, et al. **Biomed Mass Spectrom** 1980 Nov;7(11–12):565–71

Dependence on benzodiazepines. Tyrer P. **Br J Psychiatry** 1980 Dec; 137:576–7

Chlormethiazole and temazepam [letter] **Br Med J [Clin Res]** 1981 Mar 7;282(6266):825

Effect of maternal lorazepam on the neonate [letter] Johnstone M. **Br Med J [Clin Res]** 1981 Jun 13;282(6280):1973–4

Withdrawal reaction from clobazam. Petursson H, et al. **Br Med J [Clin Res]** 1981 Jun 13;282(6280):1931–2

Addiction to temazepam. Ratna L. **Br Med J [Clin Res]** 1981 Jun 6; 282(6279):1837–8

Regional release of [3H]adenosine derivatives from rat brain in vivo: effect of excitatory amino acids, opiate agonists, and benzodiazepines. Jhamandas K, et al. **Can J Physiol Pharmacol** 1980 Nov; 58(11):1262–78

Effects of uremia and hemodialysis on lormetazepam disposition. Kampf D, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):77–85

Clobazam and diazepam in anxiety. Rickels K, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):95–100

Temazepam: a review of its pharmacological properties and therapeutic efficacy as an hypnotic. Heel RC, et al. **Drugs** 1981 May; 21(5):321–40 (69 ref.)

gamma–Aminobutyric acid regulation of the benzodiazepine receptor: biochemical evidence for pharmacologically different effects of benzodiazepines and propyl beta–carboline–3–carboxylate. Ehlert FJ, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):593–5

Determination of benzodiazepines by derivative spectroscopy. Martínez D, et al. **J Anal Toxicol** 1981 Jan–Feb;5(1):10–3

Plasma concentrations of temazepam, a 3–hydroxy benzodiazepine, determined by electron–capture gas–liquid chromatography. Divoll M, et al. **J Chromatogr** 1981 Jan 2;222(1):125–8

Determination of bromazepam by gas–liquid chromatography and its application for pharmacokinetic studies in man. Klotz U. **J Chromatogr** 1981 Mar 13;222(3):501–6

Double–blind comparison of ketazolam and placebo using once–a–day dosing. Cohn JB, et al. **J Clin Pharmacol** 1980 Nov–Dec; 20(11–12):676–80

Double–blind clinical assessment of alprazolam, a new benzodiazepine derivative, in the treatment of moderate to severe anxiety. Greiss KC, et al. **J Clin Pharmacol** 1980 Nov–Dec;20(11–12):693–9

A comparison of prazepam, diazepam, lorazepam and placebo in anxious outpatients in non–psychiatric private practices. Zung WW, et al. **J Clin Psychiatry** 1981 Jul;42(7):280–4

Comparison of the therapeutic effect, tolerance and safety of ketazolam and diazepam administered for six months to out–patients with chronic anxiety neurosis. Fabre LF, et al. **J Int Med Res** 1981;9(3):191–8

The effect of bromazepam on psychomotor activity and subjective mood. Hobi V, et al. **J Int Med Res** 1981;9(2):89–97

Benzodiazepine withdrawal symptoms and propranolol. Tyrer P, et al. **Lancet** 1981 Mar 7;1(8219):520–2

Modulation by picrotoxin and IPTBO of 3H–flunitrazepam binding to the GABA/benzodiazepine receptor complex of rat cerebellum. Karobath M, et al. **Life Sci** 1981 Jan 19;28(3):307–13

Affinity of beta–carbolines on rat brain benzodiazepine and opiate binding sites. Airaksinen MM, et al. **Med Biol** 1980 Dec;58(6):341–4

Instinctive predatory behavior of mustelids (Mustela putorius f. furo, Mustela vison f. dom.) modified by benzodiazepine derivatives. Apfelbach R. **Pharmacol Biochem Behav** 1981;14 Suppl 1:43–6

Increase in 3H–flunitrazepam binding in vitro and in vivo to rat brain benzodiazepine receptors by tofizopam, a 3,4–benzo–diazepine. Saano V, et al. **Pharmacol Res Commun** 1981 Jan;13(1):75–85

gamma–Aminobutyric acid and benzodiazepine receptors: copurification and characterization. Gavish M, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1939–42

Autoradiographic localization of benzodiazepine receptors in immunocytochemically identified gamma–aminobutyrergic synapses. Möhler H, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1935–8

Rapid development of tolerance to the sedative effects of lorazepam and triazolam in rats. File SE. **Psychopharmacology (Berlin)** 1981; 73(3):240–5

[The Halcion affair (letter)] Mostert JW. **S Afr Med J** 1981 Jun 27; 59(27):967 **(Afr)**

Clinical trial of halazepam and clorazepate: considerations of a single bedtime dose [proceedings] Cohen NL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):134–5 **(eng)**

[Unusual withdrawal symptoms after long–term administration of benzodiazepines (author's transl)] Schöpf J. **Nervenarzt** 1981 May; 52(5):288–92 (Ger)

BENZODIAZEPINONES

Absorption, distribution and excretion of 14C–pirenzepine in rats. Accumulation characteristics after multiple dose regimen. Kobayashi S, et al. **Arzneimittelforsch** 1981;31(4):679–90

Quantitative analysis of CM 6912 (ethyl loflazepate) and its metabolites in plasma and urine by chemical ionization gas chromatography mass spectrometry. Application to pharmacokinetic studies in man. Cautreels W, et al. **Biomed Mass Spectrom** 1980 Nov;7(11–12):565–71

Withdrawal reaction from clobazam. Petursson H, et al. **Br Med J [Clin Res]** 1981 Jun 13;282(6280):1931–2

Benzodiazepines prevent kainate–induced loss of GABAergic and cholinergic neurons in the chick retina. Imperato A, et al. **Brain Res** 1981 May 25;213(1):205–10

Clobazam and diazepam in anxiety. Rickels K, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):95–100

Specific high–affinity saturable binding of [3H] R05–4864 to benzodiazepine binding sites in the rat cerebral cortex. Schoemaker H, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):173–5

Inhibition of carbonic anhydrase by pirenzepine. Puşcaş I, et al. **Int J Clin Pharmacol Ther Toxicol** 1981 Feb;19(2):75–7

Gas chromatographic determination of clonazepam. Larking P. **J Chromatogr** 1980 Dec 12;221(2):399–402

Double–blind comparison of ketazolam and placebo using once–a–day dosing. Cohn JB, et al. **J Clin Pharmacol** 1980 Nov–Dec; 20(11–12):676–80

Comparison of the therapeutic effect, tolerance and safety of ketazolam and diazepam administered for six months to out–patients with chronic anxiety neurosis. Fabre LF, et al. **J Int Med Res** 1981;9(3):191–8

Chemical conversion of anthramycin 11–methyl ether to didehydroanhydroanthramycin and its utilization in studies of the biosynthesis and mechanism of action of anthramycin. Malhotra RK, et al. **J Nat Prod** 1981 Jan–Feb;44(1):38–44

Investigation in man of the efficacy of a benzodiazepine antagonist, Ro 15–1788. Darragh A, et al. **Lancet** 1981 Jul 4;2(8236):8–10

In vivo effects of two novel alkylating benzodiazepines, irazepine and kenazepine. Williams EF, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):487–91

Advances in basic and clinical pharmacology of pirenzepine. Proceedings of the Second International Symposium on Pirenzepine. Hamburg, FRG, 8 June 1980. **Scand J Gastroenterol [Suppl]** 1980;15(66):1–114

Pirenzepine––a ligand with original binding properties to muscarinic receptors. Birdsall NJ, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):1–4

An international pharmacokinetic study on pirenzepine following a single oral dose. Bozler G, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):27–33

EEG and behavioral effects of pirenzepine in normal volunteers. Fink M, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):39–46

Effects of cimetidine and pirenzepine on peroperative electrical vagal stimulation of gastric acid secretion. Fritsch WP, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):95–100

Pirenzepine selectively inhibits gastric acid secretion: a comparative pharmacological study between pirenzepine and seven other antiacetylcholine drugs. Heathcote BV, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):15–26

Comparison of the action of pirenzepine and L–hyoscyamine on gastric acid secretion and other muscarinic effects. Jaup BH, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):89–94

Cerebro–spinal fluid concentrations of pirenzepine after therapeutic dosage. Jaup BH, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):35–7

Psychometric studies of pirenzepine. Kuhn E, et al. **Scand J Gastroenterol [Suppl]** 1980;15(66):47–53

The effect of pirenzepine on meal–stimulated gastrointestinal hormones. El–Sabbagh HN, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):57–61

Influence of intravenous pirenzepine on gastric acid and pepsin in man. el–Sabbagh HN, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):73–7

Clinical trial of halazepam and clorazepate: considerations of a single bedtime dose [proceedings] Cohen NL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):134–5 (eng)

[The effect of clonazepam on visual evoked potentials of the rabbit (author's transl)] Pockberger H, et al. **EEG EMG** 1981 Mar; 12(1):14–20 (Eng. Abstr.) (Ger)

BIOGENIC AMINES

Immunohistochemical characterization of monoamine–containing neurons in the central nervous system by antibodies to serotonin and noradrenalin. A study in the rat and the lamprey (Lampetra fluviatilis). Steinbusch HW, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:107–22

Biogenic amines and depression (introduction to symposium). Agurell S. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):17–9

High–performance liquid chromatographic determination of four biogenic amines in chocolate. Hurst WJ, et al. **Analyst** 1981 Apr; 106(1261):394–402

Endosymbionts, biogenic amines, and a heterodyne hypothesis for circadian rhythms. Levandowsky M. **Ann NY Acad Sci** 1981; 361:369–75

The deamination of monoamines by pig dental pulp. Norqvist A, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):403–9

Studies related to the blood–brain barrier to monoamines and protein in pia–arachnoid cultures. Hervonen H, et al. **Brain Res** 1981 Apr 6; 210(1–2):449–54

Sulphate conjugation of biologically active monoamines and their metabolites by human platelet phenolsulphotransferase. Rein G, et al. **Clin Chim Acta** 1981 Apr 9;111(2–3):247–56

Stereospecific transport carrier systems for L–tyrosine and L–tryptophan in relation to monoamine synthesis. Bruinvels J, et al. **Essays Neurochem Neuropharmacol** 1981;5:1–24 (33 ref.)

Chromatographic separation of some biogenic amines on a weakly acidic ion–exchange resin. Seki T. **J Chromatogr** 1981 Mar 20;207(2):286–7

Influence of cholecystokinin octapeptide sulfate ester on brain monoamine metabolism in rats. Fekete M, et al. **J Neural Transm** 1981; 50(2–4):81–8

Decreased transmethylation of biogenic amines after in vivo elevation of brain S–adenosyl–l–homocysteine. Schatz RA, et al. **J Neurochem** 1981 May;36(5):1739–48

An improved approach to histofluorescence using the SPG method for tissue monoamines. De la Torre JC. **J Neurosci Methods** 1980 Oct; 3(1):1–5

Unexpected differences between mazindol and its homologs on biochemical and behavioral responses. Heikkila RE, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):745–9

Effects of reserpine on monoamines and intestinal transit in the rat. Stewart JJ, et al. **J Pharmacol Exp Ther** 1981 May;217(2):357–62

Regional changes of monoamines in cerebral cortex and subcortical structures of aging rhesus monkeys. Goldman–Rakic PS, et al. **Neuroscience** 1981;6(2):177–87

Substituted phenethylamines and anorexia. Duhault J, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):341–9

Immobilization stress in rats: effect on rectal temperature and possible role of brain monoamines in hypothermia. Amar A, et al. **Psychopharmacology (Berlin)** 1981;73(2):157–60

[Modifications of cerebral amine metabolism in psychiatric illness] Linkowski P, et al. **Acta Psychiatr Belg** 1980 Sep–Oct;80(5):559–73 (38 ref.) (Fre)

[Convergence and reciprocal coupling of hypothalamic monoaminergic and peptidergic neurons (author's transl)] Barry J. **Ann Endocrinol (Paris)** 1980 Nov–Dec;41(6):457–65 (Eng. Abstr.) (Fre)

[Oxidative deamination data on biogenic monoamines in the mitochondrial fraction of rat brain and liver] Sarukhanian ZhG, et al. **Gig Tr Prof Zabol** 1981 Apr;(4):30–3 (Eng. Abstr.) (Rus)

BIPOLAR DISORDER

Estimates of the prevalence of bipolar affective disorder. Methods based on treatment with lithium. Eastwood R, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):83–90

Adolescents at risk for manic–depressive illness. Kestenbaum CJ. **Adolesc Psychiatry** 1980;8:344–66

Effects of lithium on memory. Christodoulou GN, et al. **Am J Psychiatry** 1981 Jun;138(6):847–8

Effect of lithium on glycine levels in patients with affective disorders. Deutsch SI, et al. **Am J Psychiatry** 1981 May;138(5):683–4

The effect of mianserin on urinary catecholamine excretion in psychiatric patients. Moody JP, et al. **Br J Clin Pharmacol** 1981 Jan; 11(1):103–5

Bipolar affective psychosis with onset before age 16 years: report of 10 cases. Hassanyeh F, et al. **Br J Psychiatry** 1980 Dec;137:530–9

The lithium clinic for treatment and prevention of manic depression: a cost benefit approach. Fieve RR. **Egypt J Psychiatry** 1979 Oct; 2(2):166–90

Memory processing with lithium carbonate. Marusarz TZ, et al. **J Clin Psychiatry** 1981 May;42(5):190–2

Lithium nephrotoxicity [letter] Johnson GF, et al. **Med J Aust** 1981 Apr 4;1(7):376

Estimation of lithium dose requirement by lithium clearance, serum lithium and saliva lithium following a loading dose of lithium carbonate. Tyrer SP, et al. **Neuropsychobiology** 1981;7(3):152–8

Manic–depressive disorder. Paykel ES, et al. **Practitioner** 1981 Jan; 225(1351):75–7, 79–81

Lithium in children of lithium–responding parents. McKnew DH, et al. **Psychiatry Res** 1981 Apr;4(2):171–80

Slow and rapid onset of manic episodes: implications for underlying biology. Post RM, et al. **Psychiatry Res** 1981 Apr;4(2):229–37

Prophylactic lithium with and without imipramine for bipolar I patients: a double–blind study [proceedings] Kane JM, et al.

Psychopharmacol Bull 1981 Jan;17(1):144–5

Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo–controlled comparison [proceedings] Quitkin FM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):142–4

A preliminary double–blind study on the efficacy of carbamazepine in prophylaxis of manic–depressive illness. Okuma T, et al. **Psychopharmacology (Berlin)** 1981;73(1):95–6

What to watch for with lithium. Rosenberg JM, et al. **RN** 1981 Jul; 44(7):44–6

[Lithium dose in relation to body weight and age in the preventive of relapses in manic–depressive psychosis] König L. **Agressologie** 1980; 21(A):15–7 (Eng. Abstr.) **(Ger)**

[Neurochemistry and clinical psychiatry (author's transl)] Gross G. **Fortschr Neurol Psychiatr** 1981 Jan;49(1):34–42 (Eng. Abstr.) **(Ger)**

BLOOD–BRAIN BARRIER

Studies related to the blood–brain barrier to monoamines and protein in pia–arachnoid cultures. Hervonen H, et al. **Brain Res** 1981 Apr 6; 210(1–2):449–54

Blood–brain barrier for serotonin in the eel (Anguilla anguilla L.). Genot G, et al. **Comp Biochem Physiol** [C] 1981;68C(2):247–50

Medical therapies for mood disorders alter the blood–brain barrier. Preskorn SH, et al. **Science** 1981 Jul 24;213(4506):469–71

BRADYKININ

A comparison of the actions of acetylcholine and bradykinin on the guinea pig ileum. Roberts ML. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):267–70

[Acetylcholine–bradykinin: a new peptide–amine transmitter interaction (editorial)] Pirola CJ. **Medicina (B Aires)** 1980 Nov–Dec; 40(6 Pt 2):893–5 **(Spa)**

BUTAPERAZINE

Neuroleptic–induced decrease in platelet MAO activity of schizophrenic patients. Chojnacki M, et al. **Am J Psychiatry** 1981 Jun; 138(6):838–40

BUTYLAMINES

Studies on the endoanesthetic effects of lidocaine and benzonatate on non–medullated nerve endings in the left ventricle. Thorén P, et al. **Acta Physiol Scand** 1981 Jan;111(1):51–8

BUTYROPHENONE TRANQUILIZERS

A gas chromatographic method for the determination of fluanisone, moperone, aceperone and pipamperone in human plasma. Quaglio MP, et al. **Farmaco [Prat]** 1981 Apr;36(4):204–14

BUTYROPHENONES

The relationship between loss of dopamine nerve terminals, striatal [3H]spiroperidol binding and rotational behavior in unilaterally 6–hydroxydopamine–lesioned rats. Heikkila RE, et al. **Brain Res** 1981 May 4;211(2):285–92

Biochemical mechanism of tolerance to neuroleptic drugs; regional differences in rat brain. Bacopoulos NG. **Eur J Pharmacol** 1981 Apr 9;70(4):585–6

Selective labelling of murine B lymphocytes by [3H]spiroperidol. Uzan A, et al. **J Pharm Pharmacol** 1981 Feb;33(2):102–3

Resolution of dopamine and serotonin receptor components of [3H]spiperone binding to rat brain regions. List SJ, et al. **Proc Natl Acad Sci USA** 1981 Apr;78(4):2620–4

CARBAMAZEPINE

Charcoal hemoperfusion for treatment of carbamazepine poisoning. Chan KM, et al. **Clin Chem** 1981 Jul;27(7):1300–2

Simple and rapid gas–liquid chromatographic method for estimating carbamazepine in serum. Cocks DA, et al. **J Chromatogr** 1981 Mar 13; 222(3):496–500

Rapid gas chromatography method for the determination of carbamazepine and unrearranged carbamazepine–10,11–epoxide in human plasma. Ranise A, et al. **J Chromatogr** 1981 Jan 2; 222(1):120–4

Carbamazepine–induced acute tubulointerstitial nephritis. Hogg RJ, et al. **J Pediatr** 1981 May;98(5):830–2

Induction effect of phenobarbital on the carbamazepine to carbamazepine–10, 11–epoxide pathway in rhesus monkeys. Patel IH, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):555–8

A preliminary double–blind study on the efficacy of carbamazepine in prophylaxis of manic–depressive illness. Okuma T, et al. **Psychopharmacology (Berlin)** 1981;73(1):95–6

Factors influencing simultaneous concentrations of carbamazepine and its epoxide in plasma. McKauge L, et al. **Ther Drug Monit** 1981; 3(1):63–70

GLC analysis of carbamazepine [letter] Perchalski RJ, et al. **Ther Drug Monit** 1980;2(3):289

CATECHOLAMINES

Immunofluorescent and biochemical studies on dopamine–beta–hydroxylase and catecholamines in SIF cells of the superior cervical ganglion. Heym C, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:123–9

Effect of catecholamine on fetal breathing activity in rhesus monkeys. Murata Y, et al. **Am J Obstet Gynecol** 1981 Apr 15;139(8):942–7

Cardiac catecholamine stores after cardiac sympathectomy, 6–OHDA, and cardiac denervation. Priola DV, et al. **Am J Physiol** 1981 Jun; 240(6):H889–95

Role of calmodulin in states of altered catecholamine sensitivity. Gnegy ME, et al. **Ann NY Acad Sci** 1980;356:304–18

Onset and magnitude of cardiovascular response to dobutamine and AR–L 115 BS, a new positive inotropic agent with additional vasodilating activity, in normal subjects. Benedikter L, et al. **Arzneimittelforsch** 1981; 31(1a):239–42

hypobaric hypoxia: central catecholamine levels and cortical PO2 and avoidance response in rats treated with apomorphine. Saligaut C, et al. **Aviat Space Environ Med** 1981 Mar;52(3):166–70

Catecholamines and the brain microsomal Na, K–adenosinetriphosphatase—II. The mechanism of action. Svoboda P, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):433–9

Catecholamine synthesis in the adrenal medulla of cattle and rats deficient in copper. Hesketh JE. **Biochem Soc Trans** 1981 Feb;9(1):101–2

Cyclic nucleotides of canine antral smooth muscle. Effects of acetylcholine, catecholamines and gastrin. Baur S, et al. **Biochim Biophys Acta** 1981 Jan 7;672(1):1–6

Hemodynamic responses of the pelvic vascular bed to vasoactive stimuli in pregnant sheep. Tabsh K, et al. **Biol Neonate** 1981;39(1–2):52–60

A method for the analysis of catecholamines by selected ion monitoring and 14C isotope dilution in adrenal medullary cell culture. Lhuguenot JC, et al. **Biomed Mass Spectrom** 1980 Nov;7(11–12):529–32

The effect of mianserin on urinary catecholamine excretion in psychiatric patients. Moody JP, et al. **Br J Clin Pharmacol** 1981 Jan; 11(1):103–5

Correlation between catecholamine secretion from bovine isolated chromaffin cells and [3H]–ouabain binding to plasma membranes. Aunis D, et al. **Br J Pharmacol** 1981 Jan;72(1):31–40

Further evidence for the involvement of Na+ channels in the release of adrenal catecholamine: the effect of scorpion venom and grayanotoxin I. Ito S, et al. **Br J Pharmacol** 1981 Jan;72(1):61–7

Exocytotic secretion of catecholamines from the cat adrenal medulla by sodium deprivation: involvement of calcium influx mechanism. Nishimura S, et al. **Br J Pharmacol** 1981 Feb;72(2):305–17

Liberation of catecholamines from blood platelets. Pletscher A. **Br J Pharmacol** 1981 Feb;72(2):349–54

Catecholamine synthesis regulation in hypothalamic synaptosomes. Haycock DA, et al. **Brain Res** 1981 Jun 15;214(2):371–85

Possible occurrence of Na+–dependent Ca2+ influx mechanism in isolated bovine chromaffin cells. Sorimachi M, et al. **Brain Res** 1981 Mar 16;208(2):442–6

Serotonin–immunoreactive cells in the superior cervical ganglion of the rat. Evidence for the existence of separate serotonin– and catecholamine–containing small ganglionic cells. Verhofstad AA, et al. **Brain Res** 1981 May 11;212(1):39–49

Pressor responses and adrenomedullary catecholamine release during brain stimulation in the rat. Gauthier P. **Can J Physiol Pharmacol** 1981 May; 59(5):485–92

Reflexly induced inhibition of catecholamine release through a peripheral muscarinic mechanism. Lavallée M, et al. **Can J Physiol Pharmacol** 1980 Nov;58(11):1334–41

Correlative ontogenetic development of catecholamine– and LHRH–containing nerve endings in the median eminence of the rat. Ibata Y, et al. **Cell Tissue Res** 1981;216(1):31–8

The influence of vagal afferents on the left ventricular contractile response to intracoronary administration of catecholamines in the conscious dog. Barron KW, et al. **Circ Res** 1981 Jul;49(1):159–69

The effect of charcoal hemoperfusion on the catecholamine levels in severely intoxicated patients. Verpooten GA, et al. **Clin Toxicol** 1981 Feb;18(2):127–31

Dobutamine in the rejecting transplanted heart. Edwards H, et al. **Crit Care Med** 1981 Jun;9(6):498–9

Dobutamine: a hemodynamic evaluation in human septic shock. Jardin F, et al. **Crit Care Med** 1981 Apr;9(4):329–32

The role of catecholamines in the control of gastrin and acid secretion during insulin hypoglycaemia in man. Järhult J, et al. **Digestion** 1981; 21(2):92–7

Preovulatory depletion of ovarian catecholamines in the rat. Bahr JM, et al. **Endocrinology** 1981 May;108(5):1815–20

Catecholamine turnover rates in discrete hypothalamic areas and associated changes in median eminence luteinizing hormone–releasing hormone and serum gonadotropins on proestrus and diestrous day 1.

Rance N, et al. **Endocrinology** 1981 May;108(5):1795–802

The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone-releasing hormone and the effect of prolactin on catecholamine turnover. Selmanoff M. **Endocrinology** 1981 May;108(5):1716–22

Testicular cyclic nucleotide and adrenal catecholamine metabolism following chronic exposure to cadmium. Singhal RL. **Environ Health Perspect** 1981 Apr;38:111–7

Plasma catecholamines in rats exposed to cold: effects of ganglionic and adrenoreceptor blockade. Picotti GB, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):321–9

The effect of catecholamines and their inhibitors on the solubilized adenylate cyclase activity of bovine retina. Joó I, et al. **Exp Eye Res** 1980 Dec;31(6):659–63

Autoradiographic study of catecholamine metabolism in amphibian dermis. Hadjioloff AI, et al. **Folia Morphol (Praha)** 1981;29(1):56–8

Effect of catecholamine on the contractile responses of rabbit colon and duodenum to vagus nerve stimulation in vivo. Nakahata N, et al. **Fukushima J Med Sci** 1979;26(3–4):71–7

Effect of chronic sodium depletion on cerebrospinal fluid and plasma catecholamines. Brosnihan KB, et al. **Hypertension** 1981 Mar–Apr; 3(2):233–9

The adrenergic nerve supply to bovine ovarian follicles. Morimoto K, et al. **Int J Fertil** 1981;26(1):14–9

Determination of rat brain tissue catecholamines using liquid chromatography with electrochemical detection. Hegstrand LR, et al. **J Chromatogr** 1981 Jan 2;222(1):107–11

Comparison of the sensitivity of various post-column methods for catecholamine analysis by high-performance liquid chromatography. Yui Y, et al. **J Chromatogr** 1981 Feb 27;206(3):586–8

Regulation of human leukocyte beta receptors by endogenous catecholamines: relationship of leukocyte beta receptor density to the cardiac sensitivity to isoproterenol. Fraser J, et al. **J Clin Invest** 1981 Jun;67(6):1777–84

Selectivity of dobutamine for adrenergic receptor subtypes: in vitro analysis by radioligand binding. Williams RS, et al. **J Clin Invest** 1981 Jun;67(6):1703–11

Immunocytochemical localization of catecholamine synthesizing enzymes and neuropeptides in area postrema and medial nucleus tractus solitarius of rat brain. Armstrong DM, et al. **J Comp Neurol** 1981 Mar 1; 196(3):505–17

A brainstem atlas of catecholaminergic neurons in man, using melanin as a natural marker. Bogerts B. **J Comp Neurol** 1981 Mar 20; 197(1):63–80

Evidence for a catecholaminergic projection to area X in the zebra finch. Lewis JW, et al. **J Comp Neurol** 1981 Feb 20;196(2):347–54

An immunohistochemical study of the organization of catecholaminergic cells and terminal fields in the paraventricular and supraoptic nuclei of the hypothalamus. Swanson LW, et al. **J Comp Neurol** 1981 Feb 20;196(2):271–85

Age-related changes in the catecholamine content of peripheral organs in male and female F344 rats. Martinez JL Jr, et al. **J Gerontol** 1981 May;36(3):280–4

Effect of various stimulus parameters on electrically-induced catecholamine secretion by thin slices of bovine adrenal medulla. Brooks JC, et al. **J Neural Transm** 1981;50(2–4):201–7

Application of high performance liquid chromatography with electrochemical detection to neurochemical analysis: measurement of catecholamines, serotonin and metabolites in rat brain. Mefford IN. **J Neurosci Methods** 1981 Feb;3(3):207–24 (47 ref.)

Specific enhancement of neuronal responses to catecholamine by p-tyramine. Jones RS. **J Neurosci Res** 1981;6(1):49–61

Comparison of the receptors mediating the catecholamine hyperpolarization and slow inhibitory postsynaptic potential in sympathetic ganglia. Cole AE, et al. **J Pharmacol Exp Ther** 1981 May; 217(2):440–4

Potassium-induced release of [3H]catecholamine from brain: effects of pre-exposure to catecholamine uptake inhibitors. Dembiec D, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):727–32

The actions of xylamine on central noradrenergic neurons. Dudley MW, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):834–40

Inhibitory effect of some monoamine oxidase inhibitors on fluorescence assay for the o-methylated metabolites of the catecholamines. Calverley DG, et al. **J Pharmacol Methods** 1981 Mar;5(2):179–81

Effects of chronic treatments upon the brown adipose tissue of rats. II. Comparison between the effects of catecholamine injections and cold adaptation. Mory G, et al. **J Physiol (Paris)** 1980;76(8):859–64

Effects of perhexiline on myocardial phosphorylase activity, myocardial catecholamine content and heart rate. Okabe E, et al. **Jpn Circ J** 1981 Jun;45(6):667–71

Reduced catecholamine excretion at onset of brain death [letter] Feibel JH. **Lancet** 1981 Apr 18;1(8225):890–1

Manganese as agonist and antagonist of calcium ions: dual effect upon catecholamine release from adrenal medulla. Arqueros L, et al. **Life Sci** 1981 Mar 30;28(13):1535–40

DPI, a supposed selective agonist of inhibitory dopamine receptors, strongly increases rat diuresis through alpha-adrenergic receptor activation. Baggio G, et al. **Life Sci** 1981 Mar 30;28(13):1449–56

Fluorescence histochemistry indicates damage of striatal dopamine nerve terminals in rats after multiple doses of methamphetamine. Lorez H. **Life Sci** 1981 Feb 23;28(8):911–6

Dorsal tegmental bundle destruction: effects on operant behavior, brain catecholamine levels, and behavioral suppression produced by adrenergic agonists. Morris MD, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2621–6

II. Beta-adrenergic receptors and catecholamine sensitive adenylate cyclase in the developing rat lung. Whitsett JA, et al. **Life Sci** 1981 Jan 26;28(4):339–45

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 2. Stability and restoration of activity of hormone-sensitive adenylate cyclase of adipocyte plasma membrane. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):43–50

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 3. Modified binding properties of beta-adrenoreceptor and its decreased coupling efficiency for adenylate cyclase. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):51–8

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 1. Correlation of cyclic AMP levels and initial rates of lipolysis. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):35–41

A pharmacological method to estimate the pKi of competitive inhibitors of agonist uptake processes in isolated tissues. Kenakin TP. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):89–95

Neurohistological and histochemical data on an additional fiber of some encapsulated receptors. Chelyshev YuA. **Neurosci Behav Physiol** 1980 Nov–Dec;10(6):525–9

Presence of avian pancreatic polypeptide-like immunoreactivity in catecholamine and methionine-enkephalin-containing neurones within the central nervous system. Hunt SP, et al. **Neurosci Lett** 1981 Jan 20; 21(2):125–30

Medial prefrontal cortical projections to the region of the dorsal periventricular catecholamine system. Dalsass M, et al. **Neuroscience** 1981;6(4):657–65

Effects of hypoxia lasting up to one month on the catecholamine content in rat carotid body. Hanbauer I, et al. **Neuroscience** 1981;6(1):81–6

Response of adrenal catecholamine to a newly synthesized chemical radioprotector. Hasan SS, et al. **Nuklearmedizin** 1981 Apr;20(2):82–4

Morphological and histochemical correlation of recovery after spinal transection in rat. Sahgal V, et al. **Paraplegia** 1981;19(1):1–6

Lung catecholamines and cyclic nucleotides during perinatal development in the rat. Possible relationships with biochemical and morphological differentiation. Tordet C, et al. **Pediatr Res** 1981 May;15(5):787–93

Simultaneous monoamine histofluorescence and neuropeptide immunocytochemistry: III. Ontogeny of catecholamine varicosities and neurophysin neurons in the rat supraoptic and paraventricular nuclei. Khachaturian H, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):77–95

Simultaneous monoamine histofluorescence and neuropeptide immunocytochemistry: I. Localization of catecholamines and gonadotropin-releasing hormone in the rat median eminence. McNeill TH, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):59–68

Reversal of guanethidine- and diethyldithiocarbamate-induced amnesia by peripherally-administered catecholamines. Walsh TJ, et al. **Pharmacol Biochem Behav** 1981 May;14(5):713–8

Plasma catecholamines and renin during operant blood pressure conditioning in baboons. Goldstein DS, et al. **Physiol Behav** 1981 Jan; 26(1):33–7

Plasma catecholamines in rats: daily variations in basal levels and increments in response to stress. McCarty R, et al. **Physiol Behav** 1981 Jan;26(1):27–31

Adrenal hormones and brain catecholamines responses to morning and afternoon immobilization stress in rats. Torrellas A, et al. **Physiol Behav** 1981 Jan;26(1):129–33

Effects of T-2 toxin on brain catecholamines and selected blood components in growing chickens. Chi MS, et al. **Poult Sci** 1981 Jan; 60(1):137–41

Catecholamine-mediated diuresis in turkeys. Palmore WP, et al. **Proc Soc Exp Biol Med** 1981 May;167(1):1–5

Catecholamines, acetylcholine and excitability of mechanoreceptors. Akoev GN. **Prog Neurobiol** 1980;15(4):269–94

Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Miczek KA. **Psychopharmacol Bull** 1981 Jan; 17(1):60–2

Pharmacologic manipulations of brain catecholamines and the behavior of Callithrix jacchus (marmoset). Campos F, et al. **Psychopharmacology (Berlin)** 1981;73(3):252–6

Effects of neonatal 6-hydroxydopamine treatment on catecholamine levels and behavior during development and adulthood. Fobes JL, et al. **Psychopharmacology (Berlin)** 1981;73(1):27–30

Use of 6-hydroxydopamine to deplete brain catecholamines in the rhesus monkey: effects on urinary catecholamine metabolites and behavior. Kraemer GW, et al. **Psychopharmacology (Berlin)** 1981;73(1):1–11

Catecholamine-serotonin interaction effects on activity in rats neonatally treated with 6-hydroxydopamine. Olds ME, et al.

Psychopharmacology (Berlin) 1981;73(1):31-3

[Peroperative plasma catecholamine levels during cardiovascular surgery] Caillard B, et al. **Ann Anesthesiol Fr** 1981;22(1):27-31 (Eng. Abstr.) (Fre)

[Determination of psychological stress in sea pilot based on urinary catecholamine excretion] Geister R, et al. **Zentralbl Arbeitsmed Arbeitsschutz Prophyl Ergonomie** 1980 Dec; 30(12):458-63 (Ger)

[Evaluation of catecholamine measurement of high performance liquid chromatography with electronic detector (author's transl)] Kajiwara N, et al. **Horumon To Rinsho** 1980 Oct;28(10):1205-10 (Jpn)

[Retrospect on catecholamine research in our laboratories (author's transl)] Hashimoto K. **Kokyu To Junkan** 1980 Oct;28(10):1096-101 (Jpn)

[Plasma catecholamine concentration as an index for evaluating cardiac sympathetic nerve activity (author's transl)] Miura Y, et al. **Kokyu To Junkan** 1980 Oct;28(10):1111-7 (Jpn)

[Recent advances in high-performance liquid chromatographic method for the determination of picogram amounts of catecholamines and its clinical application (author's transl)] Yui Y, et al. **Kokyu To Junkan** 1980 Oct;28(10):1125-7 (Jpn)

[Effect of endotoxin shock on endocrine function and carbohydrate metabolism (author's transl)] Matsui M. **Masui** 1981 Jan;30(1):39-46 (Eng. Abstr.) (Jpn)

[Measurement of deep body temperature difference after open heart surgery: correlations with hemodynamics, endogenous catecholamine and renin activity (author's transl)] Kawamura T, et al. **Nippon Kyobu Geka Gakkai Zasshi** 1981 Feb;29(2):211-7 (Eng. Abstr.) (Jpn)

[Catecholamines in the brain structures of rats responding differently to the 'open field' test] Belova TI, et al. **Biull Eksp Biol Med** 1981 Feb; 91(2):136-8 (Eng. Abstr.) (Rus)

CENTRAL NERVOUS SYSTEM AGENTS

Identification and quantitation of neutral and basic drugs in blood by gas chromatography and mass spectrometry. Cailleux A, et al. **J Chromatogr Sci** 1981 Apr;19(4):163-76

A clinician's guide to the use of stimulant medication for the psychiatric disorders of children. Cantwell DP. **JDPB** 1980 Sep;1(3):133-40 (58 ref.)

Drug effects on attack defense and escape in mice. Kršiak M, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:47-52

Pharmaco-ethological analysis of social behaviour of isolated mice. Poshivalov VP. **Pharmacol Biochem Behav** 1981;14 Suppl 1:53-9

CHLORDIAZEPOXIDE

Chlordiazepoxide selectively potentiates GABA conductance of spinal cord and sensory neurons in cell culture. Choi DW, et al. **J Neurophysiol** 1981 Apr;45(4):621-31

The interaction of chlordiazepoxide and sodium valproate in the nucleus accumbens of the rat. Kuruvilla A, et al. **Life Sci** 1981 Jan 26; 28(4):393-9

In defense of 'Limbitrol' [letter] Dudley RD Jr. **Minn Med** 1980 Oct; 63(10):713

Effects of morphine and chlordiazepoxide on locomotor activity in two inbred strains of mice. Cuomo V, et al. **Pharmacol Res Commun** 1981 Jan;13(1):87-93

Responders and nonresponders to chlordiazepoxide and placebo: a discriminant function analysis. Downing RW, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):405-15

Food preference following acute or chronic chlordiazepoxide administration: tolerance to an antineophobic action. Cooper SJ, et al. **Psychopharmacology (Berlin)** 1981;73(1):70-4

The partial reinforcement extinction effect after treatment with chlordiazepoxide. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):269-75

Benzodiazepine inhibition of the calcium-calmodulin protein kinase system in brain membrane. DeLorenzo RJ, et al. **Science** 1981 Jul 31; 213(4507):546-9

P-CHLOROPHENYLALANINE

Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat. Borbély AA, et al. **Behav Brain Res** 1981 Jan; 2(1):1-22

A comparison of an improved o-phthalaldehyde fluorometric method and high pressure liquid chromatography in the determination of brain 5-hydroxyindoles of rats treated with L-tryptophan and p-chlorophenyl-alanine. Curzon G, et al. **Br J Pharmacol** 1981 Jun; 73(2):555-61

The effect of para-chlorophenylalanine of thermoregulation in the Mongolian gerbil (Meriones unguiculatus). McRae MA, et al. **Comp Biochem Physiol [C]** 1981;68C(2):181-6

Effects of para-chlorophenylalanine, a brain serotonin depletor, on pituitary cyclic AMP levels in the rainbow trout, Salmo gairdneri. Olcese J, et al. **Gen Comp Endocrinol** 1981 Apr;43(4):462-6

The effect of para-chlorophenylalanine and scopolamine on passive avoidance in chicks. Mattingly BA, et al. **Pharmacol Biochem Behav** 1981 May;14(5):669-76

CHLORPROMAZINE

Reversed effect of chlorpromazine on hypothalamic serotonin levels of rats with complete deafferentation of the medial basal hypothalamus. Bánky Z, et al. **Acta Biol Acad Sci Hung** 1980;31(1-3):25-32

Influence of phenobarbital, chlorpromazine, progesterone and phenylbutazone on the biliary cholesterol excretion in rats. Barth A, et al. **Acta Biol Med Ger** 1980;39(11-12):1217-26

DL-propranolol and chlorpromazine following admission for schizophrenia. A controlled comparison. Yorkston NJ, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):13-27

The solubility of amphipathic molecules in biological membranes and lipid bilayers and its implications for membrane structure. Conrad MJ, et al. **Biochemistry** 1981 Feb 17;20(4):808-18

Analysis of chlorpromazine in plasma: effect of specimen storage. Gupta RN, et al. **Clin Chim Acta** 1981 Feb 5;109(3):351-4

Prognosis in schizophrenia: individual differences in psychological response to a test dose of antipsychotic drug and their relationship to blood and saliva levels and treatment outcome. May PR, et al. **Compr Psychiatry** 1981 Mar-Apr;22(2):147-52

Blockade of hepatic alpha-adrenergic receptors and responses by chlorpromazine and trifluoperazine. Blackmore PF, et al. **FEBS Lett** 1981 Jan 26;123(2):245-8

Inhibition of phenylephrine-stimulated gluconeogenesis by chlorpromazine is mediated by alpha-adrenergic receptors. Tilley L, et al. **FEBS Lett** 1981 Apr 20;126(2):313-7

Pharmacological studies on 1-(p-aminophenoxy)-3-[N1-(O-methoxyphenyl)-N4-piperazinyl] propane dihydrochloride (74-637). Sur RN, et al. **Indian J Exp Biol** 1980 Oct;18(10):1190-1

Simultaneous determination of diphenhydramine, methaqualone, diazepam and chlorpromazine in liver by use of enzyme digestion: a comparison of digestion procedures. Holzbecher M, et al. **J Anal Toxicol** 1981 Mar-Apr;5(2):62-4

Reversed-phase liquid chromatography for the separation of chloropromazine, imipramine and some of their metabolites. Fekete J, et al. **J Chromatogr** 1981 Jan 16;204:319-27

The separation and determination of chlorpromazine and some of its related compounds by reversed-phase high performance liquid chromatography. Smith DJ. **J Chromatogr Sci** 1981 Feb;19(2):65-71

Inhibition of riboflavin metabolism in rat tissues by chlorpromazine, imipramine, and amitriptyline. Pinto J, et al. **J Clin Invest** 1981 May; 67(5):1500-6

Drug interaction: meperidine and chlorpromazine, a toxic combination. Stambaugh JE Jr, et al. **J Clin Pharmacol** 1981 Apr;21(4):140-6

Effect of chlorpromazine administration on enzyme activity concerning phosphatidic acid metabolism in rat liver. Ide H, et al. **J Pharmacobiodyn** 1980 Nov;3(11):612-9

Differential binding of chlorpromazine to human blood cells: application of the hygroscopic desorption method. Bondy B, et al. **Life Sci** 1981 Jan 26;28(4):441-9

Chlorpromazine-induced decrease of red cell aggregability. Costa D, et al. **Med Interne** 1981 Jan-Mar;19(1):83-7

A comparative study of the interaction of chlorpromazine, trifluoperazine, and promethazine with mouse brain tubulin. Rao AG, et al. **Mol Pharmacol** 1981 Mar;19(2):295-301

Interaction of MIF-I or alpha-MSH with D-amphetamine or chlorpromazine on thermoregulation and motor activity of rats maintained at different ambient temperatures. Yehuda S, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):243-8

Effects of chlorpromazine on escape and avoidance responses: a closer look. Spirduso WW, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):433-8

Plasma levels of chlorpromazine and clinical response [proceedings] van Putten T, et al. **Psychopharmacol Bull** 1981 Jan;17(1):113-5

Effects of chlorpromazine on food-maintained and observing behavior. Dearing ME, et al. **Psychopharmacology (Berlin)** 1981;73(3):281-5

The effect of long-term concurrent administration of chlorpromazine and lithium on the striatal and frontal cortical dopamine metabolism in rats. Eroğlu L, et al. **Psychopharmacology (Berlin)** 1981;73(1):84-6

Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge. Kolakowska T, et al. **Psychopharmacology (Berlin)** 1981;72(3):283-5

Bilateral skin conductance and the pupillary light-dark reflex: manipulation by chlorpromazine, haloperidol, scopolamine, and placebo. Patterson T, et al. **Psychopharmacology (Berlin)** 1981;73(1):63-9

Concentrations of chlorpromazine and two of its active metabolites in plasma and cerebrospinal fluid of psychotic patients treated with fixed drug doses. Wode-Helgodt B, et al. **Psychopharmacology (Berlin)** 1981; 73(1):55-62

[The dynamics of the drug release from suppositories. Part 5: Liberation of chlorpromazine from suppository bases (author's transl)] Pasich J, et al. **Pharmazie** 1981;36(1):20 (Eng. Abstr.) (Ger)

[Association of chlorpromazine and essential oils of absinthium and mace on operant conditioning behavior of the rat] Fundarò A, et al. **Boll Soc Ital Biol Sper** 1980 Nov 30;56(22):2370–4 (Eng. Abstr.)(Ita)

[Effect of aminazine and majeptil on proliferation of peripheral blood lymphocytes cultivated with phytohemagglutinin] Mitkevich SP, et al. **Zh Nevropatol Psikhiatr** 1981;81(2):115–7 (Eng. Abstr.) (Rus)

CHOICE BEHAVIOR

Selective effects of barbiturate and amphetamine on information processing and response execution. Frowein HW. **Acta Psychol (Amst)** 1981 Feb;47(2):105–15

CLOMIPRAMINE

A sensitive and specific method for the determination of chlorimipramine and desmethylchlorimipramine in plasma using selected ion monitoring with chemical ionization. Lapin A, et al. **Biomed Mass Spectrom** 1980 Nov;7(11–12):588–91

Double-blind trial of amineptine and clomipramine in the treatment of depression. Lemoine P, et al. **Curr Med Res Opin** 1981;7(4):234–40

Differential effects of clomipramine and clorgyline on the sensitivity of cortical neurons to serotonin: effect of chronic treatment. Olpe HR. **Eur J Pharmacol** 1981 Jan 29;69(3):375–7

Determination of clomipramine or imipramine and their mono-demethylated metabolites in human blood or plasma by high-performance liquid chromatography. Godbillon J, et al. **J Chromatogr** 1981 Jan 16;204:303–11

Psychotropic drugs and behaviour therapy. Stern R. **Practitioner** 1981 Jan;225(1351):21–5

Pharmacokinetics of clomipramine in depressive patients. de Cuyper HJ, et al. **Psychiatry Res** 1981 Apr;4(2):147–56

COCAINE

Hepatic periportal necrosis induced by chronic administration of cocaine. Freeman RW, et al. **Biochem Pharmacol** 1981 Apr 1;30(7):777–83

Reward and detection thresholds for brain stimulation: dissociative effects of cocaine. Kornetsky C, et al. **Brain Res** 1981 Mar 30; 209(2):496–500

Prolonged effects of cocaine on hippocampal activity. Lesse H. **Commun Psychopharmacol** 1980;4(3):247–54

Interactions of cocaine and delta 9-tetrahydrocannabinol with the hypothalamic-hypophysial axis of the female rat. Steger RW, et al. **Fertil Steril** 1981 May;35(5):567–72

EENT cocaine shortage leaves mystery in its wake. **Hosp Pract** 1981 Jun;16(6):164–5

Potential errors in benzoylecgonine and cocaine analysis. Fletcher SM, et al. **J Chromatogr** 1981 Feb 6;206(1):193–5

Coca and cocaine 1981. **J Ethnopharmacol** 1981 Mar–May; 3(2–3):110–379

Cocaine pharmacokinetics in humans. Barnett G, et al. **J Ethnopharmacol** 1981 Mar–May;3(2–3):353–66

Coca and cocaine as medicines: an historical review. Grinspoon L, et al. **J Ethnopharmacol** 1981 Mar–May;3(2–3):149–59

Sundry episodes in the history of coca and cocaine. Holmstedt B, et al. **J Ethnopharmacol** 1981 Mar–May;3(2–3):113–47

Guide to the analysis of cocaine and its metabolites in biological material. Lindgren JE. **J Ethnopharmacol** 1981 Mar–May;3(2–3):337–51 (81 ref.)

Constituents of Erythroxylon coca. II. Gas-chromatographic analysis of cocaine and other alkaloids in coca leaves. Turner CE, et al. **J Ethnopharmacol** 1981 Mar–May;3(2–3):293–8

Acute cocaine intoxication in the conscious dog: studies on the mechanism of lethality. Catravas JD, et al. **J Pharmacol Exp Ther** 1981 May; 217(2):350–6

Fixed-ratio responding under second-order schedules of food presentation or cocaine injection. Goldberg SR, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):271–81

Drug-environment interaction: context dependency of cocaine-induced behavioral sensitization. Post RM, et al. **Life Sci** 1981 Feb 16; 28(7):755–60

Acute tolerance to cocaine in humans. Fischman MW, et al. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(34):241–2

The effects cocaine free extracts of the coca leaf on food consumption and locomotor activity. Bedford JA, et al. **Pharmacol Biochem Behav** 1981 May;14(5):725–8

The effects of electric shock on responding maintained by cocaine in rhesus monkeys. Bergman J, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):423–6

Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Miczek KA. **Psychopharmacol Bull** 1981 Jan; 17(1):60–2

COGNITION

Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. Cohen NJ, et al. **J Abnorm Child Psychol** 1981 Mar;9(1):43–54

Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children [proceedings] Platt JE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):123–5

COGNITION DISORDERS

[Psychomotor disturbance after an endocular operation (author's transl)] Legrand J, et al. **J Fr Ophtalmol** 1981;4(2):143–6 (Eng. Abstr.) (Fre)

CONDITIONING (PSYCHOLOGY)

Effects of diazepam on schedule-controlled and schedule-induced behavior under signaled and unsignaled shock. Hymowitz N. **J Exp Anal Behav** 1981 Jul;36(1):119–32

ACTH4—10 affects behavior but not plasma corticosterone levels in a conditioned taste aversion situation. Smotherman WP, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):207–10

Response artifact in the measurement of neuroleptic-induced anhedonia. Ettenberg A, et al. **Science** 1981 Jul 17;209(4505):357–9

CONDITIONING, CLASSICAL

Hippocampal lesion effects on conditioned taste aversion and pituitary-adrenal activity in rats. Smotherman WP, et al. **Behav Brain Res** 1981 Jan;2(1):33–48

Conditioned social aversion in the male Mongolian gerbil (Meriones unguiculatus). Pettijohn TF. **J Comp Physiol Psychol** 1981 Apr; 95(2):228–39

Aversion to the reinforcer differentially affects conditioned reinforcement and instrumental responding. Wilson CL, et al. **J Exp Psychol [Anim Behav]** 1981 Apr;7(2):165–74

Disruption of autoshaped responding to a single of brain-stimulation reward by neuroleptic drugs. Phillips AG, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):543–8

CONDITIONING, OPERANT

Alterations in brain norepinephrine metabolism and behavior induced by environmental stimuli previously paired with inescapable shock. Cassens G, et al. **Behav Brain Res** 1981 May;2(3):387–407

Regional changes in brain catecholamine turnover in the rat during performance on fixed ratio and variable interval schedules of reinforcement. Heffner TG, et al. **Brain Res** 1981 Jun 9; 214(1):215–8

Time course of chronic haloperidol and clozapine upon operant rate and duration. Faustman W, et al. **Eur J Pharmacol** 1981 Mar 5; 70(1):65–70

Aversion to the reinforcer differentially affects conditioned reinforcement and instrumental responding. Wilson CL, et al. **J Exp Psychol [Anim Behav]** 1981 Apr;7(2):165–74

Effect gamma-melanotropin (gamma-MSH) on the conditioned behavior. Oka M, et al. **J Pharmacobiodyn** 1980 Nov;3(11):628–30

Fixed-ratio responding under second-order schedules of food presentation or cocaine injection. Goldberg SR, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):271–81

Effects of combinations of phencyclidine and pentobarbital on fixed-interval performance in rhesus monkeys. Woolverton WL, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):611–8

Dorsal tegmental bundle destruction: effects on operant behavior, brain catecholamine levels, and behavioral suppression produced by adrenergic agonists. Morris MD, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2621–6

The effects of electric shock on responding maintained by cocaine in rhesus monkeys. Bergman J, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):423–6

Central 5-hydroxytryptamine and the effects of hallucinogens and phenobarbital on operant responding in rats. Commissaris RL, et al. **Pharmacol Biochem Behav** 1981 May;14(5):595–601

Plasma catecholamines and renin during operant blood pressure conditioning in baboons. Goldstein DS, et al. **Physiol Behav** 1981 Jan; 26(1):33–7

Effects of chlorpromazine on food-maintained and observing behavior. Dearing ME, et al. **Psychopharmacology (Berlin)** 1981;73(3):281–5

[Action of essential oils of chamomile, cinnamon, absinthium, mace and origanum on operant conditioning behavior of the rat] Fundarò A, et al. **Boll Soc Ital Biol Sper** 1980 Nov 30;56(22):2375–80 (Eng. Abstr.) (Ita)

[Association of chlorpromazine and essential oils of absinthium and mace on operant conditioning behavior of the rat] Fundarò A, et al. **Boll Soc Ital Biol Sper** 1980 Nov 30;56(22):2370–4 (Eng. Abstr.)(Ita)

CONFLICT (PSYCHOLOGY)

Effect of sodium dipropylacetate on conflict behavior in rats. Ohmori K, et al. **Jpn J Pharmacol** 1980 Dec;30(6):925–7

Multiple benzodiazepine receptors: evidence of dissociation between anticonflict and anticonvulsant properties by PK 8165 and PK 9084 (two quinoline derivatives). Le Fur G, et al. **Life Sci** 1981 Mar 30; 28(13):1439–48

Impact of social conflict between mice on testosterone binding in the central nervous system. Raab A, et al. **Neuroendocrinology** 1981 May; 32(5):272–7

CORTICOSTERONE

Effects of 22S–hydroxy–cholesterol and other hydroxylated sterols on the ACTH–stimulated steroid production in rat adrenal cells. Huijmans JG, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):243–50

The effect of acute neurogenic stress on corticosterone and Cu an Zn levels in rats. Armario A, et al. **Agressologie** 1980;21(5):259–62

Unconjugated cortisol and corticosterone levels in amniotic fluid [letter] Sippell WG. **Am J Obstet Gynecol** 1981 Jun 1;140(3):353–4

Dissociation of adrenal corticosteroid production from ACTH in water–restricted female rats. Doell RG, et al. **Am J Physiol** 1981 Jul; 241(1):R21–4

Circadian corticosterone rhythm and stress response in rats with adrenal autotransplants. Gibson MJ, et al. **Am J Physiol** 1981 Apr; 240(4):E363–6

Mucosal gastrin receptor. VI. Induction by corticosterone in newborn rats. Peitsch W, et al. **Am J Physiol** 1981 Jun;240(6):G442–9

Specific stimulation of steroidogenesis in rat adrenal zona glomerulosa cells by pituitary peptides. Vinson GP, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):65–72

Paradoxical effects of D–Trp6–LHRH in immature female rats correlated with changes in ACTH, prolactin, and corticosterone levels. Nekola MV, et al. **Biol Reprod** 1981 Apr;24(3):505–11

Plasma corticosterone and thyroxine concentrations during chronic ingestion of crude oil in mallard ducks (Anas platyrhynchos). Rattner BA, et al. **Comp Biochem Physiol [C]** 1981;68C(2):103–7

Adrenal sensitivity to adrenocorticotropin varies diurnally. Kaneko M, et al. **Endocrinology** 1981 Jul;109(1):70–5

Tissue culture of fetal rat islets: corticosterone promotes D cell maintenance and function. McEvoy RC, et al. **Endocrinology** 1981 Jun; 108(6):2277–82

Site and mode of action of indomethacin on the hypothalamo–hypophyseal–adrenal axis: a temporal study in intact, hypothalamic–deafferentated, and hypothalamic–lesioned male rats. Weidenfeld J, et al. **Endocrinology** 1981 Jul;109(1):205–9

Circadian rhythm of plasma corticosterone in vagotomized rats. Itoh S, et al. **Experientia** 1981 Apr 15;37(4):380–1

Plasma corticosterone fluctuations during the oestrous cycle of the house mouse. Nichols DJ, et al. **Experientia** 1981 Mar 15;37(3):319–20

Effects of hypophysectomy and corticosterone acetate treatment on hepatic lipid composition in the chick (Gallus domesticus) embryo. Doneen BA. **Gen Comp Endocrinol** 1981 Mar;43(3):284–91

Plasma concentrations and corticosterone relative to photoperiod, oviposition, and ovulation in the domestic hen. Johnson AL, et al. **Gen Comp Endocrinol** 1981 Jan;43(1):10–6

Correlation between plasma thyroxine levels and corticosterone–binding activity in intact, ovariectomized, and ovariectomized estrogen–treated rats. Calvano SE, et al. **Horm Metab Res** 1981 Mar;13(3):171–4

Concentrations of pituitary, gonadal and adrenal hormones in serum of laying and broody white rock hens (Gallus domesticus). Bedrak E, et al. **J Endocrinol** 1981 May;89(2):197–204

Serum concentrations of prolactin, luteinizing hormone, growth hormone, corticosterone, progesterone, testosterone and oestradiol in relation to broodiness in domestic turkeys (Meleagris gallopavo). Harvey S, et al. **J Endocrinol** 1981 May;89(2):187–95

Radioimmunoassay of brian tissue and cell nuclear corticosterone. McEwen BS, et al. **J Neurosci Methods** 1980 Oct;3(1):57–65

Adrenal steroids and extinction behavior: antagonism by progesterone, deoxycorticosterone and dexamethasone of a specific effect of corticosterone. Bohus B, et al. **Life Sci** 1981 Jan 26;28(4):433–40

Differential effects of cannabinoid exposure and stress on plasma prolactin, growth hormone and corticosterone levels in male mice. Dalterio SL, et al. **Life Sci** 1981 Feb 16;28(7):761–6

Thyroid hormones are required for daily rhythms of plasma corticosterone and prolactin concentration. Ottenweller JE, et al. **Life Sci** 1981 Mar 2;28(9):1033–40

Modulation by transcortin–like binding sites of uptake and distribution of glucocorticoids by dispersed pituitary cells. Koch B, et al. **Mol Cell Endocrinol** 1981 May;22(2):169–78

Effects of extracellular potassium and 4–aminopyridine on corticosteroid secretion. Lymangrover JR, et al. **Mol Cell Endocrinol** 1981 Mar; 21(3):199–210

Corticosteroid–binding globulin and corticosterone interaction with progesterone receptors [letter] Raynaud JP, et al. **Nature** 1981 May 14;291(5811):171–2

The site of inhibitory action of a natural (corticosterone) and synthetic steroid (dexamethasone) in the hypothalamic–pituitary–adrenal axis. Sakakura M, et al. **Neuroendocrinology** 1981 Mar;32(3):174–8

Adrenal steroid inhibition of the vasopressin–neurophysin neurosecretory system to the median eminence of the rat. Differential effects of corticosterone and deoxycorticosterone administration after adrenalectomy. Silverman AJ, et al. **Neuroendocrinology** 1981 Mar; 32(3):129–33

ACTH4--10 affects behavior but not plasma corticosterone levels in a conditioned taste aversion situation. Smotherman WP, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):207–10

Long–term effects of early iron deficiency on consummatory behavior in the rat. Weinberg J, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):447–53

The pituitary–adrenal response to 'minimized' schedule–induced drinking. Brett LP, et al. **Physiol Behav** 1981 Feb;26(2):153–8

Kinetic aspects of cycloheximide–induced reversal of adrenocorticotropin effects on steroidogenesis and adrenal phospholipids in vivo. Farese RV, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7189–93

Alterations of biochemical parameters by acute and repetitive stress situations in mice. Quirce CM, et al. **Psychoneuroendocrinology** 1981; 6(1):91–7

Effect of androgens on the rate of muscle protein breakdown in rats treated with glucocorticoids. Santidrian S, et al. **Reproduccion** 1980 Oct–Dec;4(4):331–3

Long–term estrogenization in mammals. IV. Body, adrenal, and testes weights; polydipsia; food intake; vasopressin administration; and serum corticosterone levels in estrogenized male Evans rats. Bischoff F, et al. **Res Commun Chem Pathol Pharmacol** 1981 May;32(2):335–54

Corticosterone increases the amount of protein 1, a neuron–specific phosphoprotein, in rat hippocampus. Nestler EJ, et al. **Science** 1981 Jun 5;212(4499):1162–4

The development and application of a direct radioimmunoassay for corticosterone. Al–Dujaili EA, et al. **Steroids** 1981 Feb;37(2):157–76

[Effect of light on corticosterone synthesis in rat adrenals in vitro] Nikitina MM. **Biol Nauki** 1981;(4):58–63 **(Rus)**

[Glucocorticoid receptor content in the cytoplasm of human peripheral leukocytes] Golikov PP. **Probl Gematol Pereliv Krovi** 1981 Feb; 26(2):22–5 (Eng. Abstr.) **(Rus)**

CORTICOTROPIN

Effects of 22S–hydroxy–cholesterol and other hydroxylated sterols on the ACTH–stimulated steroid production in rat adrenal cells. Huijmans JG, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):243–50

Dissociation of adrenal corticosteroid production from ACTH in water–restricted female rats. Doell RG, et al. **Am J Physiol** 1981 Jul; 241(1):R21–4

Corticoliberin activity of rat neurohypophysis is distinct from vasopressin. Kárteszi M, et al. **Am J Physiol** 1981 Jun;240(6):E689–93

Effects of paraventricular lesions on stimulated ACTH release and CRF in stalk–median eminence of the rat. Makara GB, et al. **Am J Physiol** 1981 Apr;240(4):E441–6

Behavioral activity of met–enkephalin and ACTH4–10 and other peptides containing a phenylalanine and methionine residue. Rigter H, et al. **Biochem Biophys Res Commun** 1981 Jan 30;98(2):424–30

Cyclic AMP is not obligatory for adrenal steroidogenesis. Salmon DM, et al. **Biochem Soc Trans** 1981 Feb;9(1):96–7

Paradoxical effects of D–Trp6–LHRH in immature female rats correlated with changes in ACTH, prolactin, and corticosterone levels. Nekola MV, et al. **Biol Reprod** 1981 Apr;24(3):505–11

Effect of stress and ACTH on dopamine metabolism in the nucleus accumbens and frontal cortex. Fadda F, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):454–8

ACTH1–24 blocks opiate – induced analgesia in the rat. Smock T, et al. **Brain Res** 1981 May 11;212(1):202–6

Adrenocortical responses to adrenocorticotrophin in the rat. Normand M, et al. **Can J Physiol Pharmacol** 1980 Nov;58(11):1279–85

Ultrastructural localization of corticotropin, beta–lipotropin, and alpha- and beta–endorphin in the porcine anterior pituitary. Dacheux F. **Cell Tissue Res** 1981;215(1):87–101

Cytological localization of alpha–MSH, ACTH and beta–endorphin in the pars intermedia of the cichiid teleost Sarotherodon mossambicus. van Eys GJ, et al. **Cell Tissue Res** 1981;215(3):625–33

Presence of beta–endorphin–like immunoreactivity in the anterior pituitary gland of rat and man and evidence for the differential localization with ACTH. Watkins WB, et al. **Cell Tissue Res** 1981; 215(3):577–89

Structure and biosynthesis of pro–adrenocorticotropin/endorphin and related peptides. Eipper BA, et al. **Endocr Rev** 1980 Winter; 1(1):1–27 (186 ref.)

Adrenal sensitivity to adrenocorticotropin varies diurnally. Kaneko M, et al. **Endocrinology** 1981 Jul;109(1):70–5

Regulation of adrenal and testicular prolactin receptors by adrenocorticotropin and luteinizing hormone. Katikineni M, et al. **Endocrinology** 1981 Jun;108(6):2367–74

Evidence for two different turnover pools of adrenocorticotropin, alpha–melanocyte–stimulating hormone, and endorphin–related peptides released by the frog pituitary neurointermediate lobe. Loh YP, et al. **Endocrinology** 1981 Jul;109(1):54–61

Brain serotonin turnover correlates inversely with plasma adrenocorticotropin during the triphasic response to adrenalectomy in

SUBJECT SECTION

rats. Van Loon GR, et al. **Endocrinology** 1981 Jun;108(6):2269–76

Site and mode of action of indomethacin on the hypothalamo–hypophyseal–adrenal axis: a temporal study in intact, hypothalamic–deafferentated, and hypothalamic–lesioned male rats. Weidenfeld J, et al. **Endocrinology** 1981 Jul;109(1):205–9

Demonstration of peptides immunologically related to vertebrate neurohormones in Dugesia lugubris (Turbellaria, Tricladida). Schilt J, et al. **Gen Comp Endocrinol** 1981 Mar;43(3):331–5

Isolation, structure and synthesis of a heptapeptide with in vitro ACTH–releasing activity from porcine hypothalamus. Chang RC, et al. **Horm Metab Res** 1981 Apr;13(4):228–32

Differentiation of MSH–, ACTH–, endorphin–, and LPH–containing cells in the hypophysis during embryonic and fetal development. Dupouy JP. **Int Rev Cytol** 1980;68:197–249 (277 ref.)

The phosphorylation of adrenal proteins in response to adrenocorticotropic hormone. Koroscil TM, et al. **J Biol Chem** 1981 Jul 10;256(13):6700–7

Effect of exogenous and endogenous ACTH on adrenocortical cyclic GMP in the rat. Guillemant J, et al. **J Steroid Biochem** 1981 Jun; 14(6):557–61

Corticotropin/beta–endorphin immunoreactivity in rat mast cells. Peptide or protease? DiAugustine RP, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2663–8

Chemistry and biosynthesis of pro–opiomelanocortin. ACTH, MSH's, endorphins and their related peptides. Chrétien M, et al. **Mol Cell Biochem** 1981 Jan 28;34(2):101–27 (232 ref.)

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 1. Correlation of cyclic AMP levels and initial rates of lipolysis. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):35–41

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 2. Stability and restoration of activity of hormone–sensitive adenylate cyclase of adipocyte plasma membrane. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):43–50

Circulating human pituitary pro–gamma–melanotropin enhances the adrenal response to ACTH. Al–Dujaili EA, et al. **Nature** 1981 May 14;291(5811):156–9

Forms and activity of high molecular weight adrenocorticotropin in guinea pig. Gasson JC. **Peptides (Fayetteville)** 1980 Fall;1(3):223–9

ACTH4––10 affects behavior but not plasma corticosterone levels in a conditioned taste aversion situation. Smotherman WP, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):207–10

Kinetic aspects of cycloheximide–induced reversal of adrenocorticotropin effects on steroidogenesis and adrenal phospholipids in vivo. Farese RV, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7189–93

Secretory granules of an anterior pituitary cell line, AtT–20, contain only mature forms of corticotropin and beta–lipotropin. Gumbiner B, et al. **Proc Natl Acad Sci USA** 1981 Jan;78(1):318–22

The regional distribution of gamma 3–melanotropin–like peptides in bovine brain is correlated with adrenocorticotropin immunoreactivity but not with beta–endorphin. Shibasaki T, et al. **Regul Pept** 1981 Apr; 2(1):43–52

Differential immunostaining of adenohypophysial cells with antisera to ACTH and beta–endorphin. Watkins WB. **Regul Pept** 1981 Mar; 1(6):375–85

Changes in the peripheral blood leucocyte populations following an injection of corticotrophin in the immature chicken. Davison TF, et al. **Res Vet Sci** 1981 Jan;30(1):79–82

CORTICOTROPIN RELEASING HORMONE

Corticoliberin activity of rat neurohypophysis is distinct from vasopressin. Kárteszi M, et al. **Am J Physiol** 1981 Jun;240(6):E689–93

Effects of paraventricular lesions on stimulated ACTH release and CRF in stalk–median eminence of the rat. Makara GB, et al. **Am J Physiol** 1981 Apr;240(4):E441–6

Isolation, structure and synthesis of a heptapeptide with in vitro ACTH–releasing activity from porcine hypothalamus. Chang RC, et al. **Horm Metab Res** 1981 Apr;13(4):228–32

CRITICAL PERIOD (PSYCHOLOGY)

Critical periods for diphenylhydantoin and phenobarbital administration during gestation. Gauron EF, et al. **Psychol Rep** 1980 Dec; 47(3 Pt 2):1163–6

DANSYL COMPOUNDS

Selective inhibition of schistosome acetylcholinesterase by dansylated acetylcholine analogs. Dotson MJ, et al. **Comp Biochem Physiol [C]** 1981;68C(2):229–30

[Dansylated amino acid separation by polyacrylamide gel electrophoresis] Svinarchuk FP, et al. **Prikl Biokhim Mikrobiol** 1981 Jan–Feb; 17(1):144–50 (Eng. Abstr.) **(Rus)**

DECISION MAKING

Drug therapy decisions. A social judgment analysis. Gillis JS, et al. **J Nerv Ment Dis** 1981 Jul;169(7):439–47

DEFENSE MECHANISMS

Drug effects on attack defense and escape in mice. Kršiak M, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:47–52

DEMENTIA

Pseudodementia and physical findings masking significant psychopathology. Good MI. **Am J Psychiatry** 1981 Jun;138(6):811–4

DEPRESSION

Recent advances in the treatment of depression. Proceedings of an international symposium, Corfu, Greece, April 16––18, 1980. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):1–477

Zimelidine to geriatric patients: a pharmacokinetic and clinical study. Dehlin O, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):410–24

Anxiety and/or the depressive syndromes. Kline NS. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):271–6

Electroconvulsive therapy and receptor sensitivity. Modigh K, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):91–9

The medically ill elderly, tricyclic response, and ECT [letter] Small G, et al. **Am J Psychiatry** 1981 May;138(5):703–4

Convulsive and drug therapies of depression. Fink M. **Annu Rev Med** 1981;32:405–12 (71 ref.)

Prophylactic effect of lithium against depression in cyclothymic patients: a life–table analysis. Peselow ED, et al. **Compr Psychiatry** 1981 May–Jun;22(3):257–64

Oxazepam in the treatment of anxiety associated with depression: results of treatment in 1600 cases (Studies in depression, VI). Bailey HR, et al. **Curr Med Res Opin** 1981;7(3):156–63

Double–blind trial of amineptine and clomipramine in the treatment of depression. Lemoine P, et al. **Curr Med Res Opin** 1981;7(4):234–40

Classification, biochemistry of depression and the mode of action of antidepressant drugs. Okasha A. **Egypt J Psychiatry** 1979 Apr; 2(1):3–18

Viloxazine and the depressed schizophrenic––methodological issues. Kurland AA, et al. **J Clin Pharmacol** 1981 Jan;21(1):37–41

A double–blind study of dothiepin hydrochloride (Prothiaden) and amitriptyline in out–patients with masked depression. Dahl LE, et al. **J Int Med Res** 1981;9(2):103–7

A comparison of the therapeutic and cardiovascular effects of a single nightly dose of Prothiaden (dothiepin, dosulepin) and Lentizol (sustained–release amitriptyline) in depressed elderly patients. Khan AU. **J Int Med Res** 1981;9(2):108–12

Antidepressant efficacy of tranylcypromine isomers: a controlled study. Moises HW, et al. **J Neural Transm** 1981;50(2–4):185–92

A preliminary evaluation of parenting, depression, and violence profiles in methadone–maintained women. Oehlberg SM, et al. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(34):380–6

Evaluation of the clinical efficacy of single daily doses of antidepressants. De Maio D, et al. **Prog Neuropsychopharmacol** 1980;4(6):607–12

Clinical response, plasma levels and pharmacokinetics of desipramine in depressed in–patients. Hrdina PD, et al. **Prog Neuropsychopharmacol** 1980;4(6):591–600

Platelet MAO activity and monoamine metabolites in cerebrospinal fluid in depressed and suicidal patients and in healthy controls. Oreland L, et al. **Psychiatry Res** 1981 Feb;4(1):21–9

The therapeutic profile of mianserin in mild elderly depressives [proceedings] Branconnier RJ, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):129–31

Vasopressin function in depression and mania [proceedings] Gold PW, et al. **Psychopharmacol Bull** 1981 Jan;17(1):7–9

Effects of phenelzine and amitriptyline on depression [proceedings] Paykel ES, et al. **Psychopharmacol Bull** 1981 Jan;17(1):104–6

The pharmacological treatment of schizoaffective disorder–depressed: a review of the literature [proceedings] Spiker DG. **Psychopharmacol Bull** 1981 Jan;17(1):75–8

Methylphenidate in depression and states of apathy. Moore DP. **South Med J** 1981 Mar;74(3):347–8

[Drug therapy of depression: benefits and limits of blood levels of tricyclic antidepressants] Baumann P. **Schweiz Med Wochenschr** 1981 Feb 14; 111(7):228–39 (112 ref.) (Eng. Abstr.) **(Fre)**

[Therapy of elderly depressive patients. Lofepramine and amitriptyline under double–blind conditions] Jessel HJ, et al. **ZFA (Stuttgart)** 1981 Apr 10;57(10):784–8 **(Ger)**

DEPRESSIVE DISORDER

The Hamilton depression scale. Evaluation of objectivity using logistic models. Bech P, et al. **Acta Psychiatr Scand** 1981 Mar;63(3):290–9

The temporo–spatial context. A neglected aspect of the depressive response. León CA. **Acta Psychiatr Scand** 1981 Feb;63(2):129–46

Depression and cerebrospinal fluid citrate. Mellerup ET, et al.

Acta Psychiatr Scand 1981 Jan;63(1):57-60

A double-blind comparison of nomifensine and amitriptyline in the treatment of depression. Ong SB, et al. **Acta Psychiatr Scand** 1981 Mar; 63(3):198-207

Plasma tryptophan binding to albumin in unipolar depressives. Riley GJ, et al. **Acta Psychiatr Scand** 1981 Feb;63(2):165-72

Recent advances in the treatment of depression. Proceedings of an international symposium, Corfu, Greece, April 16--18, 1980. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):1-477

Controlled cross-over study of a 5-HT uptake inhibiting and an NA uptake inhibiting antidepressant. Aberg A. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):244-55

Biogenic amines and depression (introduction to symposium). Agurell S. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):17-9

Zimelidine vs maprotiline in depressed outpatients. A preliminary report. d'Elia G, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):225-35

Influence of depression and antidepressants on weight. Gottfries CG. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):353-6

Depression: treatment compliance in general practice. Johnson DA. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):447-53

Anxiety and/or the depressive syndromes. Kline NS. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):271-6

Zimelidine and amitriptyline in the treatment of depressive illness in general practice. Loudon JB, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):454-63

Growth hormone response in patients with depression. Matussek N, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):122-6

A double blind comparison of zimelidine and amitriptyline in endogenous depression. Montgomery SA, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):314-27

Serotonin and noradrenaline uptake inhibitors in the treatment of depression--relationship to 5-HIAA in spinal fluid. Träskman-Bendz L, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):209-18

5-HT reuptake inhibitors plus tryptophan in endogenous depression. Wålinder J, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):179-90

Zimelidine: comparison of different dosage regimes in general practice. Watson JM, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):464-70

Antidepressant drug therapy. DeGennaro M, et al. **Am J Nurs** 1981 Jul; 81(7):1304-10

Effect of lithium on glycine levels in patients with affective disorders. Deutsch SI, et al. **Am J Psychiatry** 1981 May;138(5):683-4

Psychotic depression: a separate entity? Frances A, et al. **Am J Psychiatry** 1981 Jun;138(6):831-3

Pseudodementia and physical findings masking significant psychopathology. Good MI. **Am J Psychiatry** 1981 Jun;138(6):811-4

Effect of alcohol consumption and cigarette smoking on antidepressant levels of depressed patients. Linnoila M, et al. **Am J Psychiatry** 1981 Jun;138(6):841-2

Plasma tryptophan and five other amino acids in depressed and normal subjects. DeMyer MK, et al. **Arch Gen Psychiatry** 1981 Jun; 38(6):642-6

The effect of psychobiological research on treatment outcome. A controlled study. Kocsis JH, et al. **Arch Gen Psychiatry** 1981 May; 38(5):511-5

Correlation of individual symptoms and other clinical variables with cerebrospinal fluid amine metabolites and tryptophan in depression. Banki CM, et al. **Arch Psychiatr Nervenkr** 1981;229(4):345-53

Receptors, adenylate cyclase, depression, and lithium. Belmaker RH. **Biol Psychiatry** 1981 Apr;16(4):333-50

Cerebral evoked potential changes produced by treatment with lithium carbonate. Straumanis JJ Jr, et al. **Biol Psychiatry** 1981 Feb; 16(2):113-29

Management of depression with serotonin precursors. van Praag HM. **Biol Psychiatry** 1981 Mar;16(3):291-310

Effect of piribedil (ET-495) on plasma norepinephrine: relationship to antidepressant response. Reus VI, et al. **Commun Psychopharmacol** 1980; 4(3):207-13

Depressive illness in general practice: a pilot study. Watson JM, et al. **Health Bull (Edinb)** 1981 Mar;39(2):112-6

Viloxazine in the treatment of depressive neurosis: a placebo and standard (imipramine) controlled clinical study. Petrie WM, et al. **Int Pharmacopsychiatry** 1980;15(3):193-6

Relapse after short-term drug therapy in neurotic outpatients. Rickels K, et al. **Int Pharmacopsychiatry** 1980;15(3):186-92

Single- versus multiple-dose comparative trial of desipramine hydrochloride: a double-placebo method. Barnes RJ, et al. **J Clin Pharmacol** 1980 Nov-Dec;20(11-12):681-8

A critical appraisal of amoxapine. Smith RS Jr, et al. **J Clin Psychiatry** 1981 Jun;42(6):238-42

The clinical characteristics and treatment of atypical depression. Sovner RD. **J Clin Psychiatry** 1981 Jul;42(7):285-9

Maprotiline (Ludiomil)--another antidepressant. **Med Lett Drugs Ther** 1981 Jun 26;23(13):58-9

Relationship between response to phenelzine and MAO inhibition in a clinical trial of phenelzine, amitriptyline and placebo. Raft D, et al. **Neuropsychobiology** 1981;7(3):122-6

Serum DBH and platelet MAO in patients with depressive disorders. Honecker H, et al. **Pharmacopsychiatria** 1981 Jan;14(1 Suppl):10-4

Nortriptyline and pituitary-thyroid function in affective disorder. Nordgren L, et al. **Pharmacopsychiatria** 1981 Mar;14(2):61-5

Clinical pharmacology of viloxazine hydrochloride. Vandel B, et al. **Pharmacopsychiatria** 1981 Mar;14(2):66-70

Noradrenergic transmission in depression: under- or overfunction? Waldmeier PC. **Pharmacopsychiatria** 1981 Jan;14(1 Suppl):3-9

Interrelationship of hysteroid dysphoria and borderline personality disorder. Liebowitz MR, et al. **Psychiatr Clin North Am** 1981 Apr; 4(1):67-87

Pharmacokinetics of clomipramine in depressive patients. de Cuyper HJ, et al. **Psychiatry Res** 1981 Apr;4(2):147-56

An inverse correlation between serum levels of desmethylimipramine and melatonin-like immunoreactivity in DMI-responsive depressives. Halbreich U, et al. **Psychiatry Res** 1981 Feb;4(1):109-13

Pretreatment amine neurotransmitter system interrelationships in depression [proceedings] Bowden CL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):70-2

Clinical trials with new bicyclic and tetracyclic compounds: zimelidine and maprotiline [proceedings] Claghorn JL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):23-6

Clinical efficacy of the new antidepressant bupropion (Wellbutrin) [proceedings] Halaris AE, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):140-2

Factors which affect antidepressant drug responses in a multicenter controlled trial [proceedings] Logue JN, et al. **Psychopharmacol Bull** 1981 Jan;17(1):138-9

Novel antidepressants: a clinical trial of mianserin [proceedings] McGrath PJ, et al. **Psychopharmacol Bull** 1981 Jan;17(1):21-3

Crossover study of zimelidine and desipramine in depression: evidence for amine specificity [proceedings] Potter WZ, et al. **Psychopharmacol Bull** 1981 Jan;17(1):26-9

Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo-controlled comparison [proceedings] Quitkin FM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):142-4

Possible pathophysiological mechanisms in subtypes of unipolar depressive disorders based on differences in urinary MHPG levels [proceedings] Schildkraut JJ, et al. **Psychopharmacol Bull** 1981 Jan;17(1):90-91

Second generation antidepressants: a clinical pharmacotherapeutic research strategy [proceedings] Shopsin B. **Psychopharmacol Bull** 1981 Jan;17(1):33-5

Efficacy of desipramine in mildly depressed patients: a double-blind, placebo-controlled trial [proceedings] Stewart JW, et al. **Psychopharmacol Bull** 1981 Jan;17(1):136-8

Unexpected neuroendocrine-transmitter relationships [proceedings] Stokes PE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):72-5

Is the failure of (-)deprenyl, a selective monoamine oxidase B inhibitor, to alleviate depression related to freedom from the cheese effect? Mendis N, et al. **Psychopharmacology (Berlin)** 1981;73(1):87-90

[Management of treatment-resistant depression without ECT (author's transl)] Kielholz P, et al. **Dtsch Med Wochenschr** 1981 May 22; 106(21):671-3 (Eng. Abstr.) (Ger)

[Studies on stress in psychiatric patients (author's transl)] Ackenheil M, et al. **MMW** 1981 May 8;123(19):805-8 (Eng. Abstr.) (Ger)

[Development of biological psychiatric depression research (author's transl)] Matussek N. **MMW** 1981 May 8;123(19):793-4 (Eng. Abstr.) (Ger)

[Pharmacological treatment of affective disorders (author's transl)] Beckmann H. **Nervenarzt** 1981 Mar;52(3):135-46 (Ger)

[Treatment of depression with psychotropic drugs (author's transl)] Gastpar M. **Praxis** 1981 Feb 3;70(6):215-9 (Eng. Abstr.) (Ger)

[24 hours plasma tryptophan levels in patients with endogenous depression (author's transl)] Malatino LS, et al. **Riv Patol Nerv Ment** 1979 Nov-Dec;100(6):340-6 (Eng. Abstr.) (Ita)

[Plasma dopamine beta-hydroxylase activity in endogenous depressive syndromes] Pużyński S, et al. **Psychiatr Pol** 1980 Nov-Dec; 14(6):581-6 (Eng. Abstr.) (Pol)

DESIPRAMINE

Withdrawal from chronic phencyclidine (PCP) dependence with desipramine. Tennant FS Jr, et al. **Am J Psychiatry** 1981 Jun; 138(6):845-7

Brain distribution and kinetics of desipramine in the rat. Hrdina PD, et al. **Can J Physiol Pharmacol** 1981 Feb;59(2):163-7

Plasma desipramine levels after single dosage and at steady state in outpatients. Rudorfer MV, et al. **Commun Psychopharmacol** 1980; 4(3):185-8

'High affinity' binding of [3H]desipramine to rat cerebral cortex: relationship to tricyclic antidepressant-induced inhibition of norepinephrine uptake. Rehavi M, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):597-9

Single- versus multiple-dose comparative trial of desipramine hydrochloride: a double-placebo method. Barnes RJ, et al. **J Clin Pharmacol** 1980 Nov-Dec;20(11-12):681-8

An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment. Koide T, et al. **Life Sci** 1981 Mar 9;28(10):1139-45

Subsensitivity of the beta-adrenergic receptor-linked adenylate cyclase system of rat pineal gland following repeated treatment with desmethylimipramine and nialamide. Moyer JA, et al. **Mol Pharmacol** 1981 Mar;19(2):187-93

Subchronic treatment with the tricyclic antidepressant DMI increases isolation-induced fighting in rats. Willner P, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):475-9

Clinical response, plasma levels and pharmacokinetics of desipramine in depressed in-patients. Hrdina PD, et al. **Prog Neuropsychopharmacol** 1980;4(6):591-600

An inverse correlation between serum levels of desmethylimipramine and melatonin-like immunoreactivity in DMI-responsive depressives. Halbreich U. et al. **Psychiatry Res** 1981 Feb;4(1):109-13

Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors. Tang SW, et al. **Psychiatry Res** 1981 Apr;4(2):129-38

Crossover study of zimelidine and desipramine in depression: evidence for amine specificity [proceedings] Potter WZ, et al. **Psychopharmacol Bull** 1981 Jan;17(1):26-9

Efficacy of desipramine in mildly depressed patients: a double-blind, placebo-controlled trial [proceedings] Stewart JW, et al. **Psychopharmacol Bull** 1981 Jan;17(1):136-8

Changes in action of tricyclic and tetracyclic antidepressants: desipramine and mianserin, on avoidance behavior in the course of the chronic treatment. Hano J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):265-8

[Changes of neuronal activity in the rat's hippocampus under long-term treatment with desipramine] Jähkel M, et al. **Acta Biol Med Ger** 1980; 39(10):1083-7 (Eng. Abstr.) **(Ger)**

DESOXYCORTICOSTERONE

Metyrapone effect on blood pressure and deoxycorticosterone levels in the rat. Hauger-Klevene JH, et al. **Acta Physiol Lat Am** 1978; 28(4-5):219-21

Mineralocorticoid effects on Na-K-ATPase in individual nephron segments. Garg LC, et al. **Am J Physiol** 1981 Jun;240(6):F536-44

Deoxycorticosterone biosynthesis from progesterone in kidney tissue of the human fetus. Winkel CA, et al. **J Clin Endocrinol Metab** 1981 Jul; 53(1):10-5

Adrenal steroids and extinction behavior: antagonism by progesterone, deoxycorticosterone and dexamethasone of a specific effect of corticosterone. Bohus B, et al. **Life Sci** 1981 Jan 26;28(4):433-40

Adrenal steroid inhibition of the vasopressin-neurophysin neurosecretory system to the median eminence of the rat. Differential effects of corticosterone and deoxycorticosterone administration after adrenalectomy. Silverman AJ, et al. **Neuroendocrinology** 1981 Mar; 32(3):129-33

Plasma concentrations of 11-deoxycorticosterone in women during the menstrual cycle. Parker CR Jr, et al. **Obstet Gynecol** 1981 Jul; 58(1):26-30

Deoxycorticosterone biosynthesis in human kidney: potential for formation of a potent mineralocorticosteroid in its site of action. Winkel CA, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7069-73

5 alpha-Dihydro-11-deoxycorticosterone: effect on blood pressure in the rat. Carroll J, et al. **Steroids** 1981 Jan;37(1):111-20

19-Nor-deoxycorticosterone in the neutral fraction of human urine. Dale SL, et al. **Steroids** 1981 Jan;37(1):103-9

DEXTROAMPHETAMINE

Apparent serotonergic modulation of the dose-dependent biphasic response of neostriatal neurons produced by D-amphetamine. Rebec GV, et al. **Brain Res** 1981 Apr 6;210(1-2):277-89

Effects of intracerebroventricular injection of d-amphetamine on metabolic, respiratory, and vasomotor activities and body temperatures in the rat. Lin MT, et al. **Can J Physiol Pharmacol** 1980 Aug; 58(8):903-8

Cats develop tolerance to d-amphetamine's effects upon locomotior and stereotyped behaviors. Jacobs BL, et al. **Eur J Pharmacol** 1981 Jan 29; 69(3):353-6

A comparison of the hypothermic effects of methylphenidate and d-amphetamine. Yehuda S, et al. **Int J Neurosci** 1981;13(2-3):117-20

Growth hormone, prolactin, and growth responses in hyperkinetic males treated with d-amphetamine. Greenhill LL, et al. **J Am Acad Child Psychiatry** 1981 Winter;20(1):84-103

Effects of in vivo amphetamine administration on dopamine synthesis regulation in rat brain striatal synaptosomes. Patrick RL, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):686-91

Neurotensin blocks certain amphetamine-induced behaviours. Ervin GN, et al. **Nature** 1981 May 7;291(5810):73-6

Interaction of MIF-I or alpha-MSH with D-amphetamine or chlorpromazine on thermoregulation and motor activity of rats maintained at different ambient temperatures. Yehuda S, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):243-8

Effects of amphetamine and phenylpropanolamine on food intake in rats with ventromedial hypothalamic or dorsolateral tegmental damage. Wellman PJ, et al. **Physiol Behav** 1980 Dec;25(6):819-27

Computer analyzed EEG in amphetamine-responsive hyperactive children. McIntyre HB, et al. **Psychiatry Res** 1981 Apr;4(2):189-97

The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine. Mikkelsen E, et al. **Psychiatry Res** 1981 Apr;4(2):157-69

Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Miczek KA. **Psychopharmacol Bull** 1981 Jan; 17(1):60-2

Long-term d-amphetamine in rats: lack of change in post-synaptic dopamine receptor sensitivity. Jackson DM, et al. **Psychopharmacology (Berlin)** 1981;73(3):276-80

The effects of electroconvulsive shock on the discriminative stimulus properties of d-amphetamine and apomorphine: evidence for dopamine receptor alteration subsequent ECS. White DK, et al. **Psychopharmacology (Berlin)** 1981;73(3):211-4

The effects of d-amphetamine and potassium on serotonin release and metabolism in rat cerebral cortex tissue. Homan HD, et al. **Res Commun Chem Pathol Pharmacol** 1981 Feb;31(2):223-40

DIAZEPAM

Antagonism of 4-aminopyridine to ketamine-diazepam anesthesia in children. Martínez-Aguirre E. **Acta Anaesthesiol Belg** 1980; 31(4):289-91

Case report of unusual diazepam abstinence syndrome. Nagy BR, et al. **Am J Psychiatry** 1981 May;138(5):694-5

The effect of diazepam on the cerebral metabolic state in rats and its interaction with nitrous oxide. Carlsson C, et al. **Anesthesiology** 1981 Jun;54(6):488-95

Treatment of diazepam withdrawal syndrome with propranolol. Abernethy DR, et al. **Ann Intern Med** 1981 Mar;94(3):354-5

The role of albumin conformation in the binding of diazepam to human serum albumin. Wilting J, et al. **Biochim Biophys Acta** 1980 Dec 16; 626(2):291-8

The replicability of the psychophysiological effects of diazepam. Itil TM, et al. **Biol Psychiatry** 1981 Jan;16(1):65-70

Concentrations of N-descyclopropylmethylprazepam in whole-blood, plasma, and milk after administration of prazepam to humans. Brodie RR, et al. **Biopharm Drug Dispos** 1981 Jan-Mar;2(1):59-68

Plasma diazepam and desmethyldiazepam concentrations during long-term diazepam therapy. Greenblatt DJ, et al. **Br J Clin Pharmacol** 1981 Jan;11(1):35-40

Sex-related differences in the plasma protein binding of lignocaine and diazepam. Routledge PA, et al. **Br J Clin Pharmacol** 1981 Mar; 11(3):245-50

Benzodiazepines prevent kainate-induced loss of GABAergic and cholinergic neurons in the chick retina. Imperato A, et al. **Brain Res** 1981 May 25;213(1):205-10

The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures. Shibla DB, et al. **Brain Res** 1981 Apr 6;210(1-2):471-4

Effects of desmethyldiazepam on diazepam kinetics: a study of effects of a metabolite on parent drug disposition. Abernethy DR, et al. **Clin Pharmacol Ther** 1981 Jun;29(6):757-61

Diazepam effects and kinetics in Caucasians and Orientals. Ghoneim MM, et al. **Clin Pharmacol Ther** 1981 Jun;29(6):749-56

Diazepam interaction with antituberculosis drugs. Ochs HR, et al. **Clin Pharmacol Ther** 1981 May;29(5):671-8

Clobazam and diazepam in anxiety. Rickels K, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):95-100

Availability of isosorbide dinitrate, diazepam and chlormethiazole, from i.v. delivery systems. Cossum PA, et al. **Eur J Clin Pharmacol** 1981 Feb;19(3):181-5

Increase of benzodiazepine binding to the membranes isolated in the presence of diazepam. Korneyev AY, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):127-30

Phasic hippocampal activity during paradoxical sleep in the rat: selective suppression after diazepam administration. Monmaur P. **Experientia** 1981 Mar 15;37(3):261-2

Excessive premedication of diazepam [letter] Smith BL. **Gastrointest Endosc** 1981 May;27(2):110

Limited usefulness of the breath test in evaluation of drug metabolism: a study in human oral contraceptive users treated with dimethylaminoantipyrine and diazepam. Sonnenberg A, et al. **Hepatogastroenterology** 1980 Apr;27(2):104-8

Simultaneous determination of diphenhydramine, methaqualone, diazepam and chlorpromazine in liver by use of enzyme digestion: a comparison of digestion procedures. Holzbecher M, et al. **J Anal Toxicol** 1981 Mar-Apr;5(2):62-4

Determination of diazepam and its major metabolites in man and in the cat by high-performance liquid chromatography. Cotler S, et al.

J Chromatogr 1981 Jan 2;222(1):95–106

Comparative protein binding of diazepam and desmethyldiazepam. Allen MD, et al. **J Clin Pharmacol** 1980 Nov–Dec;20(11–12):639–43

A comparison of prazepam, diazepam, lorazepam and placebo in anxious outpatients in non-psychiatric private practices. Zung WW, et al. **J Clin Psychiatry** 1981 Jul;42(7):280–4

Effects of diazepam on schedule-controlled and schedule-induced behavior under signaled and unsignaled shock. Hymowitz N. **J Exp Anal Behav** 1981 Jul;36(1):119–32

Comparison of the therapeutic effect, tolerance and safety of ketazolam and diazepam administered for six months to out-patients with chronic anxiety neurosis. Fabre LF, et al. **J Int Med Res** 1981;9(3):191–8

Benzodiazepine withdrawal symptoms and propranolol. Tyrer P, et al. **Lancet** 1981 Mar 7;1(8219):520–2

Benzodiazepine receptor: heterogeneity in rabbit brain. Yokoi I, et al. **Life Sci** 1981 Apr 6;28(14):1591–5

The effect of diazepam on nystagmus induced by stimulation of the lateral geniculate body in the rabbit. Ishikawa M, et al. **Neuropharmacology** 1981 May;20(5):435–9

Effect of diazepam on stress induced changes in brain histamine. Mazurkiewicz-Kwilecki IM. **Pharmacol Biochem Behav** 1981 Mar; 14(3):333–8

An in vitro study of the interaction between diazepam and some antacid or excipients. Naggar VF. **Pharmazie** 1981;36(2):114–7

Psychotropic drugs and behaviour therapy. Stern R. **Practitioner** 1981 Jan;225(1351):21–5

Public judgments on the importance of valium information [proceedings] Fisher S, et al. **Psychopharmacol Bull** 1981 Jan;17(1):134

Memory and performance effects of single and 3-week administration of diazepam. Ghoneim MM, et al. **Psychopharmacology (Berlin)** 1981; 73(2):147–51

The relationships between clinical response, psychophysiological variables and plasma levels of amitriptyline and diazepam in neurotic outpatients. Johnstone EC, et al. **Psychopharmacology (Berlin)** 1981;72(3):233–40

Impairment of learning or memory in the mature and old rat by diazepam. Komiskey HL, et al. **Psychopharmacology (Berlin)** 1981;73(3):304–5

Benzodiazepine inhibition of the calcium-calmodulin protein kinase system in brain membrane. DeLorenzo RJ, et al. **Science** 1981 Jul 31; 213(4507):546–9

[Diazemuls. Diazepam in a new vehicle for parenteral use] Hüttel MS, et al. **Ugeskr Laeger** 1981 Jan;143(3):140 **(Dan)**

[A double blind trial : oxprenolol/diazepam (author's transl)] Scharbach H. **Encephale** 1981;7(1):51–8 (Eng. Abstr.) **(Fre)**

[The influence of oxazepam and diazepam on the sexual behaviour and level of GABA biogenic amines in a male rat's brain (author's transl)] Borzęcki Z, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979; 34:371–6 (Eng. Abstr.) **(Pol)**

[Role of the GABA-ergic link in the development of the tranquilizing effect in cats] Kozlovskaia MM, et al. **Biull Eksp Biol Med** 1981; 91(1):45–8 (Eng. Abstr.) **(Rus)**

DIBENZAZEPINES

The effect of mianserin on urinary catecholamine excretion in psychiatric patients. Moody JP, et al. **Br J Clin Pharmacol** 1981 Jan; 11(1):103–5

Mianserin: direct activation of brain norepinephrine neurons by blocking alpha 2-receptors. Engberg G, et al. **Commun Psychopharmacol** 1980; 4(3):233–9

The metabolism of mianserin in women, rabbits, and rats: identification of the major urinary metabolites. de Jongh GD, et al. **Drug Metab Dispos** 1981 Jan–Feb;9(1):48–53

Supersensitivity of central noradrenergic presynaptic autoreceptors following chronic treatment with the antidepressant mianserin. Cerrito F, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):425–6

Time course of chronic haloperidol and clozapine upon operant rate and duration. Faustman W, et al. **Eur J Pharmacol** 1981 Mar 5; 70(1):65–70

Cardiovascular effects of mianserin and amitriptyline in healthy volunteers. Wester HA, et al. **Int J Clin Pharmacol Ther Toxicol** 1980 Dec;18(12):513–7

Mianserin: a possible cause of neutropenia and agranulocytosis. Adverse Drug Reactions Advisory Committee. **Med J Aust** 1980 Dec 13; 2(12):673–4

Comparison of the antimuscarinic activity of mianserin and amitriptyline in the cat superior cervical ganglion. Kwok YH, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):161–4

The therapeutic profile of mianserin in mild elderly depressives [proceedings] Branconnier RJ, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):129–31

Novel antidepressants: a clinical trial of mianserin [proceedings] McGrath PJ, et al. **Psychopharmacol Bull** 1981 Jan;17(1):21–3

Changes in action of tricyclic and tetracyclic antidepressants: desipramine and mianserin, on avoidance behavior in the course of the chronic treatment. Hano J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):265–8

Clozapine: plasma levels and prolactin response. Kane JM, et al. **Psychopharmacology (Berlin)** 1981;73(2):184–7

[Does clozapine cause dependence?] Zapletálek M, et al. **Agressologie** 1990;21(A):19–21 (Eng. Abstr.) **(Ger)**

[Peculiarities and difficulties in the systematic drug therapy of chronic schizophrenics (schizophrenic 'defect')] Lange E, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1981 Jan;33(1):34–8 (Eng. Abstr.) **(Ger)**

[Therapy of elderly depressive patients. Lofepramine and amitriptyline under double-blind conditions] Jessel HJ, et al. **ZFA (Stuttgart)** 1981 Apr 10;57(10):784–8 **(Ger)**

DIBENZOTHIEPINS

High doses of clorotepin in chronic schizophrenia (preliminary report). Bastecký J, et al. **Agressologie** 1980;21(A):31–5

Simultaneous measurement of dothiepin and its major metabolites in plasma and whole blood by gas chromatography-mass fragmentography. Maguire KP, et al. **J Chromatogr** 1981 Mar 13; 222(3):399–408

A double-blind study of dothiepin hydrochloride (Prothiaden) and amitriptyline in out-patients with masked depression. Dahl LE, et al. **J Int Med Res** 1981;9(2):103–7

A comparison of the therapeutic and cardiovascular effects of a single nightly dose of Prothiaden (dothiepin, dosulepin) and Lentizol (sustained-release amitriptyline) in depressed elderly patients. Khan AU. **J Int Med Res** 1981;9(2):108–12

Clinical interpretation of pharmacokinetic data on dothiepin hydrochloride (Dosulepin, Prothiaden). Rees JA. **J Int Med Res** 1981; 9(2):98–102

[Comparison of blood and bile levels of oxyprothepine and docloxythepin in rats] Queisnerová M, et al. **Cesk Farm** 1981 Feb;30(1):14–5 (Eng. Abstr.) **(Cze)**

DIBENZOXAZEPINES

The effect of amoxapine and imipramine on serum prolactin levels. Cooper DS, et al. **Arch Intern Med** 1981 Jul;141(8):1023–5

Amoxapine: a review of literature. Ban TA, et al. **Int Pharmacopsychiatry** 1980;15(3):166–70 (21 ref.)

Postmortem blood and tissue levels of loxapine and its metabolites. Cooper TB, et al. **J Anal Toxicol** 1981 Mar–Apr;5(2):99–100

A critical appraisal of amoxapine. Smith RS Jr, et al. **J Clin Psychiatry** 1981 Jun;42(6):238–42

DIIODOTYROSINE

Changes of receptor cooperation in Tetrahymena by re-exposure to hormones. Csaba G, et al. **Acta Biol Acad Sci Hung** 1980; 31(1–3):43–7

Enhancement of the sensitivity of Tetrahymena to a second hormonal influence by hormone pretreatment. Csaba G, et al. **Acta Biol Med Ger** 1980;39(10):1027–30

Horseradish peroxidase. XLII. Oxidations of L-tyrosine and 3,5-diiodo-L-tyrosine by compound II. Ralston IM, et al. **Can J Biochem** 1980 Nov;58(11):1270–6

DISCRIMINATION (PSYCHOLOGY)

Effects of pimozide on nordiscriminated and discriminated performance in the pigeon. Tombaugh TN. **Psychopharmacology (Berlin)** 1981; 73(2):137–41

DISCRIMINATION LEARNING

Characteristics of the stimulus produced by the mixture of cannabidiol with delta 9-tetrahydrocannabinol. Zuardi AW, et al. **Arch Int Pharmacodyn Ther** 1981 Jan;249(1):137–46

Role of training conditions in discrimination of central nervous system stimulants by rats. Stolerman IP, et al. **Psychopharmacology (Berlin)** 1981;73(3):295–303

DOPA

Pronounced formation of 5-OH-dopa at enzymatic oxidation of DOPA in the presence of ascorbic acid. Hansson C, et al. **Acta Derm Venereol (Stockh)** 1981;61(2):147–8

Urinary excretion of 5-S-cysteinyldopa in healthy Japanese. Morishima T, et al. **Acta Derm Venereol (Stockh)** 1981;61(2):149–50

Specific colorimetric detection of o-diphenols and 3,4-dihydroxyphenylalanine-containing peptides. Waite JH, et al. **Anal Biochem** 1981 Feb;111(1):131–6

Formation of cysteine conjugates from dihydroxyphenylalanine and its S-cysteinyl derivatives by peroxidase-catalyzed oxidation. Ito S, et al. **Biochim Biophys Acta** 1981 Jan 21;672(2):151–7

Studies related to the blood-brain barrier to monoamines and protein in pia-arachnoid cultures. Hervonen H, et al. **Brain Res** 1981 Apr 6; 210(1–2):449–54

Identification of cysteinyldopa-derived units in eumelanins from mammalian eyes. Novellino E, et al. **FEBS Lett** 1981 Mar 9; 125(1):101–3

Chronic L–DOPA treatment of mice: a behavioural and biochemical study. Bailey R, et al. **J Neural Transm** 1981;50(2–4):209–24

DOPAMINE

The effect of dopamine on prolactin cells in vivo. Warchol JB, et al. **Acta Med Pol** 1980;21(4):403–4

Influence of estrogens on tuberoinfundibular and striatal dopaminergic systems in the rat. Labrie F, et al. **Acta Psychiatr Belg** 1980 Sep–Oct; 80(5):658–73

Changes in cardiovascular and renal function during catecholamine infusions in developing swine. Buckley NM, et al. **Am J Physiol** 1981 Apr;240(4):F276–81

Resumption of prolactin secretion after dopaminergic inhibition: differential effects of dopamine and its agonists. Woolf PD. **Am J Physiol** 1981 Jun;240(6):E700–4

Role of calmodulin in dopaminergic transmission. Hanbauer I, et al. **Ann NY Acad Sci** 1980;356:292–303

Treatment of massive phenobarbital overdose with dopamine diuresis. Costello JB, et al. **Arch Intern Med** 1981 Jun;141(7):938–40

Role of the neostriatal dopaminergic activity in sequencing and selecting behavioural strategies: facilitation of processes involved in selecting the best strategy in a stressful situation. Cools AR. **Behav Brain Res** 1980 Oct;1(5):361–78

Phenylethylamine effects on dopamine synthesis. Structure–activity relationships. Patrick RL. **Biochem Pharmacol** 1981 Jan 15; 30(2):141–6

Development of dopaminergic properties in cultured neurons from chick embryo cerebral hemispheres. Louis JC, et al. **Biochem Soc Trans** 1981 Feb;9(1):104–5

Effect of stress and ACTH on dopamine metabolism in the nucleus accumbens and frontal cortex. Fadda F, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):454–8

Ibopamine (SB 7505) in normal subjects and in chronic renal failure: a preliminary report. Stefoni S, et al. **Br J Clin Pharmacol** 1981 Jan; 11(1):69–72

Relationship between the presence of dopaminergic neurons and GABA receptors in substantia nigra: effects of lesions. Gale K. **Brain Res** 1981 Apr 6;210(1–2):401–6

Dopamine–activated adenylate cyclase of spinal cord: supersensitivity following transection of the cord. Gentleman S, et al. **Brain Res** 1981 Apr 6;210(1–2):271–5

Regional changes in brain catecholamine turnover in the rat during performance on fixed ratio and variable interval schedules of reinforcement. Heffner TG, et al. **Brain Res** 1981 Jun 9; 214(1):215–8

The relationship between loss of dopamine nerve terminals, striatal [3H]spiroperidol binding and rotational behavior in unilaterally 6–hydroxydopamine–lesioned rats. Heikkila RE, et al. **Brain Res** 1981 May 4;211(2):285–92

Regional differences in catecholamine formation and metabolism in the rat spinal cord. Karoum F, et al. **Brain Res** 1981 May 18; 212(2):361–6

Effects of methamphetamine on blood flow in the caudate–putamen after lesions of the nigrostriatal dopaminergic bundle in the rat. Lindvall O, et al. **Brain Res** 1981 Apr 27;211(1):211–6

Altered succinate dehydrogenase activity of basal ganglia following to mesotelencephalic dopaminergic projection. Marshall JF, et al. **Brain Res** 1981 May 18;212(2):367–77

The role of GABA in the regulation of the dopamine/tyrosine hydroxylase–containing neurons of the rat retina. Marshburn PB, et al. **Brain Res** 1981 Jun 15;214(2):335–47

Ontogenetic development of high potassium– and acetylcholine–induced release of dopamine from striatal slices of the rat. Nomura Y, et al. **Brain Res** 1981 Apr;227(2):171–7

Decreased dopamine turnover in the median eminence in response to suckling in the lactating rat. Selmanoff M, et al. **Brain Res** 1981 May 11;212(1):101–15

Genotypic influences on striatal dopaminergic regulation in mice. Severson JA, et al. **Brain Res** 1981 Apr 6;210(1–2):201–15

Intracranial self–stimulation: mapping against the lateral boundaries of the dopaminergic cells of the substantia nigra. Wise RA. **Brain Res** 1981 May 25;213(1):190–4

Microspectrofluorometric study of monoamines in the auricle of the heart of Protopterus aethiopicus. Scheuermann DW, et al. **Cell Tissue Res** 1981;217(2):443–9

Clinical processes and central dopaminergic activity in psychotic disorders. Bowers MB Jr, et al. **Commun Psychopharmacol** 1980; 4(3):177–83

Plasma norepinephrine, epinephrine, and dopamine concentrations in maternal and fetal sheep during spontaneous parturition and in premature sheep during cortisol–induced parturition. Eliot RJ, et al. **Endocrinology** 1981 May;108(5):1678–82

Dopamine in hypophysial portal plasma and prolactin in systemic plasma of rats treated with 5–hydroxytryptamine. Pilotte NS, et al. **Endocrinology** 1981 Jun;108(6):2137–41

Negative feedback effects of progesterone correlated with changes in hypothalamic norepinephrine and dopamine turnover rates, median eminence luteinizing hormone–releasing hormone, and peripheral plasma gonadotropins. Rance N, et al. **Endocrinology** 1981 Jun; 108(6):2194–9

The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone–releasing hormone and the effect of prolactin on catecholamine turnover. Selmanoff M. **Endocrinology** 1981 May;108(5):1716–22

Effects of estradiol and progesterone on catecholamine turnover rates in discrete hypothalamic regions in ovariectomized rats. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2186–93

Dopamine neurons of the retina: a simple method system for studying synaptic regulatory mechanisms. Iuvone PM, et al. **Essays Neurochem Neuropharmacol** 1981;5:75–94 (35 ref.)

Renal effect of SB 7505: a double–blind study. Melloni GF, et al. **Eur J Clin Pharmacol** 1981 Feb;19(3):177–80

Biochemical mechanism of tolerance to neuroleptic drugs; regional differences in rat brain. Bacopoulos NG. **Eur J Pharmacol** 1981 Apr 9;70(4):585–6

Methylphenidate–like stimulants in vitro release [3H]tyramines but not [14C]dopamine. Dyck LE. **Eur J Pharmacol** 1981 Jan 29;69(3):371–4

GABA enhancement of [3H]dopamine release from slices of rat striatum: dependence on slice size. Ennis C, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):417–20

GABA antagonists enhance dopamine turnover in the rat retina in vivo. Kamp CW, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):273–9

Postsynaptic inhibitory actions of catecholamines and opioid peptides in the bed nucleus of the stria terminalis. Sawada S, et al. **Exp Brain Res** 1981;41(3–4):264–70

Effects of the optical isomers of 2–amino–3–fluoro–1–phenylpropane (monofluoroamphetamine) hydrochloride on uptake and release of dopamine in rat striatum in vitro. Benderly A, et al. **Experientia** 1981 Mar 15;37(3):294–5

Effect of apomorphine hydrochloride administration on serum concentrations of prolactin and growth hormone in cattle. Gorewit RC. **Experientia** 1981 Feb 15;37(2):204–6

Lesions in the substantia nigra of rats induce thermoregulatory deficit in the cold. Lin MT, et al. **Experientia** 1981 Mar 15;37(3):284–6

Pharmacological characterization of the dopaminergic stimulation of mucociliary particle transport by Mytilus edulis gill. Malanga CJ, et al. **Gen Pharmacol** 1981;12(3):139–44

Catecholamine turnover in rat cerebral cortex and caudate following repeated treatment with dihydroergotoxine. Cvejić V, et al. **Gerontology** 1981;27(1–2):7–12

Studies on the uptake of [3H]dopamine by synaptic vesicle fraction isolated from bovine brain. Tsudzuki T. **J Biochem (Tokyo)** 1981 Jan; 89(1):61–9

Amine transport in chromaffin granule ghosts. pH dependence implies cationic form is translocated. Knoth J, et al. **J Biol Chem** 1981 Jul 10; 256(13):6541–3

Simultaneous determination of dopamine, DOPAC and homovanillic acid. Direct injection of supernatants from brain tissue homogenates in a liquid chromatography––electrochemical detection system. Magnusson O, et al. **J Chromatogr** 1980 Dec 12;221(2):237–47

Determination of dopamine, homovanillic acid and 3,4–dihydroxyphenylacetic acid in rat brain striatum by high–performance liquid chromatography with electrochemical detection. Saraswat LD, et al. **J Chromatogr** 1981 Mar 13; 222(3):353–62

Decreased plasma and urinary dopamine during dietary sodium depletion in man. Carey RM, et al. **J Clin Endocrinol Metab** 1981 May; 52(5):903–9

Behavioral and neurochemical effects of neonatal administration of monosodium L–glutamate in mice. Dawson R Jr, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):71–84

Chronic L–DOPA treatment of mice: a behavioural and biochemical study. Bailey R, et al. **J Neural Transm** 1981;50(2–4):209–24

3–Methoxytyramine and normetanephrine as indicators of dopamine and noradrenaline release in mouse brain in vivo. Kehr W. **J Neural Transm** 1981;50(2–4):165–78

Effects of dopamine on cyclic AMP concentration in the anterior pituitary gland in vitro. Pawlikowski M, et al. **J Neural Transm** 1981; 50(2–4):179–84

Role of phospholipids in coupling of adenosine and dopamine receptors to striatal adenylate cyclase. Anand–Srivastava MB, et al. **J Neurochem** 1981 May;36(5):1819–28

Conversion of 3, 4–dihydroxyphenylalanine and deuterated 3, 4–dihydroxyphenylalanine to alcoholic metabolites of catecholamines in rat brain. Edwards DJ, et al. **J Neurochem** 1981 May; 36(5):1641–7

The effect of mesencephalic lesions on tyramine and dopamine in the caudate nucleus of the rat. Juorio AV, et al. **J Neurochem** 1981 Jun; 36(6):1898–903

Effects of in vivo amphetamine administration on dopamine synthesis regulation in rat brain striatal synaptosomes. Patrick RL, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):686–91

Simultaneous radioenzymatic assay of dopamine and dihydroxyphenylacetic acid: an index of in vivo dopamine release. Cheng CH, et al. **J Pharmacol Methods** 1981 Mar;5(2):165–73

Cross-tolerance of dopamine metabolism to baclofen, gamma-butyrolactone and HA-966 in the striatum and olfactory tubercle of the rat. Broxterman HJ, et al. **Life Sci** 1981 Mar 2; 28(9):973–81

Decreased ability to cope with heat and cold linked to a dysfunction in a central dopaminergic pathway in elderly rats. Cox B, et al. **Life Sci** 1981 May 4;28(18):2039–44

Disruption of 5-hydroxytryptaminergic neuronal function blocks the action of morphine on tuberoinfundibular dopaminergic neurons. Demarest KT, et al. **Life Sci** 1981 Mar 23;28(12):1345–51

I. Catecholamines in developing rat lung. Gardey-Levassort C, et al. **Life Sci** 1981 Jan 26;28(4):331–7

Dopamine-inhibited adenylate cyclase in female rat adenohypophysis. Giannattasio G, et al. **Life Sci** 1981 Apr 6;28(14):1605–12

The effect of phencyclidine on dopamine metabolism in the mouse brain. Johnson KM, et al. **Life Sci** 1981 Jan 26;28(4):361–9

Passive avoidance performance correlates with catecholamine turnover in discrete limbic brain regions. Kovács GL, et al. **Life Sci** 1981 Mar 9;28(10):1109–16

Dose-dependent and reversible effects of lead on rat dopaminergic system. Memo M, et al. **Life Sci** 1981 Feb 16;28(7):795–9

Dopamine and norepinephrine uptake and metabolism by astroglial cells in culture. Pelton EW 2d, et al. **Life Sci** 1981 Apr 6;28(14):1655–63

Direct measurement of the effect of potassium, calcium, veratridine, and amphetamine on the rate of release of dopamine from superfused brain tissue. Wightman RM, et al. **Life Sci** 1981 Mar 16;28(11):1279–86

Dopamine in pediatric therapy. Foster SD. **MCN** 1981 Jul–Aug; 6(4):279

Mesocortical dopamine neurons. Lack of autoreceptors modulating dopamine synthesis. Bannon MJ, et al. **Mol Pharmacol** 1981 Mar; 19(2):270–5

Effect of calmodulin on dopamine-sensitive adenylate cyclase activity in rat striatal membranes. Gnegy M, et al. **Mol Pharmacol** 1981 Mar; 19(2):256–63

Neurotensin blocks certain amphetamine-induced behaviours. Ervin GN, et al. **Nature** 1981 May 7;291(5810):73–6

The rate constants for the efflux of deaminated metabolites of 3H-dopamine from the perfused rat heart. Bönisch H. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):231–5

Direct and indirect actions of dopamine on tracheal smooth muscle. Koga Y, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980;315(1):15–20

Experimental studies on the development of sex differences in the release of dopamine from striatal tissue fragments in vitro. Becker JB, et al. **Neuroendocrinology** 1981 Mar;32(3):168–73

Dopamine levels in hypophysial stalk plasma and prolactin levels in peripheral plasma of the lactating rat: effects of a simulated suckling stimulus. de Greef WJ, et al. **Neuroendocrinology** 1981 Apr; 32(4):229–33

Further studies on dopamine-induced suppression of pulsatile LH release in ovariectomized rats. Gallo RV. **Neuroendocrinology** 1981 Mar; 32(3):187–92

Monoamine uptake into synaptosomes from various regions of rat brain following lithium administration and withdrawal. Ahluwalia P, et al. **Neuropharmacology** 1981 May;20(5):483–7

Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat. Jones DL, et al. **Neuropharmacology** 1981 Jan;20(1):29–37

Effects of estrogens on the responses of caudate neurons to microiontophoretically applied dopamine. Arnauld E, et al. **Neurosci Lett** 1981 Feb 6;21(3):325–31

Effects of chronic estrogen treatment on dopamine concentrations and turnover in discrete brain nuclei of ovariectomized rats. Dupont A, et al. **Neurosci Lett** 1981 Feb 23;22(1):69–74

Dopaminergic mediation of reward: evidence gained using a natural reinforcer in a behavioral contrast paradigm. Royall DR, et al. **Neurosci Lett** 1981 Jan 20;21(2):223–9

Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Vachon L, et al. **Neuroscience** 1981; 6(2):189–94

Is there a non-dopaminergic nigrostriatal pathway? van der Kooy D, et al. **Neuroscience** 1981;6(3):345–57

Effects of a high-dose treatment of methamphetamine on caudate dopamine and anorexia in rats. Bittner SE, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):481–6

Septal lesions and avoidance behavior: genetic, neurochemical and behavioral considerations. Donovick PJ, et al. **Physiol Behav** 1981 Mar; 26(3):495–507

Target neuron-specific process formation by embryonic mesencephalic dopamine neurons in vitro. Hemmendinger LM, et al. **Proc Natl Acad Sci USA** 1981 Feb;78(2):1264–8

Dopamine and depolarizing agents regulate the state of phosphorylation of protein I in the mammalian superior cervical sympathetic ganglion. Nestler EJ, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7479–83

Chromosomes in living Escherichia coli cells are segregated into domains of supercoiling. Sinden RR, et al. **Proc Natl Acad Sci USA** 1981 Jan; 78(1):224–8

Dopaminergic involvement in attention. A novel animal model. Katz RJ, et al. **Prog Neuropsychopharmacol** 1980;4(6):585–90

Psychopharmacology of anorectic drugs in man. Silverstone T. **Prog Neuropsychopharmacol** 1980;4(4–5):371–4

The effect of altered dopaminergic activity on food intake in the rat: evidence for an optimal level of dopaminergic activity for behavior. Zigmond MJ, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):351–62

Slow and rapid onset of manic episodes: implications for underlying biology. Post RM, et al. **Psychiatry Res** 1981 Apr;4(2):229–37

The effect of long-term concurrent administration of chlorpromazine and lithium on the striatal and frontal cortical dopamine metabolism in rats. Eroğlu L, et al. **Psychopharmacology (Berlin)** 1981;73(1):84–6

Dopaminergic agonists differentially affect open-field activity of rats with A10 lesions. Hodge GK, et al. **Psychopharmacology (Berlin)** 1981; 73(1):39–42

Increased mesolimbic dopamine binding following chronic haloperidol treatment. Kamer RS, et al. **Psychopharmacology (Berlin)** 1981; 72(3):261–3

Is dopamine an inhibitory modulator of gastrointestinal motility? Schuurkes JA, et al. **Scand J Gastroenterol [Suppl]** 1981;67:33–6

Phosphatidate as a molecular link between depolarization and neurotransmitter release in the brain. Harris RA, et al. **Science** 1981 Jun 12;212(4500):1290–1

Cerebral blood flow and intracranial pressure in the dog during intravenous infusion of nitroglycerin alone and in combination with dopamine. von Essen C, et al. **Stroke** 1981 May–Jun;12(3):331–8

3,4,3',4'-Tetrachlorobiphenyl given to mice prenatally produces long-term decreases in striatal dopamine and receptor binding sites in the caudate nucleus. Agrawal AK, et al. **Toxicol Lett** 1981 Mar; 7(6):417–24

[A study of renovation rate of dopamine and 5-hydroxytryptamine in brain in chronic schizophrenics (author's transl)] Shen YC. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1979;12(3):158–60 (Chi)

[A case of poisoning with anuria and circulatory failure treated with dopamine infusion] Nielsen HV, et al. **Ugeskr Laeger** 1981 13 Apr; 143(16):1017–8 (Eng. Abstr.) (Dan)

[Pharmacology of dopamine] Estanove S, et al. **Ann Anesthesiol Fr** 1981; 22(1):75–83 (36 ref.) (Fre)

[The dopaminergic innervation of neostriatum: a new possibility of radioautographic investigation (author's transl)] Descarries L, et al. **J Physiol (Paris)** 1981 Apr;77(1):53–61 (Eng. Abstr.) (Fre)

[Influence of dopamine on pars reticulata neurones of substantia nigra (author's transl)] Ruffieux A, et al. **J Physiol (Paris)** 1981 Apr; 77(1):63–9 (Eng. Abstr.) (Fre)

[Dopaminergic A10 neurons and frontal system (author's transl)] Simon H. **J Physiol (Paris)** 1981 Apr;77(1):81–95 (Eng. Abstr.) (Fre)

[Effect of a new gastrokinetic drug on gastrointestinal motility: domperidone, a peripheral antidopaminergic drug] Chevrel B. **Med Chir Dig** 1981;10(2):175–8 (Fre)

[Dopamine in the management of septic shock states] Daoud A, et al. **Tunis Med** 1981 Jan–Feb;59(1):848–51 (Eng. Abstr.) (Fre)

[Effect of reserpine on monoamine uptake by rat brain synaptosomes] Blaschke M, et al. **Acta Biol Med Ger** 1980;39(11–12):1205–12 (Eng. Abstr.) (Ger)

[Effect of social isolation on the transmitter sensitivity of striatal and hippocampal neurons of the rat] Oehler J, et al. **Acta Biol Med Ger** 1980;39(10):1089–93 (Eng. Abstr.) (Ger)

[Mechanisms of the renal action of dopamine and their dependence on changes in the sodium balance. II. Studies on water-salt depletion] Agnoli GC, et al. **Boll Soc Ital Cardiol** 1979;24(12):1331–49 (Ita)

[Mechanisms of the renal action of dopamine and thier dependence on changes in sodium balance. Studies on water-salt retention] Agnoli GC, et al. **Boll Soc Ital Cardiol** 1979;24(12):1315–29 (Ita)

DOPAMINE BETA-HYDROXYLASE

Immunofluorescent and biochemical studies on dopamine-beta-hydroxylase and catecholamines in SIF cells of the superior cervical ganglion. Heym C, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:123–9

Urinary catecholamine excretion and plasma dopamine-beta-hydroxylase activity during mental work performed in some periods of menstrual cycle in women. Wasilewska E, et al. **Acta Physiol Pol** 1980; 31(6):647–51

Catecholamine synthesis in the adrenal medulla of cattle and rats deficient in copper. Hesketh JE. **Biochem Soc Trans** 1981 Feb;9(1):101–2

Effect of nerve activity on transport of nerve growth factor and dopamine beta-hydroxylase antibodies in sympathetic neurones. Lees G, et al. **Brain Res** 1981 Jun 9;214(1):186–9

Inhibition of LH and prolactin release in the cycling rat following inhibition of dopamine-beta-hydroxylase. Voogt JL, et al.

Brain Res 1981 Mar 30;209(2):411-9

Fluorimetric assay for dopamine beta-hydroxylase in rat plasma. Ohkura Y, et al. **Chem Pharm Bull (Tokyo)** 1980 Nov;28(11):3385-8

Plasma DBH activity: relation to genetic factors in schizophrenia. Baron M, et al. **Commun Psychopharmacol** 1980;4(3):197-202

Role of glucocorticoids in expression of the adrenergic phenotype in rat embryonic adrenal gland. Bohn MC, et al. **Dev Biol** 1981 Feb; 82(1):1-10

Plasma dopamine beta hydroxylase activity in chronic schizophrenic patients tested with single dose of 2-bromo-alpha ergocriptine (Parlodel). Vardi J, et al. **Encephale** 1981;7(1):95-103

Human plasma dopamine-beta-hydroxylase: oxygen and thermal stability. Dunnette J, et al. **Experientia** 1981 Feb 15;37(2):115-7

Circadian rhythms of dopamine-beta-hydroxylase and c-AMP in plasma of controls and patients with affective disorders. Markianos M, et al. **J Neural Transm** 1981;50(2-4):149-55

Phentolamine increases neuronal binding and retrograde transport of dopamine beta-hydroxylase antibodies. Lees GJ, et al. **Neurosci Lett** 1981 Mar 10;22(2):115-8

Interaction of opiate peptide and noradrenalin systems: light microscopic studies. Watson SJ, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):23-30

Serum DBH and platelet MAO in patients with depressive disorders. Honecker H, et al. **Pharmacopsychiatria** 1981 Jan;14(1 Suppl):10-4

The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine. Mikkelsen E, et al. **Psychiatry Res** 1981 Apr;4(2):157-69

[Plasma dopamine beta-hydroxylase activity in endogenous depressive syndromes] Pużyński S, et al. **Psychiatr Pol** 1980 Nov-Dec; 14(6):581-6 (Eng. Abstr.) (Pol)

DOXEPIN

Doxepin, a tricyclic antidepressant, binds to normal, intact astroglial cells in cultures and inhibits the isoproterenol-induced increase in cyclic AMP production. Hertz L, et al. **Can J Physiol Pharmacol** 1980 Dec; 58(12):1515-9

[3H]doxepin interactions with histamine H1-receptors and other sites in guinea pig and rat brain homogenates. Tran VT, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):501-9

DRUG INTERACTIONS

What to watch for with lithium. Rosenberg JM, et al. **RN** 1981 Jul; 44(7):44-6

DRUG TOLERANCE

Biochemical mechanism of tolerance to neuroleptic drugs; regional differences in rat brain. Bacopoulos NG. **Eur J Pharmacol** 1981 Apr 9;70(4):585-6

ELECTROCONVULSIVE THERAPY

Effect of antidepressants, lithium and electroconvulsive treatment on rat serum prolactin levels. Meltzer HY, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):100-21

Electroconvulsive therapy and receptor sensitivity. Modigh K, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):91-9

The medically ill elderly, tricyclic response, and ECT [letter] Small G, et al. **Am J Psychiatry** 1981 May;138(5):703-4

Convulsive and drug therapies of depression. Fink M. **Annu Rev Med** 1981;32:405-12 (71 ref.)

Auditory brain stem evoked responses in hospitalized patients undergoing drug treatment or ECT. Small JG, et al. **Biol Psychiatry** 1981 Mar; 16(3):287-90

ELECTROENCEPHALOGRAPHY

Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat. Borbély AA, et al. **Behav Brain Res** 1981 Jan; 2(1):1-22

Lisuride and cerebral electrical activity in the rabbit. Bo P, et al. **Farmaco [Sci]** 1981 May;36(5):351-8

Effect of pentobarbital on thalamo- and hippocampocortical processes in rats. Kolinová M, et al. **Physiol Bohemoslov** 1981;30(2):139-48

An objective classification of psychoactive drugs. Fink M. **Prog Neuropsychopharmacol** 1980;4(4-5):495-502

Computer analyzed EEG in amphetamine-responsive hyperactive children. McIntyre HB, et al. **Psychiatry Res** 1981 Apr;4(2):189-97

[The use of electrophysiological techniques to project typical psychotropic drug effects: some examples (author's transl)] Herrmann WM, et al. **EEG EMG** 1981 Mar;12(1):21-32 (Eng. Abstr.) (Ger)

[The effect of clonazepam on visual evoked potentials of the rabbit (author's transl)] Pockberger H, et al. **EEG EMG** 1981 Mar; 12(1):14-20 (Eng. Abstr.) (Ger)

ELECTROLYTES

Methylprednisolone stimulation of guanylate cyclase activity in rat small intestinal mucosa: possible rôle in electrolyte transport. Marnane WG, et al. **Gastroenterology** 1981 Jul;81(1):90-100

ELECTROSHOCK

Effect of stress and ACTH on dopamine metabolism in the nucleus accumbens and frontal cortex. Fadda F, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):454-8

The effects of electric shock on responding maintained by cocaine in rhesus monkeys. Bergman J, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):423-6

Repeated electroconvulsive shock prevents the sedative effect of small doses of apomorphine. Serra G, et al. **Psychopharmacology (Berlin)** 1981; 73(2):194-6

The effects of electroconvulsive shock on the discriminative stimulus properties of d-amphetamine and apomorphine: evidence for dopamine receptor alteration subsequent ECS. White DK, et al. **Psychopharmacology (Berlin)** 1981;73(3):211-4

EMOTIONS

The effect of bromazepam on psychomotor activity and subjective mood. Hobi V, et al. **J Int Med Res** 1981;9(2):89-97

[On the effect of imipramine on blood composition, glucose level and alkaline phosphatase activity of leucocytes in non-emotive Wistar rats and animals of inbred TMB strain (author's transl)] Freund D, et al. **Arzneimittelforsch** 1981;31(3):425-8 (Eng. Abstr.) (Ger)

[Catecholamines in the brain structures of rats responding differently to the 'open field' test] Belova TI, et al. **Biull Eksp Biol Med** 1981 Feb; 91(2):136-8 (Eng. Abstr.) (Rus)

ENDORPHINS

Light and electron microscopic localization of enkephalin and tyrosine hydroxylase in neostriatum of fetal and adult rat brain. Pickel VM, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:97-105

Immunoreactive endorphin peptides and prolactin in umbilical vein and maternal blood. Kimball CD, et al. **Am J Obstet Gynecol** 1981 May 15;140(2):157-64

Role of adrenergic blocking agents and glucocorticoids on the regulation of pituitary opioid peptides levels. Giagnoni G, et al. **Arch Int Pharmacodyn Ther** 1980 Dec;248(2):272-9

Met-enkephalin-Arg6-Phe7 metabolism: conversion to Met-enkephalin by brain and kidney dipeptidyl carboxypeptidases. Benuck M, et al. **Biochem Biophys Res Commun** 1981 Mar 31;99(2):630-6

The complete amino acid sequence of alpha-neo-endorphin. Kangawa K, et al. **Biochem Biophys Res Commun** 1981 Apr 15;99(3):871-8

Proposals for conformation of enkephalins related to opiate mu-pharmacophore. Maigret B, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):267-74

Beta-neo-endorphin, a new hypothalamic 'big' Leu-enkephalin of porcine origin: its purification and the complete amino acid sequence. Minamino N, et al. **Biochem Biophys Res Commun** 1981 Apr 15;99(3):864-70

Behavioral activity of met-enkephalin and ACTH4-10 and other peptides containing a phenylalanine and methionine residue. Rigter H, et al. **Biochem Biophys Res Commun** 1981 Jan 30;98(2):424-30

De novo biosynthesis of enkephalins and their homologues in the human placenta. Tan L, et al. **Biochem Biophys Res Commun** 1981 Feb 12; 98(3):752-60

Purification and substrate characterization of a human enkephalin-degrading aminopeptidase. Coletti-Previero MA, et al. **Biochim Biophys Acta** 1981 Jan 15;657(1):122-7

Serotonergic and peptidergic projections to the spinal cord demonstrated by a combined retrograde HRP histochemical and immunocytochemical staining method. Bowker RM, et al. **Brain Res** 1981 May 4; 211(2):412-7

A study of 24-hour profiles of plasma met-enkephalin in man. Shanks MF, et al. **Brain Res** 1981 May 18;212(2):403-9

Enkephalin and zinc in the hippocampal mossy fiber System. Stengaard-Pedersen K, et al. **Brain Res** 1981 May 11;212(1):230-3

Release of beta-lipotropin and beta-endorphin from rat hypothalami in vitro. Vermes I, et al. **Brain Res** 1981 Apr 27;211(1):248-54

Development of radioimmunoassayable beta-endorphin and methionine-enkephalin binding sites in regions of rat brain. Tsang D, et al. **Can J Physiol Pharmacol** 1980 Aug;58(8):947-50

Ultrastructural localization of corticotropin, beta-lipotropin, and alpha- and beta-endorphin in the porcine anterior pituitary. Dacheux F. **Cell Tissue Res** 1981;215(1):87-101

Nerves containing substance P, vasoactive intestinal polypeptide, enkephalin or somatostatin in the guinea-pig taenia coli. Distribution, ultrastructure and possible functions. Leander S, et al. **Cell Tissue Res** 1981;215(1):21-39

Cytological localization of alpha-MSH, ACTH and beta-endorphin in the pars intermedia of the cichlid teleost Sarotherodon mossambicus.

van Eys GJ, et al. **Cell Tissue Res** 1981;215(3):625–33

Presence of beta–endorphin–like immunoreactivity in the anterior pituitary gland of rat and man and evidence for the differential localization with ACTH. Watkins WB, et al. **Cell Tissue Res** 1981; 215(3):577–89

Structure and biosynthesis of pro–adrenocorticotropin/endorphin and related peptides. Eipper BA, et al. **Endocr Rev** 1980 Winter; 1(1):1–27 (186 ref.)

Effect of intraventricular injection of neurotensin and other various bioactive peptides on plasma immunoreactive somatostatin levels in rat hypophysial portal blood. Abe H, et al. **Endocrinology** 1981 May; 108(5):1939–43

Evidence for two different turnover pools of adrenocorticotropin, alpha–melanocyte–stimulating hormone, and endorphin–related peptides released by the frog pituitary neurointermediate lobe. Loh YP, et al. **Endocrinology** 1981 Jul;109(1):54–61

Comparison of acute effects of dynorphin and beta–endorphin on prolactin release in the rat. Van Vugt DA, et al. **Endocrinology** 1981 May; 108(5):2017–8

Effects of hypoxia on beta–endorphin and beta–lipotropin release in fetal, newborn, and maternal sheep. Wardlaw SL, et al. **Endocrinology** 1981 May;108(5):1710–5

Differential loss of biological activity of the enkephalins induced by current. Kitchen I, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):393–6

Postsynaptic inhibitory actions of catecholamines and opioid peptides in the bed nucleus of the stria terminalis. Sawada S, et al. **Exp Brain Res** 1981;41(3–4):264–70

Opioid peptide precursors in striatum. Beaumont A, et al. **FEBS Lett** 1980 Dec 15;122(1):135–7

Failure of somatostatin and beta–endorphin to affect bovine adrenal cortex cells in vitro. Diel F, et al. **Horm Metab Res** 1981 Feb;13(2):95–8

Endocrine effect of a methionine–enkephalin derivative (FK 33–824) in man. del Pozo E, et al. **Horm Res** 1980;13(2):90–7

Beta–endorphin: synthesis and radioligand binding activity of analogs containing cystine bridges. Blake J, et al. **Int J Pept Protein Res** 1981 Feb;17(2):239–42

Use of the chromogenic p–(p–(dimethylamino)phenylazo) benzyl (AZ) ester in the synthesis of leu–enkephalin. Reynolds GD, et al. **Int J Pept Protein Res** 1981 Feb;17(2):231–4

Human beta–endorphin: synthesis and biological activity of analogs with substitutions in positions 2, 9, 18, 27 and 31. Yeung HW, et al. **Int J Pept Protein Res** 1981 Feb;17(2):235–8

Differentiation of MSH–, ACTH–, endorphin–, and LPH–containing cells in the hypophysis during embryonic and fetal development. Dupouy JP. **Int Rev Cytol** 1980;68:197–249 (277 ref.)

Further analysis of post–translational processing of beta–endorphin in rat intermediate pituitary. Eipper BA, et al. **J Biol Chem** 1981 Jun 10; 256(11):5689–95

Differences in the post–translational processing of beta–endorphin in rat anterior and intermediate pituitary. Mains RE, et al. **J Biol Chem** 1981 Jun 10;256(11):5683–8

The interaction of N alpha–alkylenkephalins with opiate receptors. Tissue–dependent shifts in the opiate activity of methionine–enkephalin following N alpha–alkylation. Summers MC, et al. **J Biol Chem** 1981 May 25;256(10):4951–6

Diurnal rhythm of plasma immunoreactive beta–endorphin and its relationship to sleep stages and plasma rhythms of cortisol and prolactin. Dent RR, et al. **J Clin Endocrinol Metab** 1981 May;52(5):942–7

Immunohistochemical localization of substance–P, somatostatin, and methionine–enkephalin in the spinal cord and dorsal root ganglia of the North American opossum, Didelphis virginiana. Ditirro FJ, et al. **J Comp Neurol** 1981 May 10;198(2):351–63

Localization of enkephalin–like immunoreactivity to identified axonal and neuronal populations of the rat hippocampus. Gall C, et al. **J Comp Neurol** 1981 May 10;198(2):335–50

Immunohistochemical localization of leucine–enkephalin in the spinal cord of the cat: enkephalin–containing marginal neurons and pain modulation. Glazer EJ, et al. **J Comp Neurol** 1981 Mar 1;196(3):377–89

Sex differences in the content of beta–endorphin and enkephalin–like peptides in the pituitary of obese (ob/ob) mice. Govoni S, et al. **J Neurochem** 1981 May;36(5):1829–33

Alpha–N–acetyl beta–endorphins in the pituitary: immunohistochemical localization using antibodies raised against dynorphin(1–13). Weber E, et al. **J Neurochem** 1981 Jun;36(6):1977–85

The effect of captopril and ascorbic acid on nonenzymatic methionine enkephalin inactivation in the guinea–pig ileum. Greenberg R, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):750–6

Is excitation by enkephalins of hippocampal neurones in the rat due to presynaptic facilitation or to disinhibition? Haas HL, et al. **J Physiol (Lond)** 1980 Nov;308:315–30

beta–Endorphin and related peptides. Imura H. **Jpn J Pharmacol** 1980; 30(Suppl):1P

Inhibition of gastric emptying by enkephalin analogue [letter] Sullivan SN, et al. **Lancet** 1981 Jul 11;2(8237):86–7

Potent tetrapeptide enkephalins. Chipkin RE, et al. **Life Sci** 1981 Mar 30;28(13):1517–22

The effect of running on plasma beta–endorphin. Colt EW, et al. **Life Sci** 1981 Apr 6;28(14):1637–40

Corticotropin/beta–endorphin immunoreactivity in rat mast cells. Peptide or protease? DiAugustine RP, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2663–8

Comparative study on the effect of morphine and the opioid–like peptides in the vas deferens of rodents: species and strain differences, evidence for multiple opiate receptors. Huidobro–Toro JP, et al. **Life Sci** 1981 Mar 23;28(12):1331–6

Des–tyrosine–gamma–endorphin: H–reflex response similar to neuroleptics. Metz J, et al. **Life Sci** 1981 May 4;28(18):2003–8

Episodic secretion of opioid activity in human plasma and monkey CSF: evidence for a diurnal rhythm. Naber D, et al. **Life Sci** 1981 Feb 23; 28(8):931–5

Conformation of beta–endorphin analogues in cerebroside sulfate solution. Wu CS, et al. **Mol Pharmacol** 1981 Mar;19(2):302–6

Dynorphin. Nathan B. Eddy memorial award lecture. Goldstein A. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(34):1–10

Presence of avian pancreatic polypeptide–like immunoreactivity in catecholamine and methionine–enkephalin–containing neurones within the central nervous system. Hunt SP, et al. **Neurosci Lett** 1981 Jan 20; 21(2):125–30

Retention of passive avoidance behavior in rats following alpha– and gamma–endorphin administration: effects of post–learning treatments. Kovács GL, et al. **Neurosci Lett** 1981 Feb 23;22(1):79–82

In vivo release of met–enkephalin in the cat brain. Cesselin F, et al. **Neuroscience** 1981;6(3):301–13

An immunohistochemical study of enkephalins and other neuropeptides in the striatum of the cat with evidence that the opiate peptides are arranged to form mosaic patterns in register with the striosomal compartments visible by acetylcholinesterase staining. Graybiel AM, et al. **Neuroscience** 1981;6(3):377–97

Localization of [Met5]– and [Leu5]–enkephalin–like immunoreactivity in nerve terminals in human paravertebral sympathetic ganglia. Hervonen A, et al. **Neuroscience** 1981;6(3):323–30

Human spinal neurons: innervation by both substance P and enkephalin. LaMotte CC, et al. **Neuroscience** 1981;6(4):713–23

Reserpine increases opiate–like peptide content and tyrosine hydroxylase activity in adrenal medullary chromaffin cells in culture. Wilson SP, et al. **Neuroscience** 1981;6(1):71–9

Tyrosine–modified analogs of methionine–enkephalin and their effects on the mouse vas deferens. Coy DH, et al. **Peptides (Fayetteville)** 1980 Summer;1(2):175–7

Radioimmunoassay of methionine(5)–enkephalin sulphoxide: phylogenetic and anatomical distribution. King JA, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):211–6

Tobacco mosaic virus–enkephalin conjugates: potentiation of opioid activity. Kriwaczek VM, et al. **Peptides (Fayetteville)** 1981 Spring; 2(1):89–92

Enkephalinase: selective inhibitors and partial characterization. Sullivan S, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):31–5

Interaction of opiate peptide and noradrenalin systems: light microscopic studies. Watson SJ, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):23–30

A cyclic enkephalin analog with high in vitro opiate activity. DiMaio J, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7162–6

Enkephalin–like immunoreactivity of olivocochlear nerve fibers in cochlea of guinea pig and cat. Fex J, et al. **Proc Natl Acad Sci USA** 1981 Feb; 78(2):1255–9

Two adrenal opioid polypeptides: proposed intermediates in the processing of proenkephalin. Stern AS, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1962–6

Dynorphin immunocytochemical localization in brain and peripheral nervous system: preliminary studies. Watson SJ, et al. **Proc Natl Acad Sci USA** 1981 Feb;78(2):1260–3

Classification of endorphins/enkephalins in brain physiology and pathology (based on EEG and clinical study of synthetically–modified methionine–enkephalin). Roubicek J, et al. **Prog Neuropsychopharmacol** 1980;4(4–5):507–18

The regional distribution of gamma 3–melanotropin–like peptides in bovine brain is correlated with adrenocorticotropin immunoreactivity but not with beta–endorphin. Shibasaki T, et al. **Regul Pept** 1981 Apr; 2(1):43–52

Differential immunostaining of adenohypophysial cells with antisera to ACTH and beta–endorphin. Watkins WB. **Regul Pept** 1981 Mar; 1(6):375–85

Selective protection of methionine enkephalin released from brain slices by enkephalinase inhibition. Patey G, et al. **Science** 1981 Jun 5; 212(4499):1153–5

[Possibility of the proline–rich exorphins biodegradation in the gastrointestinal tract (author's transl)] Křepela E. **Cesk Gastroenterol Vyz** 1981 Mar;35(2):68–71 (Eng. Abstr.) (Cze)

[Distribution of substance P and methionine enkephalin in dorsolateral pontine tegmentum of the cat. Immunofluorescence study] Charnay Y, et al. **C R Acad Sci [D] (Paris)** 1981 Feb 2;292(5):435–40 (Eng. Abstr.) (Fre)

[Endorphins: structure, roles and biogenesis] Chrétien M, et al. **Can J Physiol Pharmacol** 1981 May;59(5):413–31 (218 ref.) (Eng. Abstr.) (Fre)

[Neuroendocrinological aspects of endorphins] Herz A. **Verh Dtsch Ges Inn Med** 1980;86:4–12 (45 ref.) (Ger)

[Prolactin secretion inhibition as affected by leucine enkephalin] Iudaev NA, et al. **Dokl Akad Nauk SSSR** 1981;256(2):500–2 (Rus)

ENURESIS

Evaluation of various methods in treatment of enuresis. Mehrotra SN, et al. **Indian Pediatr** 1980 Jun;17(6):519–22

EPHEDRINE

A clinical trial of antihistamine, decongestant, or placebo in antibiotic–treated acute otitis media followed with pneumatic otoscopy and impedance tympanometry. Lampe RM, et al. **Milit Med** 1981 Apr;146(4):259–61

EPINEPHRINE

Effects of adrenergic neuron and ganglion blockers on hemodynamics and plasma catecholamine levels after corticosteroids during hemorrhagic shock in the dog. Haglund U, et al. **Acta Anaesthesiol Scand** 1980 Dec;24(6):444–50

Changes of receptor cooperation in Tetrahymena by re–exposure to hormones. Csaba G, et al. **Acta Biol Acad Sci Hung** 1980;31(1–3):43–7

Effect of epinephrine and 5–hydroxytryptamine on in vitro thyroid iodine organification. Masini–Repiso AM, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):207–12

Thyroid hormone–catecholamine interrelationships during exposure to cold. Storm H, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):91–7

Neuropathological findings in autonomic nervous system of alimentary tract of rat after application of catecholamines. Jędrzejewska A, et al. **Acta Neuropathol [Suppl] (Berl)** 1981;7:273–5

Urinary catecholamine excretion and plasma dopamine–beta–hydroxylase activity during mental work performed in some periods of menstrual cycle in women. Wasilewska E, et al. **Acta Physiol Pol** 1980;31(6):647–51

Catecholamines and monoamine oxidase activity in anxiety. Mathew RJ, et al. **Acta Psychiatr Scand** 1981 Mar;63(3):245–52

Dose–related interaction between timolol and adrenaline. Ohrström A. **Albrecht Von Graefes Arch Klin Exp Ophthalmol** 1981;216(1):55–9

Maternal psychological and physiologic correlates of fetal–newborn health status. Lederman E, et al. **Am J Obstet Gynecol** 1981 Apr 15;139(8):956–8

Effect of counterregulatory hormones on kinetic response to ingested glucose in dogs. Saccà L, et al. **Am J Physiol** 1981 May;240(5):E465–73

Contractility of vascular smooth muscle: maximum ability to contract in response to a stimulus. Skaug N, et al. **Am J Physiol** 1981 Jun;240(6):H971–9

A comparative study on the retention of 3H lignocaine and 3H prilocaine in the presence of various vasoconstrictors. Almasi W, et al. **Aust Dent J** 1980 Dec;25(6):316–8

Induction of phosphoenolpyruvate carboxykinase by sympathetic agents in primary cultures of adult rat hepatocytes. Wölfle D, et al. **Biochem Biophys Res Commun** 1981 Feb 27;98(4):1084–90

Use of a novel rapid preparation of fat–cell plasma membranes employing Percoll to investigate the effects of insulin and adrenaline on membrane protein phosphorylation within intact fat–cells. Belsham GJ, et al. **Biochem J** 1980 Nov 15;192(2):457–67

Phosphorylation of rabbit cardiac–muscle troponin I by phosphorylase kinase. The effect of adrenaline. Moir AJ, et al. **Biochem J** 1980 Nov 1;191(2):547–54

Plasma kallikrein–generating activity evoked by rat peritoneal–fluid mast cells following treatment with epinephrine, 8–bromo–cyclic 3',5'–guanosine monophosphate or compound 48/80. Rothschild AM. **Biochem Pharmacol** 1981 Mar 1;30(5):481–7

Catecholamines and the brain microsomal Na, K–adenosinetriphosphatase—I. Protection against lipoperoxidative damage. Svoboda P, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):427–32

Reversible swelling evoked by epinephrine, 8–bromo–cyclic 3',5'–guanosine monophosphate and feeding in the mast cells of the rat. Tamburus EL, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):469–79

The influence of adrenaline on the metabolism of erythrocytes in vitro. Mairbäurl H, et al. **Biochem Soc Trans** 1981 Feb;9(1):99–100

The influences of glucagon, epinephrine and alpha– and beta–adrenergic agents on glycogenolysis in isolated rabbit hepatocytes and perfused livers. Rufo GA Jr, et al. **Biochim Biophys Acta** 1981 May 18;674(3):297–305

Type of adrenoceptors involved in induction by adrenaline of hepatic alkaline phosphatase in mice in vivo. Mary PL, et al. **Br J Pharmacol** 1981 Jan;72(1):8–9

Post–biopsy haematuria successfully treated by selective transcatheter epinephrine injection. Vaeusorn N, et al. **Br J Radiol** 1981 May;54(641):425–6

Characteristics of the beta 1–and beta 2–adrenergic–sensitive adenylate cyclases in glial cell primary cultures and their comparison with beta 2–adrenergic–sensitive adenylate cyclase of meningeal cells. Ebersolt C, et al. **Brain Res** 1981 May 25;213(1):151–61

Electrophysiological characteristics of rodent myocardium damaged by adrenaline. Gilmour RF Jr, et al. **Cardiovasc Res** 1980 Oct;14(10):582–9

Effects of calcitonin and epinephrine on serum glucose concentration in rats. Yamaguchi M. **Chem Pharm Bull (Tokyo)** 1980 Dec;28(12):3693–5

The effect of epinephrine on blood and tissue PO2 in the rabbit. Towell ME, et al. **Circ Shock** 1981;8(2):123–30

A simple chromatographic technique for the estimation of urinery levels of normetadrenaline and metadrenaline. Hanson P, et al. **Clin Biochem** 1980 Dec;13(6):262–5

Analysis of urinary metanephrines by reversed–phase high–performance liquid chromatography and electrochemical detection. Bertani–Dziedzic LM, et al. **Clin Chim Acta** 1981 Feb 19;110(1):1–8

The effect of adrenaline on peripheral vascular resistance at different temperatures in a hind part preparation of rainbow trout (Salmo gairdnerii R.). Moen KA, et al. **Comp Biochem Physiol [C]** 1981;69C(1):157–9

Plasma norepinephrine, epinephrine, and dopamine concentrations in maternal and fetal sheep during spontaneous parturition and in premature sheep during cortisol–induced parturition. Eliot RJ, et al. **Endocrinology** 1981 May;108(5):1678–82

Morphine: dual effects on plasma catecholamines. Taborsky GJ Jr, et al. **Endocrinology** 1981 Jul;109(1):319–21

In vivo and in vitro effects of adrenaline on conversion of thyroxine to triiodothyronine and to reverse–triiodothyronine in dog liver and heart. Nauman A, et al. **Eur J Clin Invest** 1980 Jun;10(3):189–92

Acute sino–aortic denervation in rats produces a selective increase of adrenaline turnover in the dorsal midline area of the caudal medulla oblongata and a reduction of adrenaline levels in the anterior and posterior hypothalamus. Yukimura T, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):361–5

Degeneration of nerve terminals in cats following systemic epinephrine: depletion of tissue norepinephrine correlated with ultrastructural changes. Flach AJ, et al. **Exp Eye Res** 1981 Apr;32(4):389–94

The effect of hormones on the haemodynamics in animals of different age groups. Frolkis VV, et al. **Exp Gerontol** 1981;16(1):1–12

The effect of phenoxybenzamine on the relationship between glycerol release and cyclic AMP levels in the presence of insulin in epinephrine–stimulated rat adipocytes. Wong EH, et al. **FEBS Lett** 1981 May 18;127(2):217–20

Influence of the hypophysio–adrenocortical system on the metabolism of 3H–adrenaline in the hypothalamus, hypophysis and the rest of the brain of rats. Parvez H, et al. **Horm Metab Res** 1981 Feb;13(2):98–102

Utilization of epinephrine–containing anesthetic solutions in the toes. Roth RD. **J Am Podiatry Assoc** 1981 Apr;71(4):189–99

Amine transport in chromaffin granule ghosts. pH dependence implies cationic form is translocated. Knoth J, et al. **J Biol Chem** 1981 Jul 10;256(13):6541–3

Novel post–column derivatization method for the fluorimetric determination of norepinephrine and epinephrine. Nimura N, et al. **J Chromatogr** 1980 Dec 12;221(2):249–55

Epinephrine plasma thresholds for lipolytic effects in man: measurements of fatty acid transport with [l–13C]palmitic acid. Galster AD, et al. **J Clin Invest** 1981 Jun;67(6):1729–38

Essential role of GTP in epinephrine stimulation of human fat cell adenylate cyclase. Katz MS, et al. **J Lipid Res** 1981 Jan;22(1):113–21

Determination of catecholamine permeability coefficients for passive diffusion across phospholipid vesicle membranes. Bochain A, et al. **J Membr Biol** 1981;60(1):73–6

Biochemical and histochemical studies on catecholamines in bullfrog spinal ganglia. Kojima H, et al. **J Neurochem** 1981 Jun;36(6):2106–9

Role of adrenergic mechanism in ketogenesis. Takabayashi Y, et al. **Keio J Med** 1980 Apr;29(1):1–8

Thyrotropin releasing factor: a putative CNS regulator of the autonomic nervous system. Brown MR. **Life Sci** 1981 Apr 13–20;28(15–16):1789–95

Glucagon and epinephrine–stimulated phospholipid methylation in hepatic microsomes. Kraus–Friedmann N, et al. **Life Sci** 1981 Mar 30;28(13):1483–8

Epinephrine–independent production of hyperuricemia by means of hypothalamic stimulation in the conscious rat. Sumi T, et al. **Life Sci** 1981 Mar 9;28(10):1183–8

Effect of epinephrine and dibutyryl cyclic AMP on delta 5–desaturation activity of rat liver microsomes. de Gomez Dumm IN, et al. **Lipids** 1980 Dec;15(12):1064–6

Distinct regulations by calcium of cyclic GMP levels and catecholamine secretion in isolated bovine adrenal chromaffin cells. Lemaire S, et al. **Metabolism** 1981 May;30(5):462–8

Active transport of biogenic amines in chromaffin granule membrane vesicles. Schuldiner S, et al. **Monogr Neural Sci** 1980;7:117–28

Sustained potentiation of transmitter release by adrenaline and dibutyryl cyclic AMP in sympathetic ganglia. Kuba K. et al. **Nature** 1981 Jun 25;291(5817):654–6

Kinetic analyses of the mechanisms of action of inhibitors of the extraneuronal uptake of adrenaline in smooth muscle cells of guinea-pig trachea. Bryan LJ, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jan;315(3):249–54

Comparison of brainstem and adrenal circadian patterns of epinephrine synthesis. Turner BB, et al. **Neuroendocrinology** 1981 May; 32(5):257–61

Effects of hypoxic and hormonal factors on ribonucleic acid content in spinal cord cells: comparison of the metabolic responses in neurons, perineuronal neuroglia and ependyma cells. Pevzner L. **Neuroscience** 1981;6(5):963–8

The effect of tryptolines (1, 2, 3, 4–tetrahydro–beta–carbolines) on monoamine metabolism and the platelet aggregation response in human platelets. Youdim MB, et al. **Neuroscience** 1981;6(4):801–10

Early effect of epinephrine on aqueous formation in the normal human eye. Nagataki S, et al. **Ophthalmology (Rochester)** 1981 Mar; 88(3):276–82

Emergence of beta–adrenergic sensitivity in the developing chicken heart. Lipshultz S, et al. **Proc Natl Acad Sci USA** 1981 Jan;78(1):288–92

Elevation of epinephrine concentration in rat brain by LY51641, a selective inhibitor of type A monoamine oxidase. Fuller RW, et al. **Res Commun Chem Pathol Pharmacol** 1981 May;32(2):207–21

In vitro response of the regenerating adrenal gland to epinephrine. Soliman KF, et al. **Res Commun Chem Pathol Pharmacol** 1981 May; 32(2):373–6

[Lactic acid in the blood of heifers after administration of adrenaline and its relationship to pregnancy] Hintnaus J. **Vet Med (Praha)** 1981 Feb; 26(2):95–100 (Eng. Abstr.) (Cze)

[Comparative pharmacology of adrenaline and noradrenaline] Martin C, et al. **Ann Anesthesiol Fr** 1981;22(1):85–96 (16 ref.) (Fre)

[Effect of adrenergic beta–receptor blockers on the oxygen consumption of narcotized rats and the calorigenic action of adrenaline] Ankermann H. **Acta Biol Med Ger** 1980;39(11–12):1227–34 (Eng. Abstr.) (Ger)

[Comparative pharmacological study of d,l–adrenaline dipivalate hydrochloride and l–adrenaline hydrochloride after local and oral administration] Eisenburger R, et al. **Arzneimittelforsch** 1981; 31(2):325–34 (Eng. Abstr.) (Ger)

[Effect of acetylcholine and adrenaline on membrane currents in ventricular muscle (author's transl)] Ochi R. **Kokyu To Junkan** 1980 Oct;28(10):1103–9 (Jpn)

[The hormonal regulation of the hepatic glycogenolysis in the newborn (author's transl)] Okazaki H. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 May;32(5):541–9 (Eng. Abstr.) (Jpn)

[Effect of adrenaline, noradrenaline and acetylcholine on rabbit and human uterine activity in vivo (author's transl)] Sakoda H. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Jun;32(6):697–705 (Eng. Abstr.) (Jpn)

ESCAPE REACTION

Alterations in brain norepinephrine metabolism and behavior induced by environmental stimuli previously paired with inescapable shock. Cassens G, et al. **Behav Brain Res** 1981 May;2(3):387–407

Effects of chlorpromazine on escape and avoidance responses: a closer look. Spirduso WW, et al. **Pharmacol Biochem Behav** 1981 Apr, 14(4):433–8

ESTRADIOL

Direct evidence in men for a role of endogenous oestrogens on gonadotrophin release. D'Agata R, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):145–9

Estrogenic and antiestrogenic effects of danazol administration in studies of estradiol receptor binding. Musich JR, et al. **Am J Obstet Gynecol** 1981 May 1;140(1):62–9

Hormonal control of postnatal development of corticosteroid–binding globulin. D'Agostino J, et al. **Am J Physiol** 1981 Apr;240(4):E402–6

Sensitivity of rat adenohypophyseal cells to estradiol and LHRH during long–term culture. Lagacé L, et al. **Am J Physiol** 1981 Jun; 240(6):E602–8

LH responses to LHRH, DBcAMP, and 17 beta–estradiol in cultures derived from aged rats. Tang LK, et al. **Am J Physiol** 1981 May; 240(5):E510–8

Effects of bromocriptine on [3H]estradiol binding in cytosol of anterior pituitary. De Nicola AF, et al. **Endocrinology** 1981 Jul;109(1):83–6

Dissociated changes of pituitary luteinizing hormone–releasing hormone (LHRH) receptors and responsiveness to the neurohormone induced by 17 beta–estradiol and LHRH in vivo in the rat. Ferland L, et al. **Endocrinology** 1981 Jul;109(1):87–93

The actions of porcine follicular fluid and estradiol on periovulatory secretion of gonadotropic hormones in rats. Rush ME, et al. **Endocrinology** 1981 Jun;108(6):2316–23

Estradiol as a gonadotropin releasing hormone in the rhesus monkey. Wildt L, et al. **Endocrinology** 1981 May;108(5):2011–3

Effects of estradiol and progesterone on catecholamine turnover rates in discrete hypothalamic regions in ovariectomized rats. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2186–93

Maintenance by L–DOPA treatment of estrous cycles and LH response to estrogen in aging female rats. Forman LJ, et al. **Exp Aging Res** 1980 Dec;6(6):547–54

A biphasic effect of estradiol on serotonin metabolism in rat pineal organ cultures. Cardinali DP, et al. **Experientia** 1981 Feb 15;37(2):203–4

Correlation between plasma thyroxine levels and corticosterone–binding activity in intact, ovariectomized, and ovariectomized estrogen–treated rats. Calvano SE, et al. **Horm Metab Res** 1981 Mar;13(3):171–4

Relationship between thyrotropin, thyroid hormones, thyroxine–binding globulin and estradiol–17 beta levels in normal pregnancy. Sawhney RC, et al. **Indian J Med Res** 1981 Jan;73:41–52

Importance of the episodic nature of luteinizing hormone secretion for normal development of the bovine testis during puberty: interference with oestradiol–17 beta. Schanbacher BD. **J Endocrinol** 1981 Mar; 88(3):393–400

Effect of oestrogen and an LH–RH agonist on the release of gonadotrophins in ovariectomized ewes deprived of LH–RH. Fraser HM, et al. **J Reprod Fertil** 1981 May;62(1):131–40

Estrogen potentiates the stereotypy induced by dopamine agonists in the rat. Chiodo LA, et al. **Life Sci** 1981 Feb 16;28(7):827–35

A dopamine agonist stimulates progesterone secretion from adrenal gland. Kalra SP, et al. **Life Sci** 1981 Mar 30;28(13):1467–9

A group–comparative study of effects of Ovestin cream versus Premarin cream in post–menopausal women with vaginal atrophy. Luisi M, et al. **Maturitas** 1980 Dec;2(4):311–9

Effects of estrogens on the responses of caudate neurons to microiontophoretically applied dopamine. Arnauld E, et al. **Neurosci Lett** 1981 Feb 6;21(3):325–31

Contrasting effects of diethylstilbestrol and estradiol on contraction of isolated rat aorta. Roesch CB, et al. **Pharmacology** 1981;22(1):15–23

Growth hormone, insulin, prolactin and total thyroxine in the plasma of sheep implanted with the anabolic steroid trenbolone acetate alone or with oestradiol. Donaldson IA, et al. **Res Vet Sci** 1981 Jan; 30(1):7–13

LH and prolactin in estrogenized female rats: response to LHRH. Vaticón MD, et al. **Rev Esp Fisiol** 1980 Dec;36(4):371–6

[Induction of lactation in cattle after short–term hormonal treatment] Manunta G, et al. **Boll Soc Ital Biol Sper** 1981 Jan 30;57(2):172–8 (Eng. Abstr.) (Ita)

[Hormonal induction of lactation after short–term treatment in sheep. III.] Manunta G, et al. **Boll Soc Ital Biol Sper** 1981 Jan 30;57(2):165–71 (Eng. Abstr.) (Ita)

[Effects of hypothalamic deafferentation and estrogen on the distribution and content of hypothalamic LHRH (author's transl)] Taketani Y. **Acta Obstet Gynaecol Jpn** 1981 May;33(5):625–34 (Eng. Abstr.) (Jpn)

EXPLORATORY BEHAVIOR

Habituation of the head–poke response: effects of an amphetamine–barbiturate mixture, PLG and fenfluramine. Koek W, et al. **Psychopharmacology (Berlin)** 1981;72(3):251–6

[Locomotor activity of rats following chronic pretreatment with haloperidol] Oehler J, et al. **Acta Biol Med Ger** 1980; 39(11–12):1235–9 (Eng. Abstr.) (Ger)

[Diphasic action of apomorphine on motility of the rat. I. Dose–effect relationship in exploratory and basal motility] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):374–80 (Eng. Abstr.) (Ita)

EXTINCTION (PSYCHOLOGY)

The partial reinforcement extinction effect after treatment with chlordiazepoxide. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):269–75

FACTITIOUS DISORDERS

Pseudodementia and physical findings masking significant psychopathology. Good MI. **Am J Psychiatry** 1981 Jun;138(6):811–4

FEAR

Differential diagnosis and treatment of panic attacks and phobic states. Liebowitz MR, et al. **Annu Rev Med** 1981;32:583–99 (46 ref.)

FENFLURAMINE

The metabolism and kinetics of tiflorex in the rat. Mas–Chamberlin C, et al. **Drug Metab Dispos** 1981 Mar–Apr;9(2):150–5

Effect of fenfluramine and related compounds on the pancreatic colipase/lipase system. Borgström B, et al. **FEBS Lett** 1981 Apr 6; 126(1):25–8

Habituation of the head-poke response: effects of an amphetamine-barbiturate mixture, PLG and fenfluramine. Koek W, et al. **Psychopharmacology (Berlin)** 1981;72(3):251–6

[Ponderal Retard] de Longraye J. **Soins** 1981 Jan 20;26(2):45–6 (Fre)

FLICKER FUSION

Critical flicker fusion (CFF) test for sedative effect of antidepressants. Holmberg G. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):289–301

FLUPHENAZINE

Late (4–8 years) outcome of treatment with megadoses of fluphenazine enanthate in drug-refractory schizophrenics. Dencker SJ, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):1–12

Depot fluphenazine maintenance treatment and associated weight changes. Marriott P, et al. **Compr Psychiatry** 1981 May–Jun;22(3):320–5

Treatment of fibromyositis with fluphenazine and amitriptyline: a preliminary report. Connolly RG. **Del Med J** 1981 Apr;53(4):189–91

Biochemical mechanism of tolerance to neuroleptic drugs; regional differences in rat brain. Bacopoulos NG. **Eur J Pharmacol** 1981 Apr 9;70(4):585–6

Prolonged dopamine receptor blockade in rats after termination of long-term depot fluphenazine [letter] Waddington JL, et al. **Lancet** 1981 Jun 20;1(8234):1375–6

Slow decline of plasma drug and prolactin levels after discontinuation of chronic treatment with depot neuroleptics [letter] Wistedt B, et al. **Lancet** 1981 May 23;1(8230):1163

Natural and therapeutic environmental indicators of maintenance dosage requirements [proceedings] Hogarty GE. **Psychopharmacol Bull** 1981 Jan;17(1):36–7

[The course of long-term care with fluphenazine decanoate (Dapotum D)] Deiser R, et al. **Psychiatr Clin (Basel)** 1980;13(3–4):193–205 (Eng. Abstr.) (Ger)

[Modification of schizophrenia by intensive neuroleptic therapy and the course of the disease after withdrawal of neuroleptic drugs] Steiner S. **Psychiatr Clin (Basel)** 1980;13(3–4):165–78 (Eng. Abstr.) (Ger)

[The influence of trihexyphenidyl on the antiamphetaminic action of fluphenazine (author's transl)] Kleinrok Z, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979;34:341–5 (Eng. Abstr.) (Pol)

[The influence of atropine on the antiamphetaminic action of fluphenazine (author's transl)] Rechberger T, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979;34:333–9 (Eng. Abstr.) (Pol)

FLURAZEPAM

Determination of flurazepam in human plasma by gas chromatography-electron capture negative chemical ionization mass spectrometry. Miwa BJ, et al. **Anal Chem** 1981 May;53(6):793–7

Tolerance during chronic benzodiazepine treatment associated with decreased receptor binding. Rosenberg HC, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):453–60

Rapid quantitation of flurazepam and its major metabolite, N-desalkylflurazepam, in human plasma by gas-liquid chromatography with electron-capture detection. Riva R, et al. **J Chromatogr** 1981 Mar 13;222(3):491–5

FOOD DEPRIVATION

Adrenergic neuroplasticity is maintained in the nutritional rehabilitated adult rat. Gottesfeld Z, et al. **Experientia** 1981 Feb 15;37(2):168–9

Intravenous self-administration of etonitazene, cocaine and phencyclidine in rats during food deprivation and satiation. Carroll ME, et al. **J Pharmacol Exp Ther** 1981 May;217(2):241–7

Pharmacokinetic study of apomorphine-induced stereotypy in food deprived rats. Watanabe H, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):493–6

FSH

Direct evidence in men for a role of endogenous oestrogens on gonadotrophin release. D'Agata R, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):145–9

Release of LH and FSH by anterior pituitary cell suspensions from female rats during the estrous cycle and from estrogen-treated ovariectomized rats. Baldwin DM, et al. **Biol Reprod** 1981 Apr;24(3):581–90

Role of the ovary in controlling luteinizing hormone, follicle stimulating hormone, and prolactin secretion during and after lactation in pigs. Stevenson JS, et al. **Biol Reprod** 1981 Mar;24(2):341–53

Increased postovulatory plasma follicle stimulating hormone levels in the luteinized unruptured follicle syndrome: a role for inhibin? Koninckx PR, et al. **Br J Obstet Gynaecol** 1981 May;88(5):525–9

A radioimmunoassay for a highly active luteinizing hormone-releasing hormone analogue and relation between the serum level of the analogue and that of gonadotropin. Yamazaki I, et al. **Endocrinol Jpn** 1980 Oct; 27(5):593–605

Stimulation of beta 2-adrenergic responsiveness by follicle-stimulating hormone in rat granulosa cells in vitro and in vivo. Adashi EY, et al. **Endocrinology** 1981 Jun;108(6):2170–8

Regulation of the second surge of follicle-stimulating hormone; effects of antiluteinizing hormone-releasing hormone serum and pentobarbital. Hasegawa Y, et al. **Endocrinology** 1981 Jul;109(1):130–5

Catecholamine turnover rates in discrete hypothalamic areas and associated changes in median eminence luteinizing hormone-releasing hormone and serum gonadotropins on proestrus and diestrous day 1. Rance N, et al. **Endocrinology** 1981 May;108(5):1795–802

The actions of porcine follicular fluid and estradiol on periovulatory secretion of gonadotropic hormones in rats. Rush ME, et al. **Endocrinology** 1981 Jun;108(6):2316–23

In vivo effect of inhibin on FSH uptake by rat testis. Vanage GR, et al. **Experientia** 1981 Apr 15;37(4):433–4

Gonadotrophin release in vitro, in the presence and absence of luteinizing hormone releasing hormone, by pituitary glands from ovariectomized and sham-operated immature female rats of various ages. Dullaart J. **J Endocrinol** 1981 Mar;88(3):375–9

Pituitary function during pseudopregnancy and lactation in the rat. Taya K, et al. **J Reprod Fertil** 1981 May;62(1):93–8

Isolation and characterization of a bovine seminal plasma protein inhibiting pituitary FSH secretion. Sairam MR, et al. **Mol Cell Endocrinol** 1981 May;22(2):231–50

[The intragonadic cybernins (author's transl)] Franchimont P. **J Gynecol Obstet Biol Reprod (Paris)** 1980;9(8):825–34 (Eng. Abstr.) (Fre)

[Orientation studies of ovulation release in mice to test gonadotropic preparations. 2. FSH, PMSG and Gn-RH activity] Bergfeld J, et al. **Arch Exp Veterinaermed** 1981;35(1):143–8 (Eng. Abstr.) (Ger)

GABA

The concentration of gamma-aminobutyric acid (GABA) in discrete areas of rat brain after chemical sympathectomy or serotoninectomy. Szkilnik R, et al. **Acta Physiol Pol** 1980;31(5):513–5

GABAergic mechanisms in blood pressure control. A pharmacological analysis in the rat. Persson B. **Acta Physiol Scand [Suppl]** 1980; 491:1–54

Inhibition of GABA metabolism in rat brain slices by halothane. Cheng SC, et al. **Anesthesiology** 1981 Jul;55(1):26–33

Isolation and identification of gamma-aminobutyric acid in Streptomyces lincolnensis. Haak WJ, et al. **Antimicrob Agents Chemother** 1981 Mar; 19(3):493

Glutamate, aspartate, and gamma-aminobutyrate transport by membrane vesicles prepared from rat brain. Roskoski R Jr, et al. **Arch Biochem Biophys** 1981 Apr 1;207(2):407–15

Absorption of 14C-clanobutin-Na in blood-perfused tied-off jejunal segments in vivo of rats. Overhoff H, et al. **Arzneimittelforsch** 1981; 31(4):670–4

Absorption of 14C-clanobutin-Na isolated perfused intestinal segments in vitro of rats. Strugala G, et al. **Arzneimittelforsch** 1981; 31(3):429–33

Studies on bicuculline binding sites on neuronal membrane using fluorescent antibody technique: comparative binding of GABA and bicuculline. Bhattacharyya A, et al. **Biochem Biophys Res Commun** 1981 Jan 30;98(2):520–6

Competitive inhibition by 3-aminopropanesulfonic acid and gamma-aminobutyric acid of carnitine transport in rat brain slices. Fariello RG, et al. **Biochem Pharmacol** 1981 May 1;30(9):1012–3

The enzymes catalysing succinic semialdehyde reduction in rat brain. Rivett AJ, et al. **Biochem Pharmacol** 1981 Apr 1;30(7):741–7

Determination of glutamic acid and gamma-aminobutyric acid in Ringer's solution without desalination at the femtomole level by gas chromatography chemical ionization mass spectrometry. Murayama K, et al. **Biomed Mass Spectrom** 1981 Apr;8(4):165–9

SL 75 102 as a gama-aminobutyric acid agonist: experiments on dorsal root ganglion neurones in vitro. Desarmenien M, et al. **Br J Pharmacol** 1981 Feb;72(2):355–64

Sensitivity of identified medial hypothalamic neurons to GABA, glycine and related amino acids; influence of bicuculline, picrotoxin and strychnine on synaptic inhibition. Blume HW, et al. **Brain Res** 1981 Mar 23;209(1):145–58

Changes of electroretinogram and neurochemical aspects of GABAergic neurons of retina after intraocular injection of kainic acid in rats. Goto M, et al. **Brain Res** 1981 May 4;211(2):305–14

Benzodiazepines prevent kainate-induced loss of GABAergic and cholinergic neurons in the chick retina. Imperato A, et al. **Brain Res** 1981 May 25;213(1):205–10

Sensitivity to GABA of neurons of the dorsal and ventral lateral geniculate nuclei in the rat. Kayama Y, et al. **Brain Res** 1981 Apr 27; 211(1):202–5

Effects of halopemide on GABA receptor binding, uptake and release. Loonen AJ, et al. **Brain Res** 1981 Apr 6;210(1–2):485–92

The role of GABA in the regulation of the dopamine/tyrosine hydroxylase-containing neurons of the rat retina. Marshburn PB, et al. **Brain Res** 1981 Jun 15;214(2):335–47

Inhibitory actions of taurocyamine, hypotaurine, homotaurine, taurine and GABA on spike discharges of Purkinje cells, and localization of sensitive sites, in guinea pig cerebellar slices. Okamoto K, et al. **Brain Res** 1981 Feb 16;206(2):371–86

Potassium-stimulated, calcium-dependent release of [3H]GABA from neuron- and glia-enriched cultures of cells dissociated from rat cerebellum. Pearce BR, et al. **Brain Res** 1981 Feb 16;206(2):485–9

Barbiturate enhancement of GABA-mediated inhibition and activation of chloride ion conductance: correlation with anticonvulsant and anesthetic actions. Schulz DW, et al. **Brain Res** 1981 Mar 23; 209(1):177–88

The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures. Shibla DB, et al. **Brain Res** 1981 Apr 6;210(1–2):471–4

Growth dependent induction of high affinity gamma-amino-butyric acid transport in cultures of a normal human brain cell line. Walum E, et al. **Brain Res** 1981 May 11;212(1):215–8

Effect of GABA agonist and antagonists on cardiovascular and sympathetic responses in SHR and WKY rats. Feuerstein G, et al. **Clin Exp Hypertens** 1981;3(2):207–18

Succinic semialdehyde dehydrogenases of Escherichia coli: their role in the degradation of p-hydroxyphenylacetate and gamma-aminobutyrate. Donnelly MI, et al. **Eur J Biochem** 1981 Jan;113(3):555–61

gamma-Aminobutyric acid regulation of the benzodiazepine receptor: biochemical evidence for pharmacologically different effects of benzodiazepines and propyl beta-carboline-3-carboxylate. Ehlert FJ, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):593–5

GABA enhancement of [3H]dopamine release from slices of rat striatum: dependence on slice size. Ennis C, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):417–20

GABA antagonists enhance dopamine turnover in the rat retina in vivo. Kamp CW, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):273–9

Molecular sizes of benzodiazepine receptors and the interacting GABA receptors in the membrane are identical. Chang LR, et al. **FEBS Lett** 1981 Apr 20;126(2):309–12

Golgi-impregnated amacrine cells and GABAergic retinal neurons: a comparison of dendritic, immunocytochemical and histochemical stratification in the inner plexiform layer of rat retina. Famiglietti EV Jr, et al. **J Comp Neurol** 1981 Mar 20;197(1):129–39

GABAergic amacrine cells in rat retina: immunocytochemical identification and synaptic connectivity. Vaughn JE, et al. **J Comp Neurol** 1981 Mar 20;197(1):113–27

The release of gamma-aminobutyric acid, glutamate, and acetylcholine from striatal slices: a mass fragmentographic study. Moroni F, et al. **J Neurochem** 1981 May;36(5):1691–9

GABA conductance of chick spinal cord and dorsal root ganglion neurons in cell culture. Choi DW, et al. **J Neurophysiol** 1981 Apr; 45(4):605–20

Chlordiazepoxide selectively potentiates GABA conductance of spinal cord and sensory neurons in cell culture. Choi DW, et al. **J Neurophysiol** 1981 Apr;45(4):621–31

GABA-mediated synaptic potentials in chick spinal cord and sensory neurons. Choi DW, et al. **J Neurophysiol** 1981 Apr;45(4):632–43

Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. III. Amacrine-mediated inhibitory influences on ganglion cell receptive-field organization: a model. Frumkes TE, et al. **J Neurophysiol** 1981 Apr;45(4):783–804

Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. I. Receptors, horizontal cells, bipolars, and G-cells. Miller RF, et al. **J Neurophysiol** 1981 Apr;45(4):743–63

Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. II. Amacrine and ganglion cells. Miller RF, et al. **J Neurophysiol** 1981 Apr;45(4):764–82

A simple perfusion chamber for studying neurotransmitter release from cells maintained in monolayer culture. Pearce BR, et al. **J Neurosci Methods** 1981 Feb;3(3):255–9

Sodium valproate enhancement of gamma-aminobutyric acid (GABA) inhibition: electrophysiological evidence for anticonvulsant activity. Balding F Jr, et al. **J Pharmacol Exp Ther** 1981 May;217(2):445–50

Modulation by picrotoxin and IPTBO of 3H-flunitrazepam binding to the GABA/benzodiazepine receptor complex of rat cerebellum. Karobath M, et al. **Life Sci** 1981 Jan 19;28(3):307–13

Cerebellar specific gamma-glutamyltranspeptidase activation by GABA and taurine in postnatal mouse brain. Lisy V, et al. **Life Sci** 1980 Dec 22–29;27(25–26):2615–20

Present status and significance of the glutamine cycle in neural tissues. Shank RP, et al. **Life Sci** 1981 Feb 23;28(8):837–42 (36 ref.)

Cortical effects of monocular deprivation: suppression or deafferentation? [news] Movshon JA. **Nature** 1981 May 28;291(5813):284–5

The role of GABAergic inhibition in the cortical effects of monocular deprivation. Sillito AM, et al. **Nature** 1981 May 28;291(5813):318–20

GABA facilitation by noradrenaline shows supersensitivity in cerebellum after 6-hydroxydopamine. Moises HC, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980;315(1):37–46

Levels of glutamate, aspartate, GABA, and taurine in different regions of the cerebellum after x-irradiation-induced neuronal loss. Rea MA, et al. **Neurochem Res** 1981 Jan;6(1):33–9

GABA and muscimol inhibit the release of prolactin from dispersed rat anterior pituitary cells. Grossman A, et al. **Neuroendocrinology** 1981 Mar;32(3):145–9

Effects of anticonvulsants on excitability and GABA sensitivity of cat dorsal root ganglion cells. Gallagher JP, et al. **Neuropharmacology** 1981 May;20(5):427–33

Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat. Jones DL, et al. **Neuropharmacology** 1981 Jan;20(1):29–37

An electrophysiological model of GABA-mediated neurotransmission. Matthews WD, et al. **Neuropharmacology** 1981 Jun;20(6):561–5

Modulatory interactions between norepinephrine and taurine, beta-alanine, gamma-aminobutyric acid and muscimol, applied iontophoretically to cerebellar Purkinje cells. Yeh HH, et al. **Neuropharmacology** 1981 Jun;20(6):549–60

Biphasic response of hippocampal pyramidal neurons to GABA. Thalmann RH, et al. **Neurosci Lett** 1981 Feb 6;21(3):319–24

Pentobarbitone slows the dissociation of GABA from rat brain synaptosomal binding sites. Willow M, et al. **Neurosci Lett** 1981 Apr 9;23(1):71–4

[3H]gamma-aminobutyrate autoradiography of the rat olfactory bulb: hypothetical grain analysis of the distribution of silver grains. Halász N, et al. **Neuroscience** 1981;6(3):473–9

Demonstration of central gamma-aminobutyrate-containing nerve terminals by means of antibodies against glutamate decarboxylase. Pérez de la Mora M, et al. **Neuroscience** 1981;6(5):875–95

Involvement of the GABAergic system on shock-induced aggressive behavior in two strains of mice. Puglisi-Allegra S, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:13–8

gamma-Aminobutyric acid and benzodiazepine receptors: copurification and characterization. Gavish M, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1939–42

Autoradiographic localization of benzodiazepine receptors in immunocytochemically identified gamma-aminobutyrergic synapses. Möhler H, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1935–8

Net uptake of gamma-aminobutyric acid by a high-affinity system of rat brain synaptosomes. Pastuszko A, et al. **Proc Natl Acad Sci USA** 1981 Feb;78(2):1242–4

Preliminary studies on CSF gamma-aminobutyric acid levels in psychiatric patients before and during treatment with different psychotropic drugs. Zimmer R, et al. **Prog Neuropsychopharmacol** 1980; 4(6):613–20

GABA depletion in chick brain-stem after intraventricular injection of cefazolin. Ientile R, et al. **Res Commun Chem Pathol Pharmacol** 1981 Feb;31(2):241–50

Stability of gamma-aminobutyric acid in human cerebrospinal fluid and plasma [letter] Löscher W, et al. **Ther Drug Monit** 1981;3(1):109

[Possible ways for the directed regulation of cerebral gamma aminobutyric acid (GABA) metabolism in local irradiation of the head (author's transl)] Savickij IV, et al. **Radiobiol Radiother (Berl)** 1980; 21(6):800–8 (Eng. Abstr.) (Ger)

[Role of the GABA-ergic link in the development of the tranquilizing effect in cats] Kozlovskaia MM, et al. **Biull Eksp Biol Med** 1981; 91(1):45–8 (Eng. Abstr.) (Rus)

[Effect of certain pharamcologic preparations and different lighting setups on human work capacity] Bogatova RI, et al. **Kosm Biol Aviakosm Med** 1981 Jan–Feb;15(1):92–3 (Rus)

[Activation of the cerebral GABA-ergic inhibiting system in stress] Pavlova VI, et al. **Patol Fiziol Eksp Ter** 1981 Jan–Feb;(1):26–30 (Eng. Abstr.) (Rus)

GALVANIC SKIN RESPONSE

The replicability of the psychophysiological effects of diazepam. Itil TM, et al. **Biol Psychiatry** 1981 Jan;16(1):65–70

Bilateral skin conductance and the pupillary light-dark reflex: manipulation by chlorpromazine, haloperidol, scopolamine, and placebo. Patterson T, et al. **Psychopharmacology (Berlin)** 1981;73(1):63–9

GLUCURONIDASE

Release of lysosomal hydrolases from bone explants affected by dental plaque. Tenovuo J, et al. **Acta Odontol Scand** 1980;38(6):355–61

The synthesis and processing of beta-glucuronidase in normal and egasyn deficient mouse kidney. Brown JA, et al. **Biochem Biophys Res Commun** 1981 Mar 31;99(2):691–9

Enzyme release and morphological changes in leukocytes induced by mechanical trauma. Dewitz TS, et al. **Blood Cells** 1979 Aug; 5(3):499–512

Inhibition by zinc of hepatic lysosomal release of beta-glucuronidase induced by phorbol-12-myristate-13-acetate (PMA). Pfeiffer CJ, et al. **Cancer Lett** 1980 Jul;10(1):51–6

Enzymatic and functional heterogeneity of lysosomes. Groh V, et al. **Cell Tissue Res** 1981;214(3):613–21

Triplex gene dosage effect of beta-glucuronidase and possible assignment to band q22 in a partial duplication 7q. Danesino C, et al. **Hum Genet** 1981;56(3):371–3

Effects of low doses of alpha-chlorohydrin on phosphatases, beta-glucosidase, beta-glucuronidase & hyaluronidase of rat testis & epididymis. Gill SK, et al. **Indian J Exp Biol** 1980 Nov; 18(11):1351–2

Hydrolysis of natural and synthetic substrates by alpha-L-fucosidase, beta-D-glucuronidase and beta-N-acetylhexosaminidase purified from molluscs. Cabezas JA, et al. **Int J Biochem** 1981;13(3):389–93

Comparative studies on postnatal development of liver beta-glucuronidase activity between Gunn rats and Wistar rats. Tamura S, et al. **J Toxicol Sci** 1980 Nov;5(4):331–8

[A cytochemical study of T, active T, non active T and B lymphocytes in respect to acid phosphatase and beta-glucuronidase activity (author's transl)] Takada K, et al. **Rinsho Byori** 1981 Feb;29(2):183–6 **(Jpn)**

GONADOTROPINS, PITUITARY

Ultrastructural localization of gonadotropin and luteinizing hormone releasing hormone in the pituitary gland of a teleost fish (the platyfish). Margolis-Kazan H, et al. **J Exp Zool** 1981 Jan;215(1):99–102

Effect of oestrogen and an LH-RH agonist on the release of gonadotrophins in ovariectomized ewes deprived of LH-RH. Fraser HM, et al. **J Reprod Fertil** 1981 May;62(1):131–40

Serotonin involvement in the regulation of gonadotropin secretion during lactation in the rat. Coppings RJ, et al. **Proc Soc Exp Biol Med** 1981 Apr;166(4):536–41

Chronic effects of the stimulatory luteinizing hormone-releasing hormone analogue D-Ser (TBU) 6-EA 10-LRH on the gonadotrophin and gonadal steroid secretion in women with amenorrhoea. Skarin G, et al. **Ups J Med Sci** 1980;85(2):103–12

[Testicular atrophy and gonadotropin activity in rats with portacaval anastomosis] Di Marcotullio A, et al. **Minerva Chir** 1980 Oct 15; 35(19):1449–54 (Eng. Abstr.) **(Ita)**

GUANETHIDINE

Autoradiographic assessment of 3H-proline uptake by osteoblasts following guanethidine-induced sympathectomy in the rat. Singh IJ, et al. **Cell Tissue Res** 1981;216(1):215–20

Intravascular guanethidine in the treatment of extravasated vasopressin [letter] Crocker MC. **N Engl J Med** 1981 Jun 4;304(23):1430

Reversal of guanethidine- and diethyldithiocarbamate-induced amnesia by peripherally-administered catecholamines. Walsh TJ, et al. **Pharmacol Biochem Behav** 1981 May;14(5):713–8

HABITUATION (PSYCHOPHYSIOLOGY)

Neuroendocrine changes following habituation of animal hypnosis in male rabbits. Farabollini F, et al. **Behav Brain Res** 1981 May;2(3):363–72

HALOPERIDOL

Haloperidol and droperidol treatment in schizophrenics. Clinical application of the 'prolactin-model'. Langer G, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):574–83

Neuroleptic-induced decrease in platelet MAO activity of schizophrenic patients. Chojnacki M, et al. **Am J Psychiatry** 1981 Jun; 138(6):838–40

Behavioral supersensitivity to methamphetamine following chronic treatment with (—)-sulpiride in the rat. Montanaro N, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):401–6

3H and 125I radioimmunoassays of haloperidol compared with fluoroimmunoassay involving antibody coupled to magnetizable solid phase. Rowell FJ, et al. **Clin Chem** 1981 Jul;27(7):1249–54

Time course of chronic haloperidol and clozapine upon operant rate and duration. Faustman W, et al. **Eur J Pharmacol** 1981 Mar 5; 70(1):65–70

A comparison of dopamine receptor blocking assay with plasma drug levels of haloperidol in schizophrenic patients. Kurland AA, et al. **J Clin Pharmacol** 1981 Jan;21(1):42–7

A comparative study of parenteral molindone and haloperidol in the acutely psychotic patient. Binder R, et al. **J Clin Psychiatry** 1981 May; 42(5):203–6

A new radioimmunoassay for haloperidol: direct measurement of serum and striatal concentrations. Wurzburger RJ, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):757–63

Chlorpromazine-induced decrease of red cell aggregability. Costa D, et al. **Med Interne** 1981 Jan–Mar;19(1):83–7

Blink rates and receptor supersensitivity. Karson CN, et al. **Neuropharmacology** 1981 Jan;20(1):91–3

Influence of substance P on the behavioral changes induced by haloperidol in rats. Jolicoeur FB, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):103–7

Disruption of autoshaped responding to a single of brain-stimulation reward by neuroleptic drugs. Phillips AG, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):543–8

An analysis of visual object reversal learning in the marmoset after amphetamine and haloperidol. Ridley RM, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):345–51

Differential prolactin responses to haloperidol and TRH in normal adult men. Hays SE, et al. **Psychoneuroendocrinology** 1981;6(1):45–52

Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children [proceedings] Platt JE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):123–5

Effects of single and long-term haloperidol administration on open field behavior of rats. Bernardi MM, et al. **Psychopharmacology (Berlin)** 1981; 73(2):171–5

Increased mesolimbic dopamine binding following chronic haloperidol treatment. Kamer RS, et al. **Psychopharmacology (Berlin)** 1981; 72(3):261–3

Bilateral skin conductance and the pupillary light-dark reflex: manipulation by chlorpromazine, haloperidol, scopolamine, and placebo. Patterson T, et al. **Psychopharmacology (Berlin)** 1981;73(1):63–9

Serum and CSF levels of haloperidol by radioimmunoassay and radioreceptor assay during high-dose therapy of resistant schizophrenic patients. Rimón R, et al. **Psychopharmacology (Berlin)** 1981; 73(2):197–9

[Locomotor activity of rats following chronic pretreatment with haloperidol] Oehler J, et al. **Acta Biol Med Ger** 1980; 39(11–12):1235–9 (Eng. Abstr.) **(Ger)**

[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Initial results] Di Giorgio RM, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):302–4 (Eng. Abstr.) **(Ita)**

HEXOBARBITAL

Effect of cannabidiol on cytochrome P-450 and hexobarbital sleep time. Bornheim LM, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):503–7

Stereoselective formation of glucuronides in metabolism of hexobarbital enantiomers in vivo: isolation and quantitation of glucuronides in rabbit urine. Miyano K, et al. **Drug Metab Dispos** 1981 Jan–Feb;9(1):60–4

Enhancement of hexobarbital-induced sleep by lysine and its metabolites. Chang YF, et al. **Life Sci** 1981 Jan 26;28(4):407–13

HISTAMINE

Additional data on the function of hypothalamic histamine. Huszti Z. **Agents Actions** 1981 Apr;11(1–2):135–42

Radical formation in single crystals of aromatic amines and radical transformation by light. Karsten W, et al. **Int J Radiat Biol** 1981 Mar; 39(3):235–52

The effect of histamine and H1 and H2 receptors on prolactin and luteinizing hormone release in humans: sex differences and the role of stress. Pontiroli AE, et al. **J Clin Endocrinol Metab** 1981 May; 52(5):924–8

Effect of diazepam on stress induced changes in brain histamine. Mazurkiewicz-Kwilecki IM. **Pharmacol Biochem Behav** 1981 Mar; 14(3):333–8

Histamine release and endothelial leakage from an intravascular contrast medium. Raininko R. **ROEFO** 1981 Apr;134(4):445–9

Histamine reactions due to ingestion of tuna fish (Thunnus argentivittatus) in patients on anti-tuberculosis therapy. Senanayake N, et al. **Toxicon** 1981;19(1):184–5

[Histamine and serotonin study in 1 blood sample] Proshina LIa. **Lab Delo** 1981;(2):90–3 (Eng. Abstr.) **(Rus)**

[Histamine and serotonin content in immunocompetent tissues and blood in vagotomized rats] Aksenova VM. **Patol Fiziol Eksp Ter** 1981 Jan–Feb;(1):23–6 (Eng. Abstr.) **(Rus)**

HISTRIONIC PERSONALITY DISORDER

Interrelationship of hysteroid dysphoria and borderline personality disorder. Liebowitz MR, et al. **Psychiatr Clin North Am** 1981 Apr; 4(1):67–87

HYDANTOINS

An improved procedure for high-sensitivity microsequencing: use of aminoethyl aminopropyl glass beads in the Beckman sequencer and the ultrasphere ODS column for PTH amino acid identification. Bhown AS, et al. **Anal Biochem** 1981 Jan 15;110(2):355–9

Rapid separation of amino acid phenylthiohydantoins by isocratic high-performance liquid chromatography. Tarr GE. **Anal Biochem** 1981 Feb;111(1):27–32

PMR and 13C-NMR spectroscopy of tropane and N-substituted nortropane spirohydantoins. Trigo GG, et al. **J Pharm Sci** 1981 Jan; 70(1):87–9

Behavioural, ECoG spectrum power and body temperature effects of BW 245C, a prostaglandin analogue after intraventricular microinjection in chicks. Rotiroti D, et al. **Neuropharmacology** 1981 May;20(5):517–20

[Establishment of the maximum permissible concentration of 5,5-dimethylhydantoin in reservoir water] Pis'ko GT, et al. **Gig Sanit** 1981 May;(5):69–70 **(Rus)**

HYDRAZINES

Development of occupational and environmental health criteria for the F–16. McLendon MH. **Aviat Space Environ Med** 1981 Mar; 52(3):145–7

A comparison of the effects of hydrallazine, diazoxide, sodium nitrite and sodium nitroprusside on human isolated arteries and veins. Moulds RF, et al. **Br J Clin Pharmacol** 1981 Jan;11(1):57–61

Differential effect of benserazide (Ro4–4602) on the concentration of indoleamines in rat pineal and hypothalamus. Arendt J, et al. **Br J Pharmacol** 1981 Feb;72(2):257–62

Deacylation of polymyxin B by hydrazine & solvolysis. Srinivasa BR, et al. **Indian J Biochem Biophys** 1980 Aug;17(4):298–302

The oxidation of hydrazine derivatives catalyzed by the purified liver microsomal FAD–containing monooxygenase. Prough RA, et al. **J Biol Chem** 1981 May 10;256(9):4178–84

Hydrazine formation from iproniazid. Hsu KY, et al. **J Pharmacobiodyn** 1980 Nov;3(11):620–7

The interaction of 2,3,4–trihydroxybenzylhydrazine with DOPA decarboxylase from pig kidney. Borri Voltattorni C, et al. **Life Sci** 1981 Jan 5;28(1):103–8

Cyclic hydrazides are mutagenic for Salmonella typhimurium. Zeiger E, et al. **Mutat Res** 1981 May;91(3):199–205

HYDRAZONES

Mechanism of action of antiviral hetarylhydrazones in vitro. Tonew M. **Acta Virol (Praha)** 1981 Mar;25(2):108–14

A novel preparation of human platelet lipoxygenase. Characteristics and inhibition by a variety of phenyl hydrazones and comparisons with other lipoxygenases. Wallach DP, et al. **Biochim Biophys Acta** 1981 Feb 23; 663(2):361–72

HYDROXYBUTYRATES

Changes in blood ketone body ratio: their significance after major hepatic resection. Ukikusa M, et al. **Arch Surg** 1981 Jun;116(6):781–5

Effect of pH and 3–hydroxybutyrate on insulin binding and action in cultured human fibroblasts. Hidaka H, et al. **Diabetes** 1981 May; 30(5):402–6

Kinetics of coupled gamma–hydroxybutyrate oxidation and D–glucuronate reduction by an NADP+–dependent oxidoreductase. Kaufman EE, et al. **J Biol Chem** 1981 Jul 10;256(13):6890–4

[Value of sodium gamma hydroxybutyrate in cerebral protection during severe hypoxia in the rat] Laborit G, et al. **Agressologie** 1980; 21(4):189–97 (Eng. Abstr.) **(Fre)**

[Lipids of the luminescent bacteria Photobacterium mandapamensis] Kalacheva GS, et al. **Mikrobiologiia** 1981 Jan–Feb;50(1):79–83 (Eng. Abstr.) **(Rus)**

HYDROXYDOPAMINE

Cardiac catecholamine stores after cardiac sympathectomy, 6–OHDA, and cardiac denervation. Priola DV, et al. **Am J Physiol** 1981 Jun; 240(6):H889–95

Effects of pre– and postnatal treatment with 6–hydroxydopamine on the development of the rat locus coeruleus. Sievers J, et al. **Bibl Anat** 1981; (19):258–63

Bradycardia following injection of 6–hydroxydopamine into the intermediate portion of nucleus tractus solitarius medialis. Healy DP, et al. **Brain Res** 1981 Feb 16;206(2):415–20

The relationship between loss of dopamine nerve terminals, striatal [3H]spiroperidol binding and rotational behavior in unilaterally 6–hydroxydopamine–lesioned rats. Heikkila RE, et al. **Brain Res** 1981 May 4;211(2):285–92

Destruction of noradrenergic cell bodies by intracerebral 6–hydroxydopamine in the newborn rat. Lanfumey L, et al. **Brain Res** 1981 Jun 15;214(2):445–50

Effects of denervation and 6–hydroxydopamine on the activity of choline acetyltransferase in the spleen of the cod, Gadus morhua. Winberg M, et al. **Comp Biochem Physiol [C]** 1981;69C(1):141–3

Neonatal intraspinal 6–hydroxydopamine: depletion of norepinephrine but not dopamine. Ings R, et al. **Eur J Pharmacol** 1981 Apr 9; 70(4):577–83

Differential effects of maternal and sibling presence of hyperactivity of 6–hydroxydopamine–treated developing rats. Teicher MH, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):134–45

The role of nigral projections to the thalamus in drug–induced circling behaviour in the rat. Reavill C, et al. **Life Sci** 1981 Mar 30; 28(13):1457–66

GABA facilitation by noradrenaline shows supersensitivity in cerebellum after 6–hydroxydopamine. Moises HC, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980;315(1):37–46

Adrenalectomy and chemical sympathectomy by 6–hydroxydopamine. Effects on basal and stimulated insulin secretion. Ahrén B, et al. **Pfluegers Arch** 1981 Apr;390(1):17–21

6–hydroxydopamine and aggression in cats. Beleslin DB, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:29–32

Effect of morphine on circling behaviour in rats with 6–hydroxydopamine striatal lesions and electrolesions of the raphe nucleus. Slater P. **Pharmacol Biochem Behav** 1981 May;14(5):625–30

Effects of neonatal 6–hydroxydopamine treatment on catecholamine levels and behavior during development and adulthood. Fobes JL, et al. **Psychopharmacology (Berlin)** 1981;73(1):27–30

Use of 6–hydroxydopamine to deplete brain catecholamines in the rhesus monkey: effects on urinary catecholamine metabolites and behavior. Kraemer GW, et al. **Psychopharmacology (Berlin)** 1981;73(1):1–11

Catecholamine–serotonin interaction effects on activity in rats neonatally treated with 6–hydroxydopamine. Olds ME, et al. **Psychopharmacology (Berlin)** 1981;73(1):31–3

[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Initial results] Di Giorgio RM, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):302–4 (Eng. Abstr.) **(Ita)**

HYDROXYINDOLEACETIC ACID

Serotonin and noradrenaline uptake inhibitors in the treatment of depression—relationship to 5–HIAA in spinal fluid. Träskman–Bendz L, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):209–18

Monoamine metabolites in CSF and suicidal behavior. Träskman L, et al. **Arch Gen Psychiatry** 1981 Jun;38(6):631–6

Correlation of individual symptoms and other clinical variables with cerebrospinal fluid amine metabolites and tryptophan in depression. Banki CM, et al. **Arch Psychiatr Nervenkr** 1981;229(4):345–53

Simultaneous determination of femtomole quantities of 5–hydroxytryptophan, serotonin and 5–hydroxyindoleacetic acid in brain using HPLC with electrochemical detection. Lacković Z, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):347–52

Levels of HIAA and VMA in C.S.F. of schizophrenics before and after treatment. Okasha A, et al. **J Egypt Med Assoc** 1978; 61(Suppl 1–2):38–50

The effect of morphine on the content of serotonin, 5–hydroxyindole acetic acid and substance–P in the nuclei raphe magnus and reticularis gigantocellularis. Lakoski JM, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2639–44

Differential effects of short and long term lithium on tryptophan uptake and serotonergic function in cat brain. Swann AC, et al. **Life Sci** 1981 Jan 26;28(4):347–54

Brain serotonin and 5–hydroxyindoleacetic acid concentrations and serotonin synthesis following tetrahydro–beta–carboline administration in mice. Buckholtz NS. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):215–21

Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Vachon L, et al. **Neuroscience** 1981; 6(2):189–94

Platelet MAO activity and monoamine metabolites in cerebrospinal fluid in depressed and suicidal patients and in healthy controls. Oreland L, et al. **Psychiatry Res** 1981 Feb;4(1):21–9

Pretreatment amine neurotransmitter system interrelationships in depression [proceedings] Bowden CL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):70–2

Cerebrospinal fluid amine metabolites and cyclic nucleotides in human aggression [proceedings] Brown GL, et al. **Psychopharmacol Bull** 1981 Jan;17(1):63–5

Unexpected neuroendocrine–transmitter relationships [proceedings] Stokes PE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):72–5

HYDROXYTRYPTOPHAN

Management of depression with serotonin precursors. van Praag HM. **Biol Psychiatry** 1981 Mar;16(3):291–310

Simultaneous determination of femtomole quantities of 5–hydroxytryptophan, serotonin and 5–hydroxyindoleacetic acid in brain using HPLC with electrochemical detection. Lacković Z, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):347–52

New and highly sensitive assay for L–5–hydroxytryptophan decarboxylase activity by high–performance liquid chromatography–voltammetry. Rahman MK, et al. **J Chromatogr** 1980 Dec 12;221(2):265–70

Denervation supersensitivity to 5–hydroxytryptophan in rats following spinal transection and 5,7–dihydroxytryptamine injection. Barbeau H, et al. **Neuropharmacology** 1981 Jun;20(6):611–6

L–5–Hydroxytryptophan–induced drinking in rats: possible mechanisms for induction. Threatte RM, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):385–91

HYPERKINESIS

Serum serotonin, free tryptophan and plasma cyclic AMP levels in autistic children –with special reference to their relation to hyperkinesia. Hoshino Y, et al. **Fukushima J Med Sci** 1979;26(3–4):79–91

Predictors of adolescent height and weight in hyperkinetic boys treated with methylphenidate [proceedings] Loney J, et al. **Psychopharmacol Bull** 1981 Jan;17(1):132–4

Analysis of pemoline in serum by high performance liquid chromatography: clinical application to optimize treatment of hyperactive children. Tomkins CP, et al. **Ther Drug Monit** 1980; 2(3):255–60

HYPERKINETIC SYNDROME

Plasma free and total tryptophan, blood serotonin, and the hyperactivity syndrome: no evidence for the serotonin deficiency hypothesis. Ferguson HB, et al. **Biol Psychiatry** 1981 Mar;16(3):231–8

Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. Cohen NJ, et al. **J Abnorm Child Psychol** 1981 Mar;9(1):43–54

Differential effects of parent training and stimulant medication with hyperactives: A progress report. Firestone P, et al. **J Am Acad Child Psychiatry** 1981 Winter;20(1):135–47

Growth hormone, prolactin, and growth responses in hyperkinetic males treated with d-amphetamine. Greenhill LL, et al. **J Am Acad Child Psychiatry** 1981 Winter;20(1):84–103

A review of some alternative approaches to drug management of hyperactivity in children. Walden EL, et al. **J Learn Disabil** 1981 Apr; 14(4):213–7, 238 (36 ref.)

'Hyperactivity' : still a maze of questions [editorial] Chamberlein HR. **JDPB** 1980 Sep;1(3):99–101

Potential risk of prolonged administration of stimulant medication for hyperactive children. Satterfield JH. et al. **JDPB** 1980 Sep; 1(3):102–7

Computer analyzed EEG in amphetamine-responsive hyperactive children. McIntyre HB, et al. **Psychiatry Res** 1981 Apr;4(2):189–97

The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine. Mikkelsen E, et al. **Psychiatry Res** 1981 Apr;4(2):157–69

IMIPRAMINE

Antidepressants and alpha 2-adrenergic autoreceptor desensitization. Siever LJ, et al. **Am J Psychiatry** 1981 May;138(5):681–2

Effects of Ro 11-2465, a new psychotropic agent on the uptake of serotonin by human platelets—in vitro determination of the IC50. Lenehan T, et al. **Arch Int Pharmacodyn Ther** 1981 Jan; 249(1):147–52

The effect of amoxapine and imipramine on serum prolactin levels. Cooper DS, et al. **Arch Intern Med** 1981 Jul;141(8):1023–5

2-nitroimipramine: a selective irreversible inhibitor of [3H] serotonin uptake and [3H] imipramine binding in platelets. Rehavi M, et al. **Biochem Biophys Res Commun** 1981 Apr 15;99(3):954–9

Regional distribution of [3H]imipramine binding in rat brain. Palkovits M, et al. **Brain Res** 1981 Apr 6;210(1–2):493–8

Reversed-phase liquid chromatography for the separation of chloropromazine, imipramine and some of their metabolites. Fekete J, et al. **J Chromatogr** 1981 Jan 16;204:319–27

Determination of clomipramine or imipramine and their mono-demethylated metabolites in human blood or plasma by high-performance liquid chromatography. Godbillon J, et al. **J Chromatogr** 1981 Jan 16;204:303–11

Inhibition of riboflavin metabolism in rat tissues by chlorpromazine, imipramine, and amitriptyline. Pinto J, et al. **J Clin Invest** 1981 May; 67(5):1500–6

Agoraphobia: the 'what if' syndrome. Fier M. **J Med Soc NJ** 1981 Apr; 78(4):286–8

Prenatal exposure to imipramine alters early behavioral development and beta adrenergic receptors in rats. Jason KM, et al. **J Pharmacol Exp Ther** 1981 May;217(2):461–6

Effect of imipramine on central 5-hydroxytryptamine turnover and metabolism in rats. Segawa T, et al. **Jpn J Pharmacol** 1980 Dec; 30(6):789–93

An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment. Koide T, et al. **Life Sci** 1981 Mar 9;28(10):1139–45

Circadian acetylcholine receptor rhythm in rat brain and its modification by imipramine. Kafka MS, et al. **Neuropharmacology** 1981 May; 20(5):421–5

Prophylactic lithium with and without imipramine for bipolar I patients: a double-blind study [proceedings] Kane JM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):144–5

Factors which affect antidepressant drug responses in a multicenter controlled trial [proceedings] Logue JN, et al. **Psychopharmacol Bull** 1981 Jan;17(1):138–9

Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo-controlled comparison [proceedings] Quitkin FM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):142–4

[On the effect of imipramine on blood composition, glucose level and alkaline phosphatase activity of leucocytes in non-emotive Wistar rats and animals of inbred TMB strain (author's transl)] Freund D, et al. **Arzneimittelforsch** 1981;31(3):425–8 (Eng. Abstr.) (Ger)

IPRONIAZID

The inhibitory action of L-dihydroxyphenylalanine (L-dopa) in the presence of a monoamine oxidase inhibitor on protein synthesis in vivo and the partial amelioration of this by methionine supplementation. Bone AH, et al. **Biochem J** 1980 Nov 15;192(2):703–7

Hydrazine formation from iproniazid. Hsu KY, et al. **J Pharmacobiodyn** 1980 Nov;3(11):620–7

ISOCARBOXAZID

Effect of adrenoceptor blocker and MAOI on postcoital utero-oviductal contractility, sperm transport, and sperm attachment to eggs in rabbits. Marsafy YM, et al. **Arch Androl** 1981 Jun;6(4):307–16

JUDGMENT

Public judgments on the importance of valium information [proceedings] Fisher S, et al. **Psychopharmacol Bull** 1981 Jan;17(1):134

LACTATES

[Lactic acid in the blood of heifers after administration of adrenaline and its relationship to pregnancy] Hintnaus J. **Vet Med (Praha)** 1981 Feb; 26(2):95–100 (Eng. Abstr.) (Cze)

LEARNING

Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Vachon L, et al. **Neuroscience** 1981; 6(2):189–94

Impairment of learning or memory in the mature and old rat by diazepam. Komiskey HL, et al. **Psychopharmacology (Berlin)** 1981;73(3):304–5

LEARNING DISORDERS

Residual attentional deficits in adolescents. Clampit MK. **J Learn Disabil** 1981 Apr;14(4):218–9

LEVODOPA

The inhibitory action of L-dihydroxyphenylalanine (L-dopa) in the presence of a monoamine oxidase inhibitor on protein synthesis in vivo and the partial amelioration of this by methionine supplementation. Bone AH, et al. **Biochem J** 1980 Nov 15;192(2):703–7

The catecholamine precursor L-3,4-dihydroxyphenylalanine inhibits both heat production and heat loss mechanisms in the rabbit. Lin MT. **Can J Physiol Pharmacol** 1980 Aug;58(8):956–64

L-dopa enhances acquisition of an inhibitory avoidance response. Martinez JL Jr, et al. **Commun Psychopharmacol** 1980;4(3):215–8

Studies on the mechanisms of L-dopa-induced salivary secretion. Pazo JH, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):255–61

Maintenance by L-DOPA treatment of estrous cycles and LH response to estrogen in aging female rats. Forman LJ, et al. **Exp Aging Res** 1980 Dec;6(6):547–54

Drugs to boost sexual potency. Kent S. **Geriatrics** 1981 Jul; 36(7):158–66

Chronic L-DOPA treatment of mice: a behavioural and biochemical study. Bailey R, et al. **J Neural Transm** 1981;50(2–4):209–24

Conversion of 3, 4-dihydroxyphenylalanine and deuterated 3, 4-dihydroxyphenylalanine to alcoholic metabolites of catecholamines in rat brain. Edwards DJ, et al. **J Neurochem** 1981 May; 36(5):1641–7

LH

Direct evidence in men for a role of endogenous oestrogens on gonadotrophin release. D'Agata R, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):145–9

Existence of multiple molecular forms of luteinizing hormone in rat: differences in immunological and biological activities between stored and circulating forms. Reddy PV, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):33–41

Qualitative and quantitative differences in the isoelectrofocusing profile of biologically active lutropin in the blood of normally menstruating and post-menopausal women. Strollo F, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):166–75

Effect of calcium and potassium on basal and gonadotrophin-releasing hormone (GnRH) stimulated release of luteinizing hormone (LH). Zolman JC, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):26–32

Differential effects of cyclic nucleotide analogues and GnRH on LH synthesis and release. Liu TC, et al. **Am J Physiol** 1981 Jul; 241(1):E6–13

Perifused pituitary cultures: a model for LHRH regulation of LH secretion. Loughlin JS, et al. **Am J Physiol** 1981 Jun;240(6):E591–6

Perifusion of rat pituitaries: requirements for optimal GnRH-stimulated LH release. Stern JE, et al. **Am J Physiol** 1981 May;240(5):E504–9

LH responses to LHRH, DBcAMP, and 17 beta-estradiol in cultures derived from aged rats. Tang LK, et al. **Am J Physiol** 1981 May; 240(5):E510–8

Effect of inhibitors of catecholamine synthesis on the pituitary response to LH-RH. Rettori V, et al. **Arch Androl** 1981 Mar;6(2):151–4

Release of LH and FSH by anterior pituitary cell suspensions from female rats during the estrous cycle and from estrogen-treated ovariectomized rats. Baldwin DM, et al. **Biol Reprod** 1981 Apr;24(3):581–90

Role of the ovary in controlling luteinizing hormone, follicle stimulating hormone, and prolactin secretion during and after lactation in pigs. Stevenson JS, et al. **Biol Reprod** 1981 Mar;24(2):341–53

Inhibition of LH and prolactin release in the cycling rat following inhibition of dopamine-beta-hydroxylase. Voogt JL, et al. **Brain Res** 1981 Mar 30;209(2):411–9

A reevaluation of the refractory period following the estrogen-induced luteinizing hormone surge in the rhesus monkey. Weick RF. **Can J Physiol Pharmacol** 1980 Aug;58(8):995–8

A radioimmunoassay for a highly active luteinizing hormone-releasing hormone analogue and relation between the serum level of the analogue and that of gonadotropin. Yamazaki I, et al. **Endocrinol Jpn** 1980 Oct; 27(5):593–605

Regulation of adrenal and testicular prolactin receptors by adrenocorticotropin and luteinizing hormone. Katikineni M, et al. **Endocrinology** 1981 Jun;108(6):2367–74

In vitro effect of danazol on luteinizing hormone-releasing hormone-stimulated luteinizing hormone release in rat anterior pituitary cell cultures in vitro. Menon M, et al. **Endocrinology** 1981 Jul; 109(1):191–6

Catecholamine turnover rates in discrete hypothalamic areas and associated changes in median eminence luteinizing hormone-releasing hormone and serum gonadotropins on proestrus and diestrous day 1. Rance N, et al. **Endocrinology** 1981 May;108(5):1795–802

The actions of porcine follicular fluid and estradiol on periovulatory secretion of gonadotropic hormones in rats. Rush ME, et al. **Endocrinology** 1981 Jun;108(6):2316–23

Maintenance by L-DOPA treatment of estrous cycles and LH response to estrogen in aging female rats. Forman LJ, et al. **Exp Aging Res** 1980 Dec;6(6):547–54

Comparison between the effects of LH-RH and raised K+ concentration on release of LH from pituitary glands of female rats in vitro. de Koning J, et al. **FEBS Lett** 1981 Apr 20;126(2):199–202

A priming effect of luteinizing hormone releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **J Anim Sci** 1981 May; 52(5):1137–42

The effect of histamine and H1 and H2 receptors on prolactin and luteinizing hormone release in humans: sex differences and the role of stress. Pontiroli AE, et al. **J Clin Endocrinol Metab** 1981 May; 52(5):924–8

Gonadotrophin release in vitro, in the presence and absence of luteinizing hormone releasing hormone, by pituitary glands from ovariectomized and sham-operated immature female rats of various ages. Dullaart J. **J Endocrinol** 1981 Mar;88(3):375–9

Importance of the episodic nature of luteinizing hormone secretion for normal development of the bovine testis during puberty: interference with oestradiol-17 beta. Schanbacher BD. **J Endocrinol** 1981 Mar; 88(3):393–400

Pituitary function during pseudopregnancy and lactation in the rat. Taya K, et al. **J Reprod Fertil** 1981 May;62(1):93–3

Effect of electrical stimulation of the dorsomedial hypothalamic nucleus on pulsatile LH release in ovariectomized rats. Gallo RV. **Neuroendocrinology** 1981 Mar;32(3):134–8

Further studies on dopamine-induced suppression of pulsatile LH release in ovariectomized rats. Gallo RV. **Neuroendocrinology** 1981 Mar; 32(3):187–92

Interrelationship between pineal gland and hypothalamic-hypophyseal complex. IV. Effect of pinealectomy on luteinizing function of rat hypophysis. Krivosheev OG, et al. **Neurosci Behav Physiol** 1980 Nov-Dec;10(6):480–4

Inhibition of LH-release by synthetic analogues of LH-RH in rat pituitary cell culture. Nikolics K, et al. **Peptides (Fayetteville)** 1981 Spring; 2(1):65–73

LH and prolactin in estrogenized female rats: response to LHRH. Vaticón MD, et al. **Rev Esp Fisiol** 1980 Dec;36(4):371–6

Delta9-tetrahydrocannabinol increase plasma testosterone concentrations in mice. Dalterio S, et al. **Science** 1981 Jul 31;213(4507):581–3

LH-FSH RELEASING HORMONE

Sensitivity of rat adenohypophyseal cells to estradiol and LHRH during long-term culture. Lagacé L, et al. **Am J Physiol** 1981 Jun; 240(6):E602–8

Differential effects of cyclic nucleotide analogues and GnRH on LH synthesis and release. Liu TC, et al. **Am J Physiol** 1981 Jul; 241(1):E6–13

Perifused pituitary cultures: a model for LHRH regulation of LH secretion. Loughlin JS, et al. **Am J Physiol** 1981 Jun;240(6):E591–6

Perifusion of rat pituitaries: requirements for optimal GnRH-stimulated LH release. Stern JE, et al. **Am J Physiol** 1981 May;240(5):E504–9

LH responses to LHRH, DBcAMP, and 17 beta-estradiol in cultures derived from aged rats. Tang LK, et al. **Am J Physiol** 1981 May; 240(5):E510–8

Effect of inhibitors of catecholamine synthesis on the pituitary response to LH-RH. Rettori V, et al. **Arch Androl** 1981 Mar;6(2):151–4

Human placental receptors for luteinizing hormone releasing hormone. Currie AJ, et al. **Biochem Biophys Res Commun** 1981 Mar 16; 99(1):332–8

A study of the applicability of QSAR calculation for peptide hormones. Nádasdi L, et al. **Biochem Biophys Res Commun** 1981 Mar 31; 99(2):451–7

Paradoxical effects of D-Trp6-LHRH in immature female rats correlated with changes in ACTH, prolactin, and corticosterone levels. Nekola MV, et al. **Biol Reprod** 1981 Apr;24(3):505–11

Increased postovulatory plasma follicle stimulating hormone levels in the luteinized unruptured follicle syndrome: a role for inhibin? Koninckx PR, et al. **Br J Obstet Gynaecol** 1981 May;88(5):525–9

Circadian variations in substance P, luliberin (LH-RH) and thyroliberin (TRH) contents in hypothalamic and extrahypothalamic brain nuclei of adult male rats. Kerdelhue B, et al. **Brain Res** 1981 Feb 16; 206(2):405–13

Ultrastructural localization of gonadotropin-releasing hormone in the porcine gonadotropic cells. Dacheux F. **Cell Tissue Res** 1981; 216(1):143–50

Correlative ontogenetic development of catecholamine- and LHRH-containing nerve endings in the median eminence of the rat. Ibata Y, et al. **Cell Tissue Res** 1981;216(1):31–8

Lack of effect of intravenous LHRH on plasma noradrenaline in man. Jürgensen HJ, et al. **Clin Endocrinol (Oxf)** 1980 Sep;13(3):249–52

The antigonadotropic activity of Lithospermum ruderale. II. The inhibition of LRF-induced gonadotropin release in vitro. Findley WE. **Contraception** 1981 Feb;23(2):157–62

Influence of the LH-RH analogue buserelin on cyclic ovarian function and on endometrium. A new approach to fertility control? Schmidt-Gollwitzer M, et al. **Contraception** 1981 Feb;23(2):187–95

A radioimmunoassay for a highly active luteinizing hormone-releasing hormone analogue and relation between the serum level of the analogue and that of gonadotropin. Yamazaki I, et al. **Endocrinol Jpn** 1980 Oct; 27(5):593–605

Binding characteristics of gonadotropin-releasing hormone receptors throughout the estrous cycle of the hamster. Adams TE, et al. **Endocrinology** 1981 Jun;108(6):2245–53

Pituitary and gonadal gonadotropin-releasing hormone receptors during sexual maturation in the rat. Dalkin AC, et al. **Endocrinology** 1981 May; 108(5):1658–64

Gonadotropin releasing hormone agonists stimulate oocyte meiosis and ovulation in hypophysectomized rats. Ekholm C, et al. **Endocrinology** 1981 May;108(5):2022–4

Dissociated changes of pituitary luteinizing hormone-releasing hormone (LHRH) receptors and responsiveness to the neurohormone induced by 17 beta-estradiol and LHRH in vivo in the rat. Ferland L, et al. **Endocrinology** 1981 Jul;109(1):87–93

Regulation of the second surge of follicle-stimulating hormone; effects of antiluteinizing hormone-releasing hormone serum and pentobarbital. Hasegawa Y, et al. **Endocrinology** 1981 Jul;109(1):130–5

Gonadotropin-releasing hormone analog and testosterone synergistically inhibit spermatogenesis. Heber D, et al. **Endocrinology** 1981 May; 108(5):2019–21

In vitro effect of danazol on luteinizing hormone-releasing hormone-stimulated luteinizing hormone release in rat anterior pituitary cell cultures in vitro. Menon M, et al. **Endocrinology** 1981 Jul; 109(1):191–6

Catecholamine turnover rates in discrete hypothalamic areas and associated changes in median eminence luteinizing hormone-releasing hormone and serum gonadotropins on proestrus and diestrous day 1. Rance N, et al. **Endocrinology** 1981 May;108(5):1795–802

Negative feedback effects of progesterone correlated with changes in hypothalamic norepinephrine and dopamine turnover rates, median eminence luteinizing hormone-releasing hormone, and peripheral plasma gonadotropins. Rance N, et al. **Endocrinology** 1981 Jun; 108(6):2194–9

The actions of porcine follicular fluid and estradiol on periovulatory secretion of gonadotropic hormones in rats. Rush ME, et al. **Endocrinology** 1981 Jun;108(6):2316–23

The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone-releasing hormone and the effect of prolactin on catecholamine turnover. Selmanoff M. **Endocrinology** 1981 May;108(5):1716–22

Estradiol as a gonadotropin releasing hormone in the rhesus monkey. Wildt L, et al. **Endocrinology** 1981 May;108(5):2011–3

Changes in radioimmunoassayable luteinizing hormone-releasing hormone in discrete brain areas of the rat at various times on proestrus, diestrous day 1, and after phenobarbital administration. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2179–85

Comparison between the effects of LH-RH and raised K+ concentration on release of LH from pituitary glands of female rats in vitro. de Koning

J, et al. **FEBS Lett** 1981 Apr 20;126(2):199-202

Synthesis, biological activity and resistance to enzymic degradation of luteinizing hormone--releasing hormone analogues modified at position 7. Hazum E, et al. **FEBS Lett** 1981 Jan 26;123(2):300-2

Results of three-times-per-week long-term administration of a luteinizing hormone-releasing hormone (LHRH) analog, D-Ser-(TBU)6-LHRH-(EA)10 in primary amenorrhea. Batrinos ML, et al. **Fertil Steril** 1981 May;35(5):515-20

TRH, GH-RIH, and LH-RH in metamorphosing Xenopus laevis. King JA, et al. **Gen Comp Endocrinol** 1981 May;44(1):20-7

Topochemically related hormone structures. Synthesis of partial retro-inverso analogs of LH-RH. Chaturvedi N, et al. **Int J Pept Protein Res** 1981 Jan;17(1):72-88

A priming effect of luteinizing hormone releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **J Anim Sci** 1981 May; 52(5):1137-42

Absence of LH-RH binding sites in corpora lutea from rhesus monkeys (Macacca mulatta). Asch RH, et al. **J Clin Endocrinol Metab** 1981 Jul; 53(1):215-17

Relationship between human follicular fluid inhibin F activity and steroid content. Channing CP, et al. **J Clin Endocrinol Metab** 1981 Jun; 52(6):1193-8

Urinary excretion of immunoreactive luteinizing hormone-releasing hormone-like material in children correlation with pubertal development. Rettig K, et al. **J Clin Endocrinol Metab** 1981 Jun; 52(6):1150-5

Pregnancy after prolonged pulsatile administration of luteinizing hormone-releasing hormone in a patient with clomiphene-resistant secondary amenorrhea. Schoemaker J, et al. **J Clin Endocrinol Metab** 1981 May;52(5):882-5

Bisexual behavior in male rats treated neonatally with antibodies to luteinizing hormone-releasing hormone. Kalcheim C, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):36-44

Gonadotrophin release in vitro, in the presence and absence of luteinizing hormone releasing hormone, by pituitary glands from ovariectomized and sham-operated immature female rats of various ages. Dullaart J. **J Endocrinol** 1981 Mar;88(3):375-9

Changes in responsiveness of dispersed pituitary cells to luteinizing hormone releasing hormone at different times of the oestrous cycle of the rat. Speight A, et al. **J Endocrinol** 1981 Apr;89(1):129-34

Changes in pituitary LHRH incorporation during the rat estrous cycle, and in rats made anovulatory by various experimental procedures. De Gaetani CF, et al. **J Endocrinol Invest** 1981 Jan-Mar;4(1):59-63

Ultrastructural localization of gonadotropin and luteinizing hormone releasing hormone in the pituitary gland of a teleost fish (the platyfish). Margolis-Kazan H, et al. **J Exp Zool** 1981 Jan;215(1):99-102

Effect of oestrogen and an LH-RH agonist on the release of gonadotrophins in ovariectomized ewes deprived of LH-RH. Fraser HM, et al. **J Reprod Fertil** 1981 May;62(1):131-40

Induction of delayed implantation in rats by LH-RH. Yoshinaga K. **J Reprod Fertil [Suppl]** 1981;29:131-3

Inhibition of HCG-induced cyclic AMP accumulation and steroidogenesis in rat luteal cells by an LHRH agonist. Massicotte J, et al. **J Steroid Biochem** 1981 Mar;14(3):239-42

Inhibition of the action of sex steroids by gonadotropin-releasing hormone (GnRH) agonists: a new biological effect. Sundaram K, et al. **Life Sci** 1981 Jan 5;28(1):83-8

The use of affinity matrices in the purification of inhibin from bovine follicular fluid. Jansen EH, et al. **Mol Cell Endocrinol** 1981 Feb; 21(2):109-17

Sertoli-Leydig cell communication via an LHRH-like factor. Sharpe RM, et al. **Nature** 1981 Apr 30;290(5809):785-7

Opiate receptors modulate LHRH and SRIF release from mediobasal hypothalamic neurons. Drouva SV, et al. **Neuroendocrinology** 1981 Mar; 32(3):163-7

Ionic channels involved in the LHRH and SRIF release from rat mediobasal hypothalamus. Drouva SV, et al. **Neuroendocrinology** 1981 Mar;32(3):155-62

Interrelationship between pineal gland and hypothalamic-hypophyseal complex. IV. Effect of pinealectomy on luteinizing function of rat hypophysis. Krivosheev OG, et al. **Neurosci Behav Physiol** 1980 Nov-Dec;10(6):480-4

Cellular characteristics of immunolabeled luteinizing hormone releasing hormone (LHRH) neurons. Kozlowski GP, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):37-46

Simultaneous monoamine histofluorescence and neuropeptide immunocytochemistry: I. Localization of catecholamines and gonadotropin-releasing hormone in the rat median eminence. McNeill TH, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):59-68

Inhibition of LH-release by synthetic analogues of LH-RH in rat pituitary cell culture. Nikolics K, et al. **Peptides (Fayetteville)** 1981 Spring; 2(1):65-73

Chromatographic and biologic analysis of ME and OVLT LHRH. Samson WK, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):97-102

LH and prolactin in estrogenized female rats: response to LHRH. Vaticón MD, et al. **Rev Esp Fisiol** 1980 Dec;36(4):371-6

Chronic effects of the stimulatory luteinizing hormone-releasing hormone analogue D-Ser (TBU) 6-EA 10-LRH on the gonadotrophin and gonadal steroid secretion in women with amenorrhoea. Skarin G, et al. **Ups J Med Sci** 1980;85(2):103-12

[Inhibin - a new ovarian hormone] Presl J. **Cesk Gynekol** 1981 Mar; 46(2):132-3 (Cze)

[Ultrastructure of female rat FSH gonadotrophs following two LH-RH stimulations (author's transl)] Seinsch W, et al. **Anat Anz** 1980; 148(3):207-13 (Eng. Abstr.) (Ger)

[Orientation studies of ovulation release in mice to test gonadotropic preparations. [illegible] FSH, PMSG and Gn-RH activity] Bergfeld J, et al. **Arch Exp Veterinaermed** 1981;35(1):143-8 (Eng. Abstr.) (Ger)

[Menstrual cycle changes during consecutive artificial insemination therapy and their treatment] Katzorke T, et al. **Fortschr Med** 1981 Apr 2;99(13):471-4 (Eng. Abstr.) (Ger)

[Endocrinology and diseases of the testis in children] Zweymüller E. **Wien Med Wochenschr** 1981 Feb 15;131(3):68-72 (Ger)

[Advances in the research of the contraceptive action of LH-RH analogs] Pardo Y, et al. **Harefuah** 1980 Oct 15;99(8):229-31 (Heb)

[Endocrinologic study of beta-thalassemia major] Monteverde R, et al. **Minerva Pediatr** 1980 Dec 15;32(23):1335-42 (Eng. Abstr.) (Ita)

[Effects of hypothalamic deafferentation and estrogen on the distribution and content of hypothalamic LHRH (author's transl)] Taketani Y. **Acta Obstet Gynaecol Jpn** 1981 May;33(5):625-34 (Eng. Abstr.) (Jpn)

[Primary amenorrhea possibly due to insufficient LH-RH secretion] Iwasa T, et al. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Oct; 32(10):1647-9 (Jpn)

LIPOTROPIN

Release of beta-lipotropin and beta-endorphin from rat hypothalami in vitro. Vermes I, et al. **Brain Res** 1981 Apr 27;211(1):248-54

Ultrastructural localization of corticotropin, beta-lipotropin, and alpha- and beta-endorphin in the porcine anterior pituitary. Dacheux F. **Cell Tissue Res** 1981;215(1):87-101

Effects of hypoxia on beta-endorphin and beta-lipotropin release in fetal, newborn, and maternal sheep. Wardlaw SL, et al. **Endocrinology** 1981 May;108(5):1710-5

Differentiation of MSH-, ACTH-, endorphin-, and LPH-containing cells in the hypophysis during embryonic and fetal development. Dupouy JP. **Int Rev Cytol** 1980;68:197-249 (277 ref.)

Chemistry and biosynthesis of pro-opiomelanocortin. ACTH, MSH's, endorphins and their related peptides. Chrétien M, et al. **Mol Cell Biochem** 1981 Jan 28;34(2):101-27 (232 ref.)

Secretory granules of an anterior pituitary cell line, AtT-20, contain only mature forms of corticotropin and beta-lipotropin. Gumbiner B, et al. **Proc Natl Acad Sci USA** 1981 Jan;78(1):318-22

LITHIUM

Preferential vulnerability of dendrites to lithium ion in rat brain and in nerve cell culture. Janka Z, et al. **Acta Neuropathol [Suppl] (Berl)** 1981; 7:44-7

The effect of chronic lithium treatment on the sialic acid content in rat brain synaptosomes. Edelfors S. **Acta Pharmacol Toxicol (Copenh)** 1981 Jan;48(1):61-4

Estimates of the prevalence of bipolar affective disorder. Methods based on treatment with lithium. Eastwood R, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):83-90

Effect of antidepressants, lithium and electroconvulsive treatment on rat serum prolactin levels. Meltzer HY, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):100-2

Lithium therapy of children with chronic neutropenia. Chan HS, et al. **Am J Med** 1981 May;70(5):1073-7

Psychotropic drugs: lithium. Harris E. **Am J Nurs** 1981 Jul; 81(7):1311-5

Effects of lithium on memory. Christodoulou GN, et al. **Am J Psychiatry** 1981 Jun;138(6):847-8

Effect of lithium on glycine levels in patients with affective disorders. Deutsch SI, et al. **Am J Psychiatry** 1981 May;138(5):683-4

A case report of megaloblastic anemia secondary to lithium. Prakash R, et al. **Am J Psychiatry** 1981 Jun;138(6):849

Receptors, adenylate cyclase, depression, and lithium. Belmaker RH. **Biol Psychiatry** 1981 Apr;16(4):333-50

Relationship between lithium levels of saliva and serum [letter] Sethi N, et al. **Biol Psychiatry** 1981 Apr;16(4):413-4

Cerebral evoked potential changes produced by treatment with lithium carbonate. Straumanis JJ Jr, et al. **Biol Psychiatry** 1981 Feb; 16(2):113-29

Lithium effect on calcitonin secretion in the rat. Dupuy B, et al. **Biomedicine** 1980 Nov;33(7):207-8

Current concepts of lithium therapy [letter] Coppen A, et al. **Br J Hosp Med** 1981 Mar;25(3):309-10

Renal function in patients receiving long-term lithium therapy. Uldall PR, et al. **Can Med Assoc J** 1981 Jun 1;124(11):1471-4

Lithium and the mitogenic response of human lymphocytes. Bray J, et al. **Clin Immunol Immunopathol** 1981 May;19(2):284-8

Prophylactic effect of lithium against depression in cyclothymic patients: a life-table analysis. Peselow ED, et al. **Compr Psychiatry** 1981 May-Jun;22(3):257-64

The antidepressant effect of lithium. Arieli A, et al. **Curr Dev Psychopharmacol** 1981;6:165-90 (58 ref.)

Lithium updated. **Drug Ther Bull** 1981 Mar 13;19(6):21-4

The lithium clinic for treatment and prevention of manic depression: a cost benefit approach. Fieve RR. **Egypt J Psychiatry** 1979 Oct; 2(2):166-90

Effect of potassium and lithium ions on protein synthesis in the sea urchin embryo. Wolcott DL. **Exp Cell Res** 1981 Apr;132(2):464-7

Granulopoietic effects of lithium on human bone marrow in vitro. Richman CM, et al. **Exp Hematol** 1981 Apr;9(4):449-55

The spectrum of neutrons from A238Pu-Li source. Ing H, et al. **Health Phys** 1981 Mar;40(3):345-50

Adjuvant effects of lithium chloride on human mononuclear cells in suppressor-enriched and suppressor-depleted systems. Shenkman L, et al. **Immunopharmacology** 1981 Feb;3(1):1-8

Lithium response in the treatment of manic symptomatology. Channabasavanna SM, et al. **Indian J Med Res** 1980 Dec;72:908-9

Effects of indomethacin and methylprednisolone on renal elimination of lithium in the rat. Imbs JL, et al. **Int Pharmacopsychiatry** 1980; 15(3):143-9

Lithium induces abnormal calcium-regulated PTH release in dispersed bovine parathyroid cells. Brown EM. **J Clin Endocrinol Metab** 1981 May;52(5):1046-8

Steady-state lithium blood level fluctuations in man following administration of a lithium carbonate conventional and controlled-release dosage form. Caldwell HC, et al. **J Clin Pharmacol** 1981 Feb-Mar;21(2):106-9

Memory processing with lithium carbonate. Marusarz TZ, et al. **J Clin Psychiatry** 1981 May;42(5):190-2

Evidence that lithium alters phosphoinositide metabolism: chronic administration elevates primarily D-myo-inositol-1-phosphate in cerebral cortex of the rat. Sherman WR, et al. **J Neurochem** 1981 Jun; 36(6):1947-51

Lithium and the kidney. Singer I. **Kidney Int** 1981 Feb;19(2):374-87

Differential effects of short and long term lithium on tryptophan uptake and serotonergic function in cat brain. Swann AC, et al. **Life Sci** 1981 Jan 26;28(4):347-54

Lithium nephrotoxicity [letter] Johnson GF, et al. **Med J Aust** 1981 Apr 4;1(7):376

Effect of monovalent cations on the aggregation of tobacco mosaic virus by chondroitin sulfate. Sano Y, et al. **Microbiol Immunol** 1981; 25(2):155-61

The inhibitory effect of lithium of high-K induced contraction in guinea-pig taenia coli. Kishimoto T, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980;315(1):69-76

Monoamine uptake into synaptosomes from various regions of rat brain following lithium administration and withdrawal. Ahluwalia P, et al. **Neuropharmacology** 1981 May;20(5):483-7

Paradoxical effects of lithium on field potentials of dentate granule cells in slices of rat hippocampus. MacVicar BA, et al. **Neuropharmacology** 1981 May;20(5):489-96

Estimation of lithium dose requirement by lithium clearance, serum lithium and saliva lithium following a loading dose of lithium carbonate. Tyrer SP, et al. **Neuropsychobiology** 1981;7(3):152-8

Unit activity changes elicited in amygdala and neocortex of anaesthetized rats by intraperitoneal injection of lithium chloride. Reddy MM, et al. **Neurosci Lett** 1981 Mar 10;22(2):169-72

Feeding and selection of saccharin after injections of bombesin, LiCl, and NaCl. Kulkosky PJ, et al. **Peptides (Fayetteville)** 1981 Spring; 2(1):61-4

Particle size effects in thermoluminescent lithium fluoride. Driscoll CM, et al. **Phys Med Biol** 1981 Mar;26(2):321-7

Effects of dorsolateral tegmental lesions on amphetamine- and lithium-induced taste aversions. Wellman PJ, et al. **Physiol Behav** 1981 Feb;26(2):341-4

Lithium: some drug interactions. Kamlana SH, et al. **Practitioner** 1980 Dec;224(1350):1291-2

Manic-depressive disorder. Paykel ES, et al. **Practitioner** 1981 Jan; 225(1351):75-7, 79-81

Lithium in children of lithium-responding parents. McKnew DH, et al. **Psychiatry Res** 1981 Apr;4(2):171-80

Prophylactic lithium with and without imipramine for bipolar I patients: a double-blind study [proceedings] Kane JM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):144-5

Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children [proceedings] Platt JE, et al. **Psychopharmacol Bull** 1981 Jan;17(1):123-5

Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo-controlled comparison [proceedings] Quitkin FM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):142-4

Effect of lithium on reaction time—a study of diurnal variations. Elsass P, et al. **Psychopharmacology (Berlin)** 1981;72(3):279-82

The effect of long-term concurrent administration of chlorpromazine and lithium on the striatal and frontal cortical dopamine metabolism in rats. Eroglu L, et al. **Psychopharmacology (Berlin)** 1981;73(1):84-6

Effects of lithium carbonate on methylphenidate-induced mood, behavior, and cognitive processes. Huey LY, et al. **Psychopharmacology (Berlin)** 1981;73(2):161-4

Lithium effects on citrate metabolism in humans and rats. Mellerup ET, et al. **Psychopharmacology (Berlin)** 1981;73(1):75-6

Effects of lithium on behavioral reactivity: relation to increases in brain cholinergic activity. Russell RW, et al. **Psychopharmacology (Berlin)** 1981;73(2):120-5

What to watch for with lithium. Rosenberg JM, et al. **RN** 1981 Jul; 44(7):44-6

Lithium and T cell colonies. Fernandez LA, et al. **Scand J Haematol** 1980 Nov;25(5):382-4

Lithium and mania. Tosteson DC. **Sci Am** 1981 Apr; 244(4):164-6, 168, 171-2 et passim

Medical therapies for mood disorders alter the blood-brain barrier. Preskorn SH, et al. **Science** 1981 Jul 24;213(4506):469-71

[Lithium dosage and age] Kijne B, et al. **Ugeskr Laeger** 1981 Jan; 143(3):119-20 (Eng. Abstr.) **(Dan)**

[Lithium dose in relation to body weight and age in the preventive of relapses in manic-depressive psychosis] König L. **Agressologie** 1980; 21(A):15-7 (Eng. Abstr.) **(Ger)**

[Pharmacokinetic study of delayed-action lithium in affective psychoses] Molcan J, et al. **Agressologie** 1980;21(A):11-4 (Eng. Abstr.) **(Ger)**

[Lithium prophylaxis and renal function. Conclusions and guidelines for treatment control (author's transl)] Müller-Oerlinghausen B, et al. **Nervenarzt** 1981 Feb;52(2):113-5 **(Ger)**

[Endocrinological aspects of long-term lithium therapy] Jonderko G, et al. **Z Gesamte Inn Med** 1981 Feb 1;36(3):79-82 (Eng. Abstr.) **(Ger)**

[Lithium. A practical clinical review] Malt U. **Tidsskr Nor Laegeforen** 1981 Mar 30;101(9-10):549-54 (Eng. Abstr.) **(Nor)**

[Long-term use of lithium salts - endocrinological and biochemical aspects] Jonderko G, et al. **Pol Tyg Lek** 1981 Jan 5;36(1):23-5 (Eng. Abstr.) **(Pol)**

[Effect of lithium chloride on lymphocyte transformation] Sierakowski S, et al. **Pol Tyg Lek** 1981 Jan 12;36(2):63-4 (Eng. Abstr.) **(Pol)**

[Influence of lithium ions on glycolytic and oxidative enzymes of the subcellular fractions and synaptosome fractions of the rat cortex] Busuioc A, et al. **Rev Med Chir Soc Med Nat Iasi** 1980 Jul-Sep; 84(3):515-20 (Eng. Abstr.) **(Rum)**

[Geographical gradients of lithium concentration in surface and drinking waters and in plasma of exposed subjects in Northern Chile (author's transl)] Zaldivar R. **Rev Med Chil** 1980 Sep;108(9):822-4 (Eng. Abstr.) **(Spa)**

MATERNAL BEHAVIOR

Pituitary-adrenal responsiveness of mothers to pups in mice of two inbred strains. Hennessy MB, et al. **Behav Neural Biol** 1981 Mar; 31(3):304-13

Mother-infant interaction in rhesus monkeys treated clinically with delta-9-tetrahydrocannabinol. Golub MS, et al. **Child Dev** 1981 Mar; 52(1):389-92

Concentrations of pituitary, gonadal and adrenal hormones in serum of laying and broody white rock hens (Gallus domesticus). Bedrak E, et al. **J Endocrinol** 1981 May;89(2):197-204

Serum concentrations of prolactin, luteinizing hormone, growth hormone, corticosterone, progesterone, testosterone and oestradiol in relation to broodiness in domestic turkeys (Meleagris gallopavo). Harvey S, et al. **J Endocrinol** 1981 May;89(2):187-95

MEMORY

Impaired speed of visual information processing in marijuana intoxication. Braff DL, et al. **Am J Psychiatry** 1981 May;138(5):613-7

Effects of lithium on memory. Christodoulou GN, et al. **Am J Psychiatry** 1981 Jun;138(6):847-8

The pharmacology of memory: a neurobiological perspective. Squire LR, et al. **Annu Rev Pharmacol Toxicol** 1981;21:323-56 (203 ref.)

The effects of colchicine and vinblastine on memory in chicks. Bell GA, et al. **Behav Brain Res** 1981 May;2(3):301-22

Memory processing with lithium carbonate. Marusarz TZ, et al. **J Clin Psychiatry** 1981 May;42(5):190-2

Time dependent changes in anterograde scopolamine-induced amnesia in rats. Moss DE, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):321-3

Reversal of guanethidine- and diethyldithiocarbamate-induced amnesia by peripherally-administered catecholamines. Walsh TJ, et al. **Pharmacol Biochem Behav** 1981 May;14(5):713-8

Memory and performance effects of single and 3-week administration of diazepam. Ghoneim MM, et al. **Psychopharmacology (Berlin)** 1981; 73(2):147-51

Impairment of learning or memory in the mature and old rat by diazepam. Komiskey HL, et al. **Psychopharmacology (Berlin)** 1981;73(3):304-5

[Formation and preservation of conditioned taste aversion in dogs] Vavilova NM, et al. **Zh Vyssh Nerv Deiat** 1981 Jan-Feb;31(1):171-2 **(Rus)**

MENTAL DISORDERS

Treatment of the seriously disturbed adolescent. Miller D. **Adolesc Psychiatry** 1980;8:469–81

An interdisciplinary comparison of consultation outcomes. Psychiatry vs cardiology. Popkin MK, et al. **Arch Gen Psychiatry** 1981 Jul; 38(7):821–5

Low blood pressure in psychiatric inpatients. Masterton G, et al. **Br Heart J** 1981 Apr;45(4):442–6

The psychiatrically violent patient [letter] **Br Med J [Clin Res]** 1981 Mar 7;282(6266):821

Adverse effects of antidepressant drugs. Part 2: 'Second generation' antidepressants and rational decision making in antidepressant therapy. Blackwell B. **Drugs** 1981 Apr;21(4):273–82 (120 ref.)

Folic acid and B12 in autism and neuropsychiatric disturbances of childhood. Lowe TL, et al. **J Am Acad Child Psychiatry** 1981 Winter; 20(1):104–11

What's so special about my specialty? Psychiatric med nursing. Harvey S. **J Pract Nurs** 1981 Jun;31(6):27, 32

Self-medication of psychiatric patients. Lane DE. **J Psychiatr Nurs** 1981 May;19(5):27–8

A clinician's guide to the use of stimulant medication for the psychiatric disorders of children. Cantwell DP. **JDPB** 1980 Sep;1(3):133–40 (58 ref.)

Psychiatry. 4. Drugged to the eyeballs. Ross T. **Nurs Mirror** 1981 Apr 16;152(16):16–8

Psychiatric treatment in the aged. Jacobson SB. **NY State J Med** 1981 Apr;81(5):802–4

Methods of multicenter trials in psychiatry. Part I: Review. Fischer-Cornelssen KA. **Prog Neuropsychopharmacol** 1980; 4(6):545–60

Classification of drugs and patients to achieve maximum therapeutic response. Kline NS. **Prog Neuropsychopharmacol** 1980;4(4–5):491–4

Preliminary studies on CSF gamma-aminobutyric acid levels in psychiatric patients before and during treatment with different psychotropic drugs. Zimmer R, et al. **Prog Neuropsychopharmacol** 1980; 4(6):613–20

[Sultopride used at low doses in the older child and adolescent.] Hugonenq H, et al. **Neuropsychiatr Enfance Adolesc** 1980 Dec;28(12):593–7 (Fre)

[Neuropeptides and psychiatry report presented at the French-Swiss Psychiatric meeting in Bel-Air, Geneva, 4 May 1980] Taban CH. **Schweiz Arch Neurol Neurochir Psychiatr** 1981;128(1):85–103 (Eng. Abstr.) (Fre)

[Cooperation of pharmacotherapy and psychotherapy: an experimental illustration] Caplová T, et al. **Agressologie** 1980;21(A):37–9 (Eng. Abstr.) (Ger)

[Experience with reactivant in psychiatric patients] Guensberger E, et al. **Agressologie** 1980;21(A):63–5 (Eng. Abstr.) (Ger)

[Documentation of psychopathological data in psychopharmacotherapy] Kühne GE, et al. **Agressologie** 1980;21(A):1–5 (Eng. Abstr.) (Ger)

[Psychopharmacology in gerontopsychiatry] Kümpel Q. **Agressologie** 1980;21(A):67–9 (Eng. Abstr.) (Ger)

[Biologic psychiatric research and psychiatric pharmacotherapy. Critical remarks on methods (author's transl)] Benkert O, et al. **MMW** 1981 May 8;123(19):795–9 (Eng. Abstr.) (Ger)

[Psychopharmacology for the practising physician (author's transl)] Laemmel K. **Praxis** 1981 Feb 3;70(6):192–9 (Eng. Abstr.) (Ger)

[The course of long-term care with fluphenazine decanoate (Dapotum D)] Deiser R, et al. **Psychiatr Clin (Basel)** 1980;13(3–4):193–205 (Eng. Abstr.) (Ger)

[Psychopathologic changes during 20 days of antidepressive or neuroleptic therapy] Woggon B. **Psychiatr Clin (Basel)** 1980;13(3–4):150–64 (Eng. Abstr.) (Ger)

[Rehabilitation of persons with psychic disorders or handicaps in transitional facilities and its place within the social security system (author's transl)] Stroebel H. **Rehabilitation (Stuttg)** 1981 Feb; 20(1):42–4 (Eng. Abstr.) (Ger)

[Current extent of biological therapy of mental disorder. II.] Predescu V, et al. **Rev Med Interna [Neurol Psihiatr]** 1980 Oct–Dec; 25(4):241–51 (205 ref.) (Rum)

MENTAL PROCESSES

[Psychotropic drugs and imprisonment in a psychiatric hospital for political reasons] Drucker H. **Acta Med Leg Soc (Liege)** 1980; 30(1):189–210 (Fre)

[Psychotropic drugs and imprisonment] Maltaverne S. **Acta Med Leg Soc (Liege)** 1980;30(1):185–8 (Fre)

[Effect of certain pharamcologic preparations and different lighting setups on human work capacity] Bogatova RI, et al. **Kosm Biol Aviakosm Med** 1981 Jan–Feb;15(1):92–3 (Rus)

MEPROBAMATE

Severe meprobamate intoxication treated by hemoperfusion over amberlite resin. Freund LG. **Artif Organs** 1981 Feb;5(1):80–1

The poisoned pen. A case report. Vanstratt W. **Forensic Sci Int** 1981 Mar–Apr;17(2):152–6

[The influence of the polymorphism of the active substance on the properties of tablets. Part 3. Compressional behaviour of meprobamate (author's transl)] Burger A, et al. **Pharmazie** 1981;36(1):41–6 (Eng. Abstr.) (Ger)

METHYLPHENIDATE

Gas chromatographic/mass spectrometric analysis of methylphenidate (ritalin) in serum. Chan YM, et al. **Clin Biochem** 1980 Dec; 13(6):266–72

Effect of methylphenidate on young adult's vigilance and event-related potentials. Coons HW, et al. **Electroencephalogr Clin Neurophysiol** 1981 Apr;51(4):373–87

Methylphenidate-like stimulants in vitro release [3H]tyramines but not [14C]dopamine. Dyck LE. **Eur J Pharmacol** 1981 Jan 29;69(3):371–4

A comparison of the hypothermic effects of methylphenidate and d-amphetamine. Yehuda S, et al. **Int J Neurosci** 1981;13(2–3):117–20

Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. Cohen NJ, et al. **J Abnorm Child Psychol** 1981 Mar;9(1):43–54

Differential effects of parent training and stimulant medication with hyperactives: A progress report. Firestone P, et al. **J Am Acad Child Psychiatry** 1981 Winter;20(1):135–47

Potential risk of prolonged administration of stimulant medication for hyperactive children. Satterfield JH, et al. **JDPB** 1980 Sep; 1(3):102–7

Predictors of adolescent height and weight in hyperkinetic boys treated with methylphenidate [proceedings] Loney J, et al. **Psychopharmacol Bull** 1981 Jan;17(1):132–4

Effects of lithium carbonate on methylphenidate-induced mood, behavior, and cognitive processes. Huey LY, et al. **Psychopharmacology (Berlin)** 1981;73(2):161–4

Methylphenidate in depression and states of apathy. Moore DP. **South Med J** 1981 Mar;74(3):347–8

METHYSERGIDE

Effects of the interaction between methysergide and clonidine on growth hormone and prolactin secretion in normal man. Agnati LF, et al. **Neurosci Lett** 1981 Feb 6;21(3):333–8

MMPI

Psychotherapeutic drug recommendations based on the Mini-Mult. Siddall JW, et al. **Psychol Rep** 1980 Dec;47(3 Pt 2):1283–8

MOTIVATION

The central basis of motivation: intracranial self-stimulation studies. Olds ME, et al. **Annu Rev Psychol** 1981;32:523–74 (246 ref.)

Reward and detection thresholds for brain stimulation: dissociative effects of cocaine. Kornetsky C, et al. **Brain Res** 1981 Mar 30; 209(2):496–500

MOTOR ACTIVITY

Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat. Borbély AA, et al. **Behav Brain Res** 1981 Jan; 2(1):1–22

Behavioral supersensitivity to methamphetamine following chronic treatment with (—)-sulpiride in the rat. Montanaro N, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):401–6

Dopamine receptor changes following destruction of the nigrostriatal pathway: lack of a relationship to rotational behavior. Staunton DA, et al. **Brain Res** 1981 May 4;211(2):315–27

Intraventricular carbachol mimics the phase-shifting effect of light on the circadian rhythm of wheel-running activity. Zatz M, et al. **Brain Res** 1981 May 11;212(1):234–8

Cats develop tolerance to d-amphetamine's effects upon locomotion and stereotyped behaviors. Jacobs BL, et al. **Eur J Pharmacol** 1981 Jan 29; 69(3):353–6

Involvement of both dopaminergic and alpha-adrenergic receptors in the hypomotility induced by dibenzoyl-6,7-ADTN. Sumners C, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):541–50

Differential effects of maternal and sibling presence of hyperactivity of 6-hydroxydopamine-treated developing rats. Teicher MH, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):134–45

The effect of bromazepam on psychomotor activity and subjective mood. Hobi V, et al. **J Int Med Res** 1981;9(2):89–97

Chronic L-DOPA treatment of mice: a behavioural and biochemical study. Bailey R, et al. **J Neural Transm** 1981;50(2–4):209–24

The effects of p-chloroamphetamine administration on locomotor activity and serotonin in neonatal and adult rats. Lucot JB, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):738–44

Drug-environment interaction: context dependency of cocaine-induced behavioral sensitization. Post RM, et al. **Life Sci** 1981 Feb 16;

28(7):755–60

The role of nigral projections to the thalamus in drug-induced circling behaviour in the rat. Reavill C, et al. **Life Sci** 1981 Mar 30; 28(13):1457–66

Similar motor effects of 5-HT and TRH in rats following chronic spinal transection and 5.7-dihydroxytryptamine injection. Barbeau H, et al. **Neuropharmacology** 1981 May;20(5):477–81

Self-stimulation and locomotor changes indicating 'latent' anticholinergic activity by an atypical neuroleptic (thioridazine). Herberg LJ, et al. **Neuropharmacology** 1981 Jan;20(1):55–60

Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat. Jones DL, et al. **Neuropharmacology** 1981 Jan;20(1):29–37

Apomorphine-induced circling behaviour in hamsters following unilateral injection of scrapie gent in the striatum. Gorde JM, et al. **Neurosci Lett** 1981 Mar 10;22(2):201–4

Influence of substance P on the behavioral changes induced by haloperidol in rats. Jolicoeur FB, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):103–7

Interaction of MIF-I or alpha-MSH with D-amphetamine or chlorpromazine on thermoregulation and motor activity of rats maintained at different ambient temperatures. Yehuda S, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):243–8

The effects cocaine free extracts of the coca leaf on food consumption and locomotor activity. Bedford JA, et al. **Pharmacol Biochem Behav** 1981 May;14(5):725–8

Different effects of apomorphine on locomotor activity in C57BL/6 and DBA/2 mice. Sansone M, et al. **Pharmacol Biochem Behav** 1981 May; 14(5):741–3

Effects of morphine and chlordiazepoxide on locomotor activity in two inbred strains of mice. Cuomo V, et al. **Pharmacol Res Commun** 1981 Jan;13(1):87–93

Role of the pulvinar-lateral posterior nucleus complex in turning behavior. Motles E, et al. **Physiol Behav** 1980 Dec;25(6):921–9

Effects of propranolol on the locomotor stimulation induced by activation of postsynaptic catecholamine receptors. Hallberg H, et al. **Psychopharmacology (Berlin)** 1981;72(3):227–31

Dopaminergic agonists differentially affect open-field activity of rats with A10 lesions. Hodge GK, et al. **Psychopharmacology (Berlin)** 1981; 73(1):39–42

Lesion of serotonergic neurons antagonizes clonidine induced suppression of avoidance behavior and locomotor activity in rats. Kostowski W, et al. **Psychopharmacology (Berlin)** 1981;73(3):261–4

[Locomotor activity of rats following chronic pretreatment with haloperidol] Oehler J, et al. **Acta Biol Med Ger** 1980; 39(11–12):1235–9 (Eng. Abstr.) **(Ger)**

[Evaluation of motor behavior in conditions of hyperprolactinemia] Rampello L, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):297–301 (Eng. Abstr.) **(Ita)**

[Diphasic action of apomorphine on motility of the rat. I. Dose-effect relationship in exploratory and basal motility] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):374–80 (Eng. Abstr.) **(Ita)**

[Diphasic action of apomorphine on motility in the rat. II. Time aspects of the effect of a single dose] Vaccheri A, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):381–6 (Eng. Abstr.) **(Ita)**

[Certain biochemical and behavioral effects of morphine in rats following amyzil administration] Bandman AL, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):185–8 (Eng. Abstr.) **(Rus)**

[State of the endocrine glands in hypodynamia (a review of the literature)] Korkach VI. **Vrach Delo** 1981 Feb;(2):11–6 (73 ref.) **(Rus)**

MSH

Cytological localization of alpha-MSH, ACTH and beta-endorphin in the pars intermedia of the cichlid teleost Sarotherodon mossambicus. van Eys GJ, et al. **Cell Tissue Res** 1981;215(3):625–33

Evidence for two different turnover pools of adrenocorticotropin, alpha-melanocyte-stimulating hormone, and endorphin-related peptides released by the frog pituitary neurointermediate lobe. Loh YP, et al. **Endocrinology** 1981 Jul;109(1):54–61

Differentiation of MSH-, ACTH-, endorphin-, and LPH-containing cells in the hypophysis during embryonic and fetal development. Dupouy JP. **Int Rev Cytol** 1980;68:197–249 (277 ref.)

Effect gamma-melanotropin (gamma-MSH) on the conditioned behavior. Oka M, et al. **J Pharmacobiodyn** 1980 Nov;3(11):628–30

Chemistry and biosynthesis of pro-opiomelanocortin. ACTH, MSH's, endorphins and their related peptides. Chrétien M, et al. **Mol Cell Biochem** 1981 Jan 28;34(2):101–27 (232 ref.)

Circulating human pituitary pro-gamma-melanotropin enhances the adrenal response to ACTH. Al-Dujaili EA, et al. **Nature** 1981 May 14;291(5811):156–9

The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Yamada K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):155–60

Interaction of MIF-I or alpha-MSH with D-amphetamine or chlorpromazine on thermoregulation and motor activity of rats maintained at different ambient temperatures. Yehuda S, et al. **Peptides (Fayetteville)** 1980 Fall;1(3):243–8

Localization of gamma-melanocyte stimulating hormone (gamma MSH) immunoreactivity in rat brain and pituitary. Bloom FE, et al. **Regul Pept** 1980 Dec;1(3):205–22

The regional distribution of gamma 3-melanotropin-like peptides in bovine brain is correlated with adrenocorticotropin immunoreactivity but not with beta-endorphin. Shibasaki T, et al. **Regul Pept** 1981 Apr; 2(1):43–52

NEUROREGULATORS

An introduction to the immunocytochemical localization of neuropeptides and neurotransmitters. van Leeuwen FW. **Acta Histochem [Suppl] (Jena)** 1981;24:49–77 (162 ref.)

Ultrastructural and morphometric investigations on the mechanism of neurotransmitter release from synaptic vesicles. Dymecki J, et al. **Acta Neuropathol [Suppl] (Berl)** 1981;7:381–5

Role of calmodulin in neurotransmitter release and synaptic function. DeLorenzo RJ. **Ann NY Acad Sci** 1980;356:92–109

Dietary precursors and brain neurotransmitter formation. Fernstrom JD. **Annu Rev Med** 1981;32:413–25 (49 ref.)

Hypothalamic hypophysiotropic hormones and neurotransmitter regulation: current views. Meites J, et al. **Annu Rev Pharmacol Toxicol** 1981;21:295–322 (160 ref.)

Excitatory amino acid transmitters. Watkins JC, et al. **Annu Rev Pharmacol Toxicol** 1981;21:165–204 (294 ref.)

Biochemical specificity of septal hyperreactivity: a behavioral discrimination. Chafetz MD, et al. **Behav Brain Res** 1981 May; 2(3):409–20

Morphological and biochemical studies on the ontogenesis of the nucleus locus coeruleus. Sievers J, et al. **Bibl Anat** 1981;(19):52–130

Neurochemistry of man: noninvasive approaches. Agranoff BW. **Biol Psychiatry** 1981 Mar;16(3):211–2

Glutamate mimics the afferent transmitter in the Xenopus laevis lateral line. Bobbin RP, et al. **Birth Defects** 1980;16(4):107–9

The role of calcium in the effects of noradrenaline and phenoxybenzamine on adrenergic transmitter release from atria: no support for negative feedback of release. Kalsner S. **Br J Pharmacol** 1981 Jun; 73(2):363–71

An examination of the residual calcium theory for facilitation of transmitter release. Bittner GD, et al. **Brain Res** 1981 Apr 6; 210(1–2):431–6

Monoaminergic afferents to the neocortex: a developmental histofluorescence study in normal and Reeler mouse embryos. Caviness VS Jr, et al. **Brain Res** 1981 Mar 23;209(1):1–9

The influence of striatal stimulation and putative neurotransmitters on identified neurones in the rat substantia nigra. Collingridge GL, et al. **Brain Res** 1981 May 18;212(2):345–59

Neuronal, glial and meningeal localizations of neurotransmitter-sensitive adenylate cyclases in cerebral cortex of mice. Ebersolt C, et al. **Brain Res** 1981 May 25;213(1):139–50

The membrane potential of cat hippocampal neurons recorded in vivo displays four different reaction-mechanisms to iontophoretically applied transmitter agonists. Herrling PL. **Brain Res** 1981 May 18; 212(2):331–43

Behavioral evidence that substance P may be a spinal cord sensory neurotransmitter. Piercey MF, et al. **Brain Res** 1981 Apr 6; 210(1–2):407–12

Barbiturates and transmitter release at the frog neuromuscular junction. Pincus JH, et al. **Brain Res** 1981 May 25;213(1):127–37

Characterization of the isolated perfused mouse brain as a system for neurochemical studies. Towell JF, et al. **Brain Res** 1981 Mar 30; 209(2):476–81

Baclofen modifies via the release of monoamines the synaptic depression, frequency facilitation, and posttetanic potentiation observed at an identified cholinergic synapse of Aplysia californica. Philippe E, et al. **Can J Physiol Pharmacol** 1981 Mar;59(3):244–52

Effects of precursors on brain neurotransmitter synthesis and brain functions. Fernstrom JD. **Diabetologia** 1981 Mar;20 Suppl:281–9 (43 ref.)

Octopamine—after a decade as a putative neuroregulator. Robertson HA. **Essays Neurochem Neuropharmacol** 1981;5:47–73 (83 ref.)

Neurotransmitter control of hypothalamic-pituitary-thyroid function in rats. Morley JE, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):263–71

Localization of putative amino acid neurotransmitters in the human retina. Lam DM, et al. **Exp Eye Res** 1980 Dec;31(6):729–32

A simple perfusion chamber for studying neurotransmitter release from cells maintained in monolayer culture. Pearce BR, et al. **J Neurosci Methods** 1981 Feb;3(3):255–9

The K+ liquid ion exchange electrode system: responses to drugs and neurotransmitters. Kuramoto T, et al. **J Neurosci Res** 1951; 6(1):37–48

Calcium dependence of evoked transmitter release at very low quantal contents at the frog neuromuscular junction. Andreu R, et al. **J Physiol (Lond)** 1980 Nov;308:79–97

Possible embryogenetical differences of the dog venous system in sensitivity to vasoactive substances. Ishikawa N, et al.

Jpn J Pharmacol 1980 Dec;30(6):807-18

Pharmacological antagonists of excitant amino acid action. Evans RH, et al. **Life Sci** 1981 Mar 23;28(12):1303-8

Role of intracellular proteins in the regulation of calcium action and transmitter release during exocytosis. Pollard HB, et al. **Monogr Neural Sci** 1980;7:106-16

Contralateral denervation causes enhanced transmitter release from frog motor nerve terminals. Herrera AA, et al. **Nature** 1981 Jun 11; 291(5815):495-7

Sustained potentiation of transmitter release by adrenaline and dibutyryl cyclic AMP in sympathetic ganglia. Kuba K, et al. **Nature** 1981 Jun 25;291(5817):654-6

Possible role of 'prenervous' neurotransmitters in cellular interactions of early embryogenesis: a hypothesis. Buznikov GA, et al. **Neurochem Res** 1981 Jan;6(1):55-68

Regional distribution of neurohumoral responsive adenylate cyclase in rabbit brain microvessels. Palmer GC. **Neurosci Lett** 1981 Jan 20; 21(2):207-10

Excitatory amino acids as transmitter candidates of vibrissae afferent fibres to the rat trigeminal nucleus caudalis. Salt TE, et al. **Neurosci Lett** 1981 Mar 10;22(2):183-7

Modelling the postsynaptic location and magnitude of tonic conductance changes resulting from neurotransmitters or drugs. Carlen PL, et al. **Neuroscience** 1981;6(5):839-46

Biochemical evidence for glutamate as neurotransmitter in corticostriatal and corticothalamic fibres in rat brain. Fonnum F, et al. **Neuroscience** 1981;6(5):863-73

Regional changes of monoamines in cerebral cortex and subcortical structures of aging rhesus monkeys. Goldman-Rakic PS, et al. **Neuroscience** 1981;6(2):177-87

Substance P as a baro- and chemoreceptor afferent neurotransmitter: immunocytochemical and neurochemical evidence in the rat. Helke CJ, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):1-9

Brain neurotransmitters regulating TRH producing neurons. Annunziato L, et al. **Pharmacol Res Commun** 1981 Jan;13(1):1-10 (47 ref.)

Intracellular injection of t he catalytic subunit of cyclic AMP-dependent protein kinase simulates facilitation of transmitter release underlying behavioral sensitization in Aplysia. Castellucci VF, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7492-6

Central neurotransmitter mechanisms involved in the control of urinary bladder function. An experimental study in the rat. Sillén U. **Scand J Urol Nephrol [Suppl]** 1980;58:1-45

Pentapeptide (proctolin) associated with an identified neuron. O'Shea M, et al. **Science** 1981 Jul 31;213(4507):567-9

[Information transfer in the brain puzzles neuroscientists] Hyyppä MT. **Duodecim** 1980;96(11):769-72 (Fin)

[In vitro study of the interaction between neuromediators and neuropeptides involved in hypothalamic neurosecretion control (author's transl)] Epelbaum J, et al. **Ann Endocrinol (Paris)** 1980 Nov-Dec;41(6):478-86 (35 ref.) (Eng. Abstr.) (Fre)

[Neuropeptides and psychiatry report presented at the French-Swiss Psychiatric meeting in Bel-Air, Geneva, 4 May 1980] Taban CH. **Schweiz Arch Neurol Neurochir Psychiatr** 1981;128(1):85-103 (Eng. Abstr.) (Fre)

[Biologic psychiatric research and psychiatric pharmacotherapy. Critical remarks on methods (author's transl)] Benkert O, et al. **MMW** 1981 May 8;123(19):795-9 (Eng. Abstr.) (Ger)

[Mechanism of action of antiepileptic drugs. Experimental results on the role of neurotransmitters (author's transl)] Löscher W. **Nervenarzt** 1981 Feb;52(2):61-7 (Ger)

[Functional anatomy of the neuroendocrine system] Weindl A, et al. **Verh Dtsch Ges Inn Med** 1980;86:12-25 (36 ref.) (Ger)

[The vasoactive intestinal polypeptide (VIP). Its role in the physiology of the digestive system] Leonardi R, et al. **Minerva Med** 1981 Apr 2; 72(13):801-5 (Eng. Abstr.) (Ita)

[Reactions of an identified edible snail neuron to application of peptides, mediators, prostaglandins, and cyclic nucleotides] Osipovskiĭ SA, et al. **Neirofiziologiia** 1981;13(1):80-7 (Eng. Abstr.) (Rus)

[Parameters of a model of transmitter depletion in synapses of identified snail neurons] Voronin LL, et al. **Neirofiziologiia** 1981;13(1):88-97 (Eng. Abstr.) (Rus)

[Significance of neuroregulatory interrelationships in the science of transplantation] Konevskiĭ AG, et al. **Vestn Khir** 1980 Dec; 125(12):88-91 (Eng. Abstr.) (Rus)

[Acetylcholine-bradykinin: a new peptide-amine transmitter interaction (editorial)] Pirola CJ. **Medicina (B Aires)** 1980 Nov-Dec; 40(6 Pt 2):893-5 (Spa)

NEUROTENSIN

Plasma neurotensin in term and preterm neonates. Lucas A, et al. **Acta Paediatr Scand** 1981 Mar;70(2):201-6

Neurotensin release by rat hypothalamic fragments in vitro. Maeda K, et al. **Brain Res** 1981 Apr 6;210(1-2):261-9

Neurotensin receptor localization by light microscopic autoradiography in rat brain. Young WS 3d, et al. **Brain Res** 1981 Feb 16; 206(2):273-85

Effect of intraventricular injection of neurotensin and other various bioactive peptides on plasma immunoreactive somatostatin levels in rat hypophysial portal blood. Abe H, et al. **Endocrinology** 1981 May; 108(5):1939-43

The hypotensive effect of centrally administered neurotensin in rats. Rioux F, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):241-7

Neurotensin blocks certain amphetamine-induced behaviours. Ervin GN, et al. **Nature** 1981 May 7;291(5810):73-6

Bacterial peptides with C-terminal similarities to bovine neurotensin. Bhatnagar YM, et al. **Peptides (Fayetteville)** 1981 Spring;2(1):51-9

Immunochemical characterization of neurotensin-like peptides in chicken. Carraway R, et al. **Peptides (Fayetteville)** 1980 Summer;1(2):159-65

Isolation, structure and biologic activity of chicken intestinal neurotensin. Carraway R, et al. **Peptides (Fayetteville)** 1980 Summer;1(2):167-74

NEUROTIC DISORDERS

The relationships between clinical response, psychophysiological variables and plasma levels of amitriptyline and diazepam in neurotic outpatients. Johnstone EC, et al. **Psychopharmacology (Berlin)** 1981;72(3):233-40

NIALAMIDE

Inhibition of monoamine oxidase activity after combined action of chlordimeform with the antidepressant nialamide. Kaloyanova F, et al. **Arch Environ Contam Toxicol** 1981;10(1):1-8

Subsensitivity of the beta-adrenergic receptor-linked adenylate cyclase system of rat pineal gland following repeated treatment with desmethylimipramine and nialamide. Moyer JA, et al. **Mol Pharmacol** 1981 Mar;19(2):187-93

NOREPINEPHRINE

Effects of adrenergic neuron and ganglion blockers on hemodynamics and plasma catecholamine levels after corticosteroids during hemorrhagic shock in the dog. Haglund U, et al. **Acta Anaesthesiol Scand** 1980 Dec;24(6):444-50

Further evidence of the dual role of noradrenaline in regulation of thyrotrophin secretion in male rats. Männistö PT, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):213-20

Thyroid hormone-catecholamine interrelationships during exposure to cold. Storm H, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):91-7

Immunohistochemical characterization of monoamine-containing neurons in the central nervous system by antibodies to serotonin and noradrenalin. A study in the rat and the lamprey (Lampetra fluviatilis). Steinbusch HW, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:107-22

Neuropathological findings in autonomic nervous system of alimentary tract of rat after application of catecholamines. Jędrzejewska A, et al. **Acta Neuropathol [Suppl] (Berl)** 1981;7:273-5

Effect of prostaglandin synthesis inhibition on the central activity of noradrenaline in rats. Brus R, et al. **Acta Physiol Pol** 1981 Jan-Feb; 32(1):47-51

Urinary catecholamine excretion and plasma dopamine-beta-hydroxylase activity during mental work performed in some periods of menstrual cycle in women. Wasilewska E, et al. **Acta Physiol Pol** 1980; 31(6):647-51

Autoinhibition versus transsynaptic control of noradrenaline secretion in the rabbit kidney. Hedqvist P. **Acta Physiol Scand** 1980 Dec; 110(4):441-3

Catecholamines and monoamine oxidase activity in anxiety. Mathew RJ, et al. **Acta Psychiatr Scand** 1981 Mar;63(3):245-52

Controlled cross-over study of a 5-HT uptake inhibiting and an NA uptake inhibiting antidepressant. Aberg A. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):244-55

Specific norepinephrine and serotonin uptake inhibitors in man: a crossover study with pharmacokinetic, biochemical, neuroendocrine and behavioral parameters. Potter WZ, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):152-65

Serotonin and noradrenaline uptake inhibitors in the treatment of depression--relationship to 5-HIAA in spinal fluid. Träskman-Bendz L, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):209-18

Glomerular architectural changes after a two-hour infusion of norepinephrine. Bulger RE, et al. **Am J Anat** 1980 Dec; 159(4):379-84

Changes in cardiovascular and renal function during catecholamine infusions in developing swine. Buckley NM, et al. **Am J Physiol** 1981 Apr;240(4):F276-81

Cardiac cyclic nucleotides and norepinephrine during neural sympathetic stimulation. Pindok MT, et al. **Am J Physiol** 1981 Apr; 240(4):H630-5

Adrenergically induced renin release in conscious indomethacin-treated dogs and rats. Seymour AA, et al. **Am J Physiol** 1981 Jun; 240(6):F515-21

Contractility of vascular smooth muscle: maximum ability to contract in response to a stimulus. Skaug N, et al. **Am J Physiol** 1981 Jun; 240(6):H971-9

Increased activity of carotid sinus baroreceptors by sympathetic stimulation and norepinephrine. Tomomatsu E, et al. **Am J Physiol** 1981 Apr;240(4):H650-8

Alternation by histamine receptor agonists of the release of adrenergic transmitter in the isolated perfused rabbit kidney. Ercan ZS, et al. **Arch Int Pharmacodyn Ther** 1981 Feb;249(2):203-12

Antinoradrenergic activity of thymoxamine and its metabolites in rats. Roquebert J, et al. **Arch Int Pharmacodyn Ther** 1981 Jan; 249(1):12-25

Effect of SQ 14225 and SQ 20881 on the norepinephrine contents of the central nervous system. Dominguez AE, et al. **Arch Int Physiol Biochim** 1981 Feb;89(1):89-90

A comparative study on the retention of 3H lignocaine and 3H prilocaine in the presence of various vasoconstrictors. Almasi W, et al. **Aust Dent J** 1980 Dec;25(6):316-8

Alterations in brain norepinephrine metabolism and behavior induced by environmental stimuli previously paired with inescapable shock. Cassens G, et al. **Behav Brain Res** 1981 May;2(3):387-407

Induction of phosphoenolpyruvate carboxykinase by sympathetic agents in primary cultures of adult rat hepatocytes. Wölfle D, et al. **Biochem Biophys Res Commun** 1981 Feb 27;98(4):1084-90

Changes in fatty acyl chain composition of rat heart phospholipids induced by noradrenaline. Emilsson A, et al. **Biochim Biophys Acta** 1981 Apr 23;664(1):82-8

Solubilization and reconstitution of the adenosine 5'-triphosphate dependent noradrenaline uptake system of bovine chromaffin granule membrane. Isambert MF, et al. **Biochimie** 1981 Mar;63(3):211-9

Vesicular noradrenaline stores in peripheral nerves of the rat and their modification by tranylcypromine. Fillenz M, et al. **Br J Pharmacol** 1981 Jun;73(2):401-4

The role of calcium in the effects of noradrenaline and phenoxybenzamine on adrenergic transmitter release from atria: no support for negative feedback of release. Kalsner S. **Br J Pharmacol** 1981 Jun; 73(2):363-71

Effects of nerve stimulation and of administration of noradrenaline or potassium chloride upon the release of prostaglandins, I2, E2, and F2 alpha from te perfused mesenteric arterial bed of the rabbit. Pipili E, et al. **Br J Pharmacol** 1981 Jan;72(1):89-93

Noradrenaline augments tetanic potentiation of transmitter release by a calcium dependent process. Bergman H, et al. **Brain Res** 1981 Jun 9; 214(1):200-4

Evidence that the noradrenergic coerulospinal projection decussates at the spinal level. Commissiong JW. **Brain Res** 1981 May 11; 212(1):145-51

Regional changes in brain catecholamine turnover in the rat during performance on fixed ratio and variable interval schedules of reinforcement. Heffner TG, et al. **Brain Res** 1981 Jun 9; 214(1):215-8

Regional differences in catecholamine formation and metabolism in the rat spinal cord. Karoum F, et al. **Brain Res** 1981 May 18; 212(2):361-6

Destruction of noradrenergic cell bodies by intracerebral 6-hydroxydopamine in the newborn rat. Lanfumey L, et al. **Brain Res** 1981 Jun 15;214(2):445-50

Mechanisms of norepinephrine actions on hippocampal pyramidal cells in vitro. Langmoen IA, et al. **Brain Res** 1981 Mar 16;208(2):349-62

Noradrenergic responses in rat hippocampus: evidence for medication by alpha and beta receptors in the in vitro slice. Mueller AL, et al. **Brain Res** 1981 Jun 9;214(1):113-26

Increased concentration and accelerated synaptosomal uptake of noradrenaline in the central nervous tissues of neonatally hemispherectomized adult rats. Toyama M, et al. **Brain Res** 1981 Mar 16;208(2):447-50

Antagonism of the inhibitory effect of the polychlorinated biphenyl preparation, aroclor 1242, on color changes of the fiddler crab, Uca pugilator, by norepinephrine and drugs affecting noradrenergic neurotransmission. Hanumante MM, et al. **Bull Environ Contam Toxicol** 1981 Apr;26(4):479-84

Noradrenaline-induced calorigenesis in warm- and cold-acclimated rats: relations between concentration of noradrenaline in arterial plasma, blood flow to differently located masses of brown adipose tissue, and calorigenic response. Foster DO, et al. **Can J Physiol Pharmacol** 1980 Aug;58(8):915-24

Evidence against noradrenergic regulation of vasodilation in rat brown adipose tissue. Foster DO, et al. **Can J Physiol Pharmacol** 1980 Dec; 58(12):1418-25

Different influences of two types of diets commonly used for rats on a series of parameters related to the metabolism of central serotonin and noradrenaline. Héroux O, et al. **Can J Physiol Pharmacol** 1981 Feb; 59(2):108-12

Release of noradrenaline from the rat tail artery induced by inhibition of the sodium pump in calcium-free solution. Palatý V. **Can J Physiol Pharmacol** 1981 Apr;59(4):347-50

The load clamp analysis of mammalian heart contraction in the presence of noradrenaline. Rosenshtraukh LV, et al. **Can J Physiol Pharmacol** 1980 Dec;58(12):1504-8

Correlations between hemodynamic parameters of the liver and norepinephrine release upon hepatic nerve stimulation in the dog. Yamaguchi N, et al. **Can J Physiol Pharmacol** 1980 Nov; 58(11):1347-55

Microspectrofluorometric study of monoamines in the auricle of the heart of Protopterus aethiopicus. Scheuermann DW, et al. **Cell Tissue Res** 1981;217(2):443-9

Effects of norepinephrine and dibutyryl adenosine 3',5'-cyclic monophosphate on the ultrastructure of pineal cells in monolayer culture. Steinberg V, et al. **Cell Tissue Res** 1981;216(1):181-91

Lack of effect of intravenous LHRH on plasma noradrenaline in man. Jürgensen HJ, et al. **Clin Endocrinol (Oxf)** 1980 Sep;13(3):249-52

Age-dependence of noradrenaline kinetics in normal subjects. Esler M, et al. **Clin Sci** 1981 Feb;60(2):217-9

Mianserin: direct activation of brain norepinephrine neurons by blocking alpha 2-receptors. Engberg G, et al. **Commun Psychopharmacol** 1980; 4(3):233-9

Effect of piribedil (ET-495) on plasma norepinephrine: relationship to antidepressant response. Reus VI, et al. **Commun Psychopharmacol** 1980; 4(3):207-13

Plasma norepinephrine, epinephrine, and dopamine concentrations in maternal and fetal sheep during spontaneous parturition and in premature sheep during cortisol-induced parturition. Eliot RJ, et al. **Endocrinology** 1981 May;108(5):1678-82

The role of central adrenoreceptors in the control of vasopressin release and blood pressure. Kimura T, et al. **Endocrinology** 1981 May; 108(5):1829-36

Negative feedback effects of progesterone correlated with changes in hypothalamic norepinephrine and dopamine turnover rates, median eminence luteinizing hormone-releasing hormone, and peripheral plasma gonadotropins. Rance N, et al. **Endocrinology** 1981 Jun; 108(6):2194-9

The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone-releasing hormone and the effect of prolactin on catecholamine turnover. Selmanoff M. **Endocrinology** 1981 May;108(5):1716-22

Morphine: dual effects on plasma catecholamines. Taborsky GJ Jr, et al. **Endocrinology** 1981 Jul;109(1):319-21

Effects of estradiol and progesterone on catecholamine turnover rates in discrete hypothalamic regions in ovariectomized rats. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2186-93

Reversal of noradrenaline denervation-induced increase of beta-adrenoreceptor binding in rat neocortex by noradrenaline infusion. Biswas B, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):341-6

Calcium-sensitive accumulation of norepinephrine in rat cerebral cortex. Burrows GH, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):301-12

Supersensitivity of central noradrenergic presynaptic autoreceptors following chronic treatment with the antidepressant mianserin. Cerrito F, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):425-6

Neonatal intraspinal 6-hydroxydopamine: depletion of norepinephrine but not dopamine. Ings R, et al. **Eur J Pharmacol** 1981 Apr 9; 70(4):577-83

'High affinity' binding of [3H]desipramine to rat cerebral cortex: relationship to tricyclic antidepressant-induced inhibition of norepinephrine uptake. Rehavi M, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):597-9

Comparison of two alpha-noradrenergic agonists (clonidine and guanfacine) on norepinephrine turnover in the cortex of rats during morphine abstinence. Zigun JR, et al. **Eur J Pharmacol** 1981 Apr 9; 70(4):565-70

Postsynaptic inhibitory actions of catecholamines and opioid peptides in the bed nucleus of the stria terminalis. Sawada S, et al. **Exp Brain Res** 1981;41(3-4):264-70

Degeneration of nerve terminals in cats following systemic epinephrine: depletion of tissue norepinephrine correlated with ultrastructural changes. Flach AJ, et al. **Exp Eye Res** 1981 Apr;32(4):389-94

Effect of monoamines on firing rate and thermal sensitivity of neurons in the preoptic area of awake rabbits. Gordon CJ, et al. **Exp Neurol** 1981 May;72(2):352-65

Electro-osmotic and iontophoretic release of noradrenaline from micropipettes. Bevan P, et al. **Experientia** 1981 Mar 15;37(3):296-7

Differential sensitivity of the two phases of ear artery contraction to intimal and adventitial norepinephrine. McCalden TA, et al. **Experientia** 1981 Mar 15;37(3):268-9

Vasoconstrictor effects of tyramine and noradrenaline on goat brain vessels. Marin J, et al. **Gen Pharmacol** 1981;12(3):187-91

Catecholamine turnover in rat cerebral cortex and caudate following repeated treatment with dihydroergotoxine. Cvejić V, et al. **Gerontology** 1981;27(1-2):7-12

The detection by x-ray microanalysis of noradrenaline in sympathetic nerve terminals of the rat vas deferens. Santer RM, et al. **Histochemistry** 1981;71(1):155-60

Compartmentation of adenine nucleotides in the isolated working guinea pig heart stimulated by noradrenaline. Soboll S, et al. **Hoppe Seylers Z Physiol Chem** 1981 Feb;362(2):125-32

Circadian rhythm and hormonal sensitivity of lipoprotein lipase activity in cold acclimated rats. Goubern M, et al. **Horm Metab Res** 1981 Feb;

13(2):73–7
Binding of noradrenaline to bovine serum albumin. Farre ER, et al. **Int J Nucl Med Biol** 1981;8(1):65–75
Myocardial norepinephrine turnover during induced hypothermia and rewarming. Jones SB. **J Appl Physiol** 1981 May;50(5):962–6
Amine transport in chromaffin granule ghosts. pH dependence implies cationic form is translocated. Knoth J, et al. **J Biol Chem** 1981 Jul 10; 256(13):6541–3
Novel post-column derivatization method for the fluorimetric determination of norepinephrine and epinephrine. Nimura N, et al. **J Chromatogr** 1980 Dec 12;221(2):249–55
Age-related elevation of plasma catecholamine concentration and reduced responsiveness of lymphocyte adenylate cyclase. Krall JF, et al. **J Clin Endocrinol Metab** 1981 May;52(5):863–7
3-Methoxytyramine and normetanephrine as indicators of dopamine and noradrenaline release in mouse brain in vivo. Kehr W. **J Neural Transm** 1981;50(2–4):165–78
Individually reared rats: alteration in noradrenergic brain functions. Kraeuchi K, et al. **J Neural Transm** 1981;50(2–4):103–12
The functional role of the noradrenergic neurons in the thermoregulatory circuits in mice. Schelkunov EL, et al. **J Neural Transm** 1981; 50(2–4):113–37
Reduction of Vanadate by ascorbic acid and noradrenaline in synaptosomes. Adám-Vizi V, et al. **J Neurochem** 1981 May; 36(5):1616–20
Conversion of 3, 4-dihydroxyphenylalanine and deuterated 3, 4-dihydroxyphenylalanine to alcoholic metabolites of catecholamines in rat brain. Edwards DJ, et al. **J Neurochem** 1981 May; 36(5):1641–7
Biochemical and histochemical studies on catecholamines in bullfrog spinal ganglia. Kojima H, et al. **J Neurochem** 1981 Jun;36(6):2106–9
The inhibition by flunarizine of the norepinephrine-evoked contraction and calcium influx in rat aorta and mesenteric arteries. Godfraind T, et al. **J Pharmacol Exp Ther** 1981 May;217(2):510–5
Thyrotropin releasing factor: a putative CNS regulator of the autonomic nervous system. Brown MR. **Life Sci** 1981 Apr 13–20; 28(15–16):1789–95
I. Catecholamines in developing rat lung. Gardey-Levassort C, et al. **Life Sci** 1981 Jan 26;28(4):331–7
Passive avoidance performance correlates with catecholamine turnover in discrete limbic brain regions. Kovács GL, et al. **Life Sci** 1981 Mar 9;28(10):1109–16
Dopamine and norepinephrine uptake and metabolism by astroglial cells in culture. Pelton EW 2d, et al. **Life Sci** 1981 Apr 6;28(14):1655–63
Action of colchicine on cholinergic and adrenergic mechanisms in guinea pig vas deferens. Takeyasu K, et al. **Life Sci** 1981 Feb 23; 28(8):851–60
Stimulatory effect of somatostatin on norepinephrine release from rat brain cortex slices. Tsujimoto A, et al. **Life Sci** 1981 Feb 23;28(8):903–10
Urinary excretion of radiolabelled norepinephrine after release from renal sympathetic nerves. Willis LR, et al. **Life Sci** 1980 Dec 22–29; 27(25–26):2541–6
Distinct regulations by calcium of cyclic GMP levels and catecholamine secretion in isolated bovine adrenal chromaffin cells. Lemaire S, et al. **Metabolism** 1981 May;30(5):462–8
The effect of phencyclidine on noradrenaline uptake by bovine chromaffin granules. Amir A, et al. **Monogr Neural Sci** 1980;7:129–37
The participation of cyclic nucleotides and protein kinase in the regulation of norepinephrine synthesis and release during nerve stimulation. Weiner N. **Monogr Neural Sci** 1980;7:146–60
The inhibition by (+/–)-propranolol of the positive inotropic effects of (+/–)-isoprenaline and (–)-noradrenaline. Competitive antagonism and saturable uptake. Ebner F. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):96–107
GABA facilitation by noradrenaline shows supersensitivity in cerebellum after 6-hydroxydopamine. Moises HC, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980;315(1):37–46
Monoamine uptake into synaptosomes from various regions of rat brain following lithium administration and withdrawal. Ahluwalia P, et al. **Neuropharmacology** 1981 May;20(5):483–7
Effects of phenytoin on mouse cerebellar 5-hydroxytryptamine and norepinephrine. Fry BW, et al. **Neuropharmacology** 1981 Jun; 20(6):623–5
Modulatory interactions between norepinephrine and taurine, beta-alanine, gamma-aminobutyric acid and muscimol, applied iontophoretically to cerebellar Purkinje cells. Yeh HH, et al. **Neuropharmacology** 1981 Jun;20(6):549–60
Influence of castration and testosterone propionate on [3H]noradrenaline metabolism in various structures of male rat brain. Bekhtereva EP. **Neurosci Behav Physiol** 1980 Nov–Dec;10(6):471–3
Noradrenaline content correlated to matrix density in small noradrenergic vesicles from rat seminal ducts. Fried G, et al. **Neuroscience** 1981; 6(4):787–800
Norepinephrine-containing terminals in kitten visual cortex: laminar distribution and ultrastructure. Itakura T, et al. **Neuroscience** 1981; 6(2):159–75
Fine structure of rat cerebellar noradrenaline terminals as visualized by potassium permanganate 'in situ perfusion' fixation method. Kimoto Y, et al. **Neuroscience** 1981;6(1):47–58
Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Va[illegible] L, et al. **Neuroscience** 1981; 6(2):189–94
Cholecystokinin acts on the hypothalamic 'noradrenergic system' involved in feeding. McCaleb ML, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):47–9
Influence of noradrenaline on blood flow to brown adipose tissue in rats exhibiting diet-induced thermogenesis. Rothwell NJ, et al. **Pflugers Arch** 1981 Mar;389(3):237–42
Regional responses of rat brain noradrenergic neurones to acute intense stress. Nakagawa R, et al. **Pharmacol Biochem Behav** 1981 May; 14(5):729–32
Mechanism of stress-induced subsensitivity to norepinephrine. Stone EA. **Pharmacol Biochem Behav** 1981 May;14(5):719–23
Noradrenergic transmission in depression: under- or overfunction? Waldmeier PC. **Pharmacopsychiatria** 1981 Jan;14(1 Suppl):3–9
Septal lesions and avoidance behavior: genetic, neurochemical and behavioral considerations. Donovick PJ, et al. **Physiol Behav** 1981 Mar; 26(3):495–507
The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine. Mikkelsen E, et al. **Psychiatry Res** 1981 Apr;4(2):157–69
The specific activity of platelet monoamine oxidase varies with platelet count during severe exercise and noradrenaline infusion. Gawel MJ, et al. **Psychopharmacology (Berlin)** 1981;72(3):275–7
Increased brain serotonergic and noradrenergic activity after repeated systemic administration of the beta-2 adrenoceptor agonist salbutamol, a putative antidepressant drug. Hallberg H, et al. **Psychopharmacology (Berlin)** 1981;73(3):201–4
Electrophysiologic interactions of antipsychotic drugs with central noradrenergic pathways. Marwaha J, et al. **Psychopharmacology (Berlin)** 1981;73(2):126–33
Two pools of amines in synaptic vesicles of rat pineal nerves. Pellegrino de Iraldi A, et al. **Rev Can Biol** 1981 Mar;40(1):101–9
Influence of sympathetic tonus and plasma noradrenaline on urethral pressure. Nordling J, et al. **Scand J Urol Nephrol** 1981;15(1):1–6
[Short-term submaximum work and its effect on plasma noradrenaline levels (author's transl)] Stejskal P. **Cas Lek Cesk** 1981 Feb 26; 120(8):218–23 (Eng. Abstr.) (Cze)
[Comparative pharmacology of adrenaline and noradrenaline] Martin C, et al. **Ann Anesthesiol Fr** 1981;22(1):85–96 (16 ref.) (Fre)
[Effect of social isolation on the transmitter sensitivity of striatal and hippocampal neurons of the rat] Oehler J, et al. **Acta Biol Med Ger** 1980;39(10):1089–93 (Eng. Abstr.) (Ger)
[Development of biological psychiatric depression research (author's transl)] Matussek N. **MMW** 1981 May 8;123(19):793–4 (Eng. Abstr.) (Ger)
[Modulation of the effect of morphine on the isolated guinea pig intestine by noradrenaline and serotonin] Sarto G. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):394–400 (Eng. Abstr.) (Ita)
[Studies on the mechanism of the hypertropic action of hydrocortisone on the secretory tubules of the mouse submandibular glands. 3) Effect of hydrocortisone acetate on the noradrenaline stimulation to submandibular glands (author's transl)] Maruyama S, et al. **Josai Shika Daigaku Kiyo** 1980;1(9):29–34 (Eng. Abstr.) (Jpn)
[Effect of adrenaline, noradrenaline and acetylcholine on rabbit and human uterine activity in vivo (author's transl)] Sakoda H. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Jun;32(6):697–705 (Eng. Abstr.) (Jpn)
[Changes in the morphofunctional status of the capillary system of the cerebral cortex in cats exposed to adrenergic stimulation while prostaglandin biosynthesis is inhibited] Gabrielian ES, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):173–5 (Eng. Abstr.) (Rus)
[Noradrenaline as a RNA and Na K ATPase biosynthesis regulator in the neurons] Elaev NR. **Probl Endokrinol (Mosk)** 1981 Jan–Feb; 27(1):58–62 (Eng. Abstr.) (Rus)
[Effect of Arzni carbonate mineral baths on labeled noradrenaline uptake by myocardial sections and the activity of mitochondrial monoamine oxidase] Mirzoian SA, et al. **Vopr Kurortol Fizioter Lech Fiz Kult** 1981 Mar–Apr;(2):42–5 (Rus)

NORMETANEPHRINE

A simple chromatographic technique for the estimation of urinary levels of normetadrenaline and metadrenaline. Hanson P, et al. **Clin Biochem** 1980 Dec;13(6):262–5
Analysis of urinary metanephrines by reversed-phase high-performance liquid chromatography and electrochemical detection. Bertani-Dziedzic LM, et al. **Clin Chim Acta** 1981 Feb 19;110(1):1–8
3-Methoxytyramine and normetanephrine as indicators of dopamine and noradrenaline release in mouse brain in vivo. Kehr W. **J Neural Transm** 1981;50(2–4):165–78

NORTRIPTYLINE

Saliva secretion following long-term antidepressant treatment with nortriptyline controlled by plasma levels. Bertram U, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):357–63

Effect of alcohol consumption and cigarette smoking on antidepressant levels of depressed patients. Linnoila M, et al. **Am J Psychiatry** 1981 Jun;138(6):841–2

Pharmacokinetics of nortriptyline in elderly volunteers. Turbott J, et al. **Commun Psychopharmacol** 1980;4(3):225–31

Excretion of nortriptyline into saliva. Virtanen R. **Int J Clin Pharmacol Ther Toxicol** 1981 Feb;19(2):78–81

Slow hydroxylation of nortriptyline and concomitant poor debrisoquine hydroxylation: clinical implications [letter] Bertilsson L, et al. **Lancet** 1981 Mar 7;1(8219):560–1

Nortriptyline and pituitary-thyroid function in affective disorder. Nordgren L, et al. **Pharmacopsychiatria** 1981 Mar;14(2):61–5

OBSESSIVE-COMPULSIVE DISORDER

Review of behavioral psychotherapy, I: Obsessive-compulsive disorders. Marks IM. **Am J Psychiatry** 1981 May;138(5):584–92 (45 ref.)

Psychotropic drugs and behaviour therapy. Stern R. **Practitioner** 1981 Jan;225(1351):21–5

OXAZEPAM

Oxazepam in the treatment of anxiety associated with depression: results of treatment in 1600 cases (Studies in depression, VI). Bailey HR, et al. **Curr Med Res Opin** 1981;7(3):156–63

Oxazepam esters. 3. Intrinsic activity, selectivity, and prodrug effect. Maksay G, et al. **J Med Chem** 1981 May;24(5):499–502

[The influence of oxazepam and diazepam on the sexual behaviour and level of GABA biogenic amines in a male rat's brain (author's transl)] Borzęcki Z, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979; 34:371–6 (Eng. Abstr.) **(Pol)**

PARANOID DISORDERS

An obligation to treat vs. a right to refuse. Davis AJ. **Am J Nurs** 1981 Jul;81(7):1370

PARASYMPATHOMIMETICS

Role of cyclic GMP in cholinergic activation of Na-K pump in duck salt gland. Stewart DJ, et al. **Am J Physiol** 1981 May; 240(5):C207–14

Actions of various muscarinic agonists on membrane potential, potassium efflux, and contraction of longitudinal muscle of guinea-pig intestine. Bolton TB, et al. **Br J Pharmacol** 1981 Feb;72(2):319–34

Cholinergic effect of 4-aminopyridine and adrenergic effect of 4-methyl-2-aminopyridine in cardiac muscle. Glover WE. **Eur J Pharmacol** 1981 Apr 24;71(1):21–31

Molecular requirements of the active sites of the cholinergic receptors. XVI – Synthesis and cholinergic activity of 2- or 5-alkyl or 5-phenyl-4-methyl-3-oxo-1-dimethylaminomethylcyclopentane methiodide. Pigini M, et al. **Farmaco [Sci]** 1981 Feb;36(2):152–8

Conformational analysis of the reverse ester of acetylcholine, cholinergic potency, and cholinergic models. Reed KW, et al. **Gen Pharmacol** 1981; 12(3):177–85

Fluorescence and N.M.R. studies of the binding of cholinergic fluorescent probes to horse serum cholinesterase. Narayanan R, et al. **Int J Pept Protein Res** 1981 Feb;17(2):170–80

Molecular requirements of the active site of cholinergic receptors XV: Synthesis and biological activity of 2,3-dehydrodeoxamuscarone and 2,3-dehydrodeoxamuscarines. Angeli P, et al. **J Pharm Sci** 1981 May; 70(5):489–92

Pre- and postsynaptic effects of muscarinic agonists in the guinea-pig ileum. Kilbinger H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):259–66

Interaction of morphine with the cholinergic system on prolactin release. Fanjul LF, et al. **Proc Soc Exp Biol Med** 1981 Apr;166(4):542–5

[Effects of parasympathomimetic and sympathomimetic drugs on the sublingual glands of rats] Abe K, et al. **Gifu Shika Gakkai Zasshi** 1980 Jun;8(1):36–52 (Eng. Abstr.) **(Jpn)**

PARGYLINE

Effects of pargyline and diethyldithiocarbamate in vivo treatment on aldehyde dehydrogenase activities of submitochondrial fractions. Nakanishi S, et al. **Arch Toxicol** 1980 Dec;46(3–4):241–8

Studies on the pargyline-binding site of different types of monoamine oxidase. Yu PH. **Can J Biochem** 1981 Jan;59(1):30–7

PEMOLINE

Reversed-phase high-performance liquid chromatographic detection of pemoline in doping control. Cartoni GP, et al. **J Chromatogr** 1980 Dec 5;202(1):131–3

Analysis of pemoline in serum by high performance liquid chromatography: clinical application to optimize treatment of hyperactive children. Tomkins CP, et al. **Ther Drug Monit** 1980; 2(3):255–60

[Effect of a combined geriatric preparation on serum proteins and liver tests (author's transl)] Kocián J, et al. **Cesk Gastroenterol Vyz** 1981 Mar; 35(2):49–53 (Eng. Abstr.) **(Cze)**

PENTOBARBITAL

Selective effects of barbiturate and amphetamine on information processing and response execution. Frowein HW. **Acta Psychol (Amst)** 1981 Feb;47(2):105–15

Induction of hyperphagia in rats by intracerebroventricular infusion of sodium pentobarbital. A method for testing anorexigenic compounds. Kaufmann SH, et al. **Arzneimittelforsch** 1981;31(2):335–7

Barbiturate enhancement of GABA-mediated inhibition and activation of chloride ion conductance: correlation with anticonvulsant and anesthetic actions. Schulz DW, et al. **Brain Res** 1981 Mar 23; 209(1):177–88

The inhibition and potentiation of procarbazine on hepatic mixed-function oxidases in phenobarbital tolerant and nontolerant mice. Onoda K, et al. **Drug Chem Toxicol** 1980;3(2):185–200

The effect of pentobarbital on central somatosensory conduction time in the rat. Shaw NA, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jun;51(6):674–7

Regulation of the second surge of follicle-stimulating hormone; effects of antiluteinizing hormone-releasing hormone serum and pentobarbital. Hasegawa Y, et al. **Endocrinology** 1981 Jul;109(1):130–5

Effects of combinations of phencyclidine and pentobarbital on fixed-interval performance in rhesus monkeys. Woolverton WL, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):611–8

Pentobarbitone slows the dissociation of GABA from rat brain synaptosomal binding sites. Willow M, et al. **Neurosci Lett** 1981 Apr 9;23(1):71–4

Effect of pentobarbital on thalamo- and hippocampocortical processes in rats. Kolinová M, et al. **Physiol Bohemoslov** 1981;30(2):139–48

[Effect of the administration of sodium pentobarbital on tolerance to acute hypoxia in albino rats] Quatrini U, et al. **Boll Soc Ital Biol Sper** 1981 Feb 15;57(3):333–9 **(Ita)**

PEPTIDES

An introduction to the immunocytochemical localization of neuropeptides and neurotransmitters. van Leeuwen FW. **Acta Histochem [Suppl] (Jena)** 1981;24:49–77 (162 ref.)

Specific colorimetric detection of o-diphenols and 3,4-dihydroxyphenylalanine-containing peptides. Waite JH, et al. **Anal Biochem** 1981 Feb;111(1):131–6

Thyrotropin-releasing hormone and a homologous peptide in the reproductive system of the female rat and pig. Pekary AE, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):73–80

Specific stimulation of steroidogenesis in rat adrenal zona glomerulosa cells by pituitary peptides. Vinson GP, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):65–72

Ordered conformation of polypeptides and proteins in acidic dodecyl sulfate solution. Wu CS, et al. **Biochemistry** 1981 Feb 3;20(3):566–70

The effects of substance P and related peptides on alpha-amylase release from rat parotid gland slices. Brown CL, et al. **Br J Pharmacol** 1981 Jun;73(2):517–23

Human insulin: study of safety and efficacy in man. Owens DR, et al. **Br Med J [Clin Res]** 1981 Apr 18;282(6272):1264–6

Immunocytochemical demonstration of peptidergic neurons in the central nervous system of the pond snail Lymnaea stagnalis with antisera raised to biologically active peptides of vertebrates. Schot LP, et al. **Cell Tissue Res** 1981;216(2):273–91

Microsuperfusion of neurointermediate lobes of Xenopus laevis: concomitant and coordinately controlled release of newly synthesized peptides. Martens GJ, et al. **Comp Biochem Physiol [C]** 1981; 69C(1):75–82

Neuropeptides: central nervous system effects on nutrient metabolism. Brown M. **Diabetologia** 1981 Mar;20 Suppl:299–304 (28 ref.)

The effect of somatostatin on bombesin-stimulated serum gastrin and gastric acid secretion in man. Jansen JB, et al. **Digestion** 1981; 21(4):193–7

Evidence for two different turnover pools of adrenocorticotropin, alpha-melanocyte-stimulating hormone, and endorphin-related peptides released by the frog pituitary neurointermediate lobe. Loh YP, et al. **Endocrinology** 1981 Jul;109(1):54–61

Heterogeneity of somatostatin-like peptides in rat brain, pancreas, and gastrointestinal tract. Trent DF, et al. **Endocrinology** 1981 Jun; 108(6):2033–8

Effects of somatostatin-14 and somatostatin-28 on bombesin-stimulated release of gastrin, insulin, and glucagon in the dog. Veyne N, et al. **Endocrinology** 1981 May;108(5):1843–7

Active chloride transport by the skin of a marine teleost is stimulated by urotensin I and inhibited by urotensin II. Marshall WS, et al. **Gen Comp Endocrinol** 1981 Apr;43(4):484-91

Isolation, structure and synthesis of a heptapeptide with in vitro ACTH-releasing activity from porcine hypothalamus. Chang RC, et al. **Horm Metab Res** 1981 Apr;13(4):228-32

Studies on protein semisynthesis. I. Formation of esters, hydrazides, and substituted hydrazides of peptides by the reverse reaction of trypsin. Yagisawa S. **J Biochem (Tokyo)** 1981 Feb;89(2):491-501

Characterization and determination of neuropeptides by high-performance liquid chromatography and radioimmunoassay. McDermott JR, et al. **J Chromatogr** 1981 Mar 13;222(3):371-9

Association of the transformation-specific protein pp60src with the membrane of an avian sarcoma virus. Bunte T, et al. **J Virol** 1981 Jun; 38(3):1034-47

Corticotropin/beta-endorphin immunoreactivity in rat mast cells. Peptide or protease? DiAugustine RP, et al. **Life Sci** 1980 Dec 22-29; 27(25-26):2663-8

Comparative study on the effect of morphine and the opioid-like peptides in the vas deferens of rodents: species and strain differences, evidence for multiple opiate receptors. Huidobro-Toro JP, et al. **Life Sci** 1981 Mar 23;28(12):1331-6

Bacterial peptides with C-terminal similarities to bovine neurotensin. Bhatnagar YM, et al. **Peptides (Fayetteville)** 1981 Spring;2(1):51-9

Immunochemical characterization of neurotensin-like peptides in chicken. Carraway R, et al. **Peptides (Fayetteville)** 1980 Summer;1(2):159-65

Feeding and selection of saccharin after injections of bombesin, LiCl, and NaCl. Kulkosky PJ, et al. **Peptides (Fayetteville)** 1981 Spring; 2(1):61-4

Failure of peptides (angiotensin, bradykinin, substance P, physalaemin, Met-enkephalin) to influence the cardiac action potential. Iven H, et al. **Pharmacology** 1980;21(6):403-6

Effects of hyperthermia on binding, internalization, and degradation of epidermal growth factor. Magun BE, et al. **Radiat Res** 1981 Apr; 86(1):133-46

Immunohistochemical evidence of gastro-entero-pancreatic neurohormonal peptides of vertebrate type in the nervous system of the larva of a dipteran insect, the hoverfly, Eristalis aeneus. El-Salhy M, et al. **Regul Pept** 1980 Dec;1(3):187-204

[Convergence and reciprocal coupling of hypothalamic monoaminergic and peptidergic neurons (author's transl)] Barry J. **Ann Endocrinol (Paris)** 1980 Nov-Dec;41(6):457-65 (Eng. Abstr.) **(Fre)**

[Biosynthesis of some hypothalamic neuropeptides. Identification of precursor forms (author's transl)] Camier M, et al. **Ann Endocrinol (Paris)** 1980 Nov-Dec;41(6):466-77 (37 ref.) (Eng. Abstr.) **(Fre)**

[In vitro study of the interaction between neuromediators and neuropeptides involved in hypothalamic neurosecretion control (author's transl)] Epelbaum J, et al. **Ann Endocrinol (Paris)** 1980 Nov-Dec;41(6):478-86 (35 ref.) (Eng. Abstr.) **(Fre)**

[The intragonadic cybernins (author's transl)] Franchimont P. **J Gynecol Obstet Biol Reprod (Paris)** 1980;9(8):825-34 (Eng. Abstr.) **(Fre)**

[Gut-brain peptides-structures and functions (author's transl)] Yanaihara N. **Horumon To Rinsho** 1980 Oct;28(10):1153-60 (34 ref.) **(Jpn)**

[Reactions of an identified edible snail neuron to application of peptides, mediators, prostaglandins, and cyclic nucleotides] Osipovskii SA, et al. **Neirofiziologiia** 1981;13(1):80-7 (Eng. Abstr.) **(Rus)**

PERPHENAZINE

Effects of bromocriptine and perphenazine on male accessory sex glands. I. The seminal vesicles. Krall A, et al. **Arch Androl** 1981 Jun; 6(4):295-300

Radioimmunoassay for perphenazine in human plasma. Midha KK, et al. **Br J Clin Pharmacol** 1981 Jan;11(1):85-8

PERSONALITY DISORDERS

Attitudes toward medication change among chronically impaired psychiatric patients. Lesser IM, et al. **Am J Psychiatry** 1981 Jun; 138(6):801-3

Current concepts in psychiatry: borderline personality disorder. Groves JE. **N Engl J Med** 1981 Jul 30;305(5):259-62

Interrelationship of hysteroid dysphoria and borderline personality disorder. Liebowitz MR, et al. **Psychiatr Clin North Am** 1981 Apr; 4(1):67-87

The interaction of psychopharmacology and psychoanalysis in the borderline patient. Snyder S. **Psychiatr Q** 1980 Winter;52(4):240-50 (51 ref.)

PHENCYCLIDINE

Withdrawal from chronic phencyclidine (PCP) dependence with desipramine. Tennant FS Jr, et al. **Am J Psychiatry** 1981 Jun; 138(6):845-7

Phencyclidine intoxication: clinical experience in 27 cases confirmed by urine assay. Barton CH, et al. **Ann Emerg Med** 1981 May; 10(5):243-6

Effect of chronic administration of phencyclidine on hepatic mixed-function oxidases in the mouse. Ho IK, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):545-7

An improved method for the quantitation of phencyclidine (PCP) in biological samples utilizing nitrogen-detection gas chromatography. Miceli JN, et al. **J Anal Toxicol** 1981 Jan-Feb;5(1):2[illegible]-32

Analytical determination of purity of 1-piperidinocyclohexanecarbonitrile and its hydrobromide salt. Soine WH. **J Pharm Sci** 1981 Jan; 70(1):106-8

The effect of phencyclidine on the turnover rate of acetylcholine in various regions of rat brain. Murray TF, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):733-7

Effects of N-substituted analogs and metabolites of phencyclidine on avoidance behavior in the rat. Shannon HE, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):55-62

Effects of combinations of phencyclidine and pentobarbital on fixed-interval performance in rhesus monkeys. Woolverton WL, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):611-8

Interactions of tricyclic antidepressants with a synaptic ion channel. Aronstam RS. **Life Sci** 1981 Jan 5;28(1):59-64

The identification of a new metabolite of phencyclidine. Cho AK, et al. **Life Sci** 1981 Mar 2;28(9):1075-9

The effect of phencyclidine on dopamine metabolism in the mouse brain. Johnson KM, et al. **Life Sci** 1981 Jan 26;28(4):361-9

Disposition of [3H] phencyclidine in the rat after single and multiple doses. Misra AL, et al. **Life Sci** 1980 Dec 22-29;27(25-26):2501-8

The effect of phencyclidine on noradrenaline uptake by bovine chromaffin granules. Amir A, et al. **Monogr Neural Sci** 1980;7:129-37

Phencyclidine inhibition of cerebellar Purkinje neurons. Marwaha J, et al. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(34):187-92

Differential electrophysiological and behavioral responses to optically active derivatives of phencyclidine. Marwaha J, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jan;315(3):203-9

[3H]Phencyclidine: a probe for the ionic channel of the nicotinic receptor. Eldefrawi ME, et al. **Proc Natl Acad Sci USA** 1980 Dec; 77(12):7458-62

Metabolic disposition and irreversible binding of phencyclidine in rats. Law FC. **Toxicol Appl Pharmacol** 1981 Feb;57(2):263-72

PHENCYCLIDINE ABUSE

Phencyclidine intoxication: clinical experience in 27 cases confirmed by urine assay. Barton CH, et al. **Ann Emerg Med** 1981 May; 10(5):243-6

Analytical determination of purity of 1-piperidinocyclohexanecarbonitrile and its hydrobromide salt. Soine WH. **J Pharm Sci** 1981 Jan; 70(1):106-8

PHENELZINE

Phenelzine and exposure in the treatment of phobias. Solyom C, et al. **Biol Psychiatry** 1981 Mar;16(3):239-47

Determination of phenelzine in human plasma with gas chromatography-mass spectrometry using an isotope labeled internal standard. Jindal SP, et al. **J Chromatogr** 1980 Dec 12;221(2):301-8

Agoraphobia: the 'what if' syndrome. Fier M. **J Med Soc NJ** 1981 Apr; 78(4):286-8

Relationship between response to phenelzine and MAO inhibition in a clinical trial of phenelzine, amitriptyline and placebo. Raft D, et al. **Neuropsychobiology** 1981;7(3):122-6

Effects of phenelzine and amitriptyline on depression [proceedings] Paykel ES, et al. **Psychopharmacol Bull** 1981 Jan;17(1):104-6

PHENETHYLAMINES

Type B monoamine oxidase activities toward beta-phenylethylamine in discrete hypothalamic and circumventricular nuclei of the rat. Kim JS, et al. **Biochem Pharmacol** 1981 Apr;30(8):893-5

Phenylethylamine effects on dopamine synthesis. Structure-activity relationships. Patrick RL. **Biochem Pharmacol** 1981 Jan 15; 30(2):141-6

Effect of hyperoxia on uptake and metabolism of 5-hydroxytryptamine and beta-phenylethylamine in rat lung: a sex difference. Ben-Harari RR, et al. **Br J Pharmacol** 1981 Jun;73(2):461-6

Quantitation of biologically important primary amines as their isothiocyanate derivatives by gas chromatography using nitrogen detector and validation by selected ion monitoring. Narasimhachari N, et al. **Clin Chim Acta** 1981 Mar 5;110(2-3):235-43

Toxicological analysis of phenylethylamines by high performance reversed-phase ion-pair partition thin-layer and liquid chromatographies. Verbiese-Genard N, et al. **Clin Toxicol** 1981; 18(4):391-400

Preferential blockade of postsynaptic alpha-adrenoceptors by BE 2254. Göthert M, et al. **Eur J Pharmacol** 1981 Mar 5;70(1):35-42

Secoverine selectively antagonizes muscarinic effects in various in vivo preparations. Zwagemakers JM, et al. **Eur J Pharmacol** 1981 Apr 24; 71(1):165-8

Radical formation in single crystals of aromatic amines and radical transformation by light. Karsten W, et al. **Int J Radiat Biol** 1981 Mar; 39(3):235-52

Physiologic effects and plasma kinetics of phenylethanolamine and its N-methyl homolog in the dog. Shannon HE, et al. **J Pharmacol Exp Ther** 1981 May;217(2):379-85

Substituted phenethylamines and anorexia. Duhault J, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):341-9

Is the failure of (-)deprenyl, a selective monoamine oxidase B inhibitor, to alleviate depression related to freedom from the cheese effect? Mendis N, et al. **Psychopharmacology (Berlin)** 1981;73(1):87-90

[Release of norfenefrine from sustained-release formulations by an in vitro dissolution model. Simulation of 'drug levels' by calculation using pharmacokinetical constants and comparison with in vivo course of action (author's transl)] Laven R, et al. **Arzneimittelforsch** 1981; 31(2):353-6 (Eng. Abstr.) (Ger)

[Comparison of the tocolytic efficacy of hexoprenaline and ritodrine in prostaglandin-induced labor] Brabec W, et al. **Gynaekol Rundsch** 1980 Jun;20 Suppl 2:230-4 (Ger)

[Mechanism of inhibition by chlorgyline and deprenyl of tyramine deamination by mitochondrial monoamine oxidase of rat liver] Deverina IS. **Biokhimiia** 1980 Oct;45(10):1897-908 (Eng. Abstr.) (Rus)

PHENMETRAZINE

Correction of drug names [letter] Hamer R. **Ann Emerg Med** 1981 Jul; 10(7):395

A study of phenmetrazine (Preludin) abuse. Chambers CD, et al. **Chem Depend** 1980;4(1-2):101-11

PHENOBARBITAL

Influence of phenobarbital, chlorpromazine, progesterone and phenylbutazone on the biliary cholesterol excretion in rats. Barth A, et al. **Acta Biol Med Ger** 1980;39(11-12):1217-26

Serum digoxin concentrations in dogs before, during, and after concomitant treatment with phenobarbital. Pedersoli WM, et al. **Am J Vet Res** 1980 Oct;41(10):1639-42

Serum concentrations of primidone and its metabolites, phenylethylmalonamide and phenobarbital, in the dog. Yeary RA. **Am J Vet Res** 1980 Oct;41(10):1643-5

Low blood levels of phenobarbital due to poor gastrointestinal solubility of phenobarbital tablets [letter] Alvarez N, et al. **Ann Neurol** 1981 Mar; 9(3):309-10

Treatment of massive phenobarbital overdose with dopamine diuresis. Costello JB, et al. **Arch Intern Med** 1981 Jun;141(7):938-40

Alterations in rabbit liver protein synthesis as a result of phenobarbital treatment. DiLella AG, et al. **Biochem Biophys Res Commun** 1981 Feb 12;98(3):628-34

Induction of translationally active rat liver glutathione S-transferase B messenger RNA by phenobarbital. Pickett CB, et al. **Biochem Biophys Res Commun** 1981 Apr 15;99(3):1002-10

Sequential translocation of two phenobarbital-induced polysomal messenger ribonucleic acids from the nuclear envelope to the endoplasmic reticulum. Gonzalez FJ, et al. **Biochemistry** 1981 Apr 14; 20(8):2292-8

Barbiturates and transmitter release at the frog neuromuscular junction. Pincus JH, et al. **Brain Res** 1981 May 25;213(1):127-37

Barbiturate enhancement of GABA-mediated inhibition and activation of chloride ion conductance: correlation with anticonvulsant and anesthetic actions. Schulz DW, et al. **Brain Res** 1981 Mar 23; 209(1):177-88

Effects of phenobarbital upon triacylglycerol metabolism in the guinea pig. Goldberg DM, et al. **Can J Biochem** 1981 Jan;59(1):48-53

A comparison of the effects of pretreatment with phenobarbitone and 3-methylcholanthrene on the metabolism of aflatoxin B1 by rat liver microsomes and isolated hepatocytes in vitro. Metcalfe SA, et al. **Chem Biol Interact** 1981 May;35(2):145-57

Enzyme immunoassay for phenobarbital. Aoki K, et al. **Chem Pharm Bull (Tokyo)** 1980 Nov;28(11):3291-5

Barbiturate and hypnosedative withdrawal by a multiple oral phenobarbital loading dose technique. Robinson GM, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):71-6

The effect of phenobarbital and beta-naphthoflavone induction on the metabolism of biphenyl in the rat and mouse. Halpaap-Wood K, et al. **Drug Metab Dispos** 1981 Mar-Apr;9(2):97-102

The effect of 3-methylcholanthrene, Aroclor 1254, and phenobarbital induction on the metabolism of biphenyl by rat and mouse 9000g supernatant liver fractions. Halpaap-Wood K, et al. **Drug Metab Dispos** 1981 Mar-Apr;9(2):103-7

Changes in radioimmunoassayable luteinizing hormone-releasing hormone in discrete brain areas of the rat at various times on proestrus, diestrous day 1, and after phenobarbital administration. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2179-85

Structural gene products of the murine Ah complex. Differences in ontogenesis and glucosamine incorporation between liver microsomal cytochromes P1-450 and P-448 induced by polycyclic aromatic compounds. Negishi M, et al. **Eur J Biochem** 1981 Apr; 115(3):585-94

Influence of phenobarbital treatment on cimetidine kinetics. Somogyi A, et al. **Eur J Clin Pharmacol** 1981;19(5):343-7

In vivo and in vitro availability of commercial phenytoin formulations containing phenobarbitone. Shukla UA, et al. **Indian J Med Res** 1980 Dec;72:910-5

Selective induction of two different molecular species of cytochrome P-450 by phenobarbital and 3-methylcholanthrene. Harada N, et al. **J Biochem (Tokyo)** 1981 Jan;89(1):237-48

An immunohistochemical study on the localization and distributions of phenobarbital- and 3-methylcholanthrene-inducible cytochromes P-450 within the livers of untreated rats. Baron J, et al. **J Biol Chem** 1981 Jun 10;256(11):5931-7

The effects of phenytoin on phenobarbitone and primidone metabolism. Lambie DG, et al. **J Neurol Neurosurg Psychiatry** 1981 Feb; 44(2):148-51

Interactions among chloramphenicol, phenytoin, and phenobarbital in a pediatric patient. Powell DA, et al. **J Pediatr** 1981 Jun;98(6):1001-3

Evidence for a synergistic interaction between phenytoin and phenobarbital in experimental animals. Masuda Y, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):805-11

Induction effect of phenobarbital on the carbamazepine to carbamazepine-10, 11-epoxide pathway in rhesus monkeys. Patel IH, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):555-8

Effects of aging and phenobarbital on the rat liver microsomal drug-metabolizing system. Schmucker DL, et al. **Mech Ageing Dev** 1981 Feb;15(2):189-202

Central 5-hydroxytryptamine and the effects of hallucinogens and phenobarbital on operant responding in rats. Commissaris RL, et al. **Pharmacol Biochem Behav** 1981 May;14(5):595-601

Effect of phenobarbital on the level of translatable rat liver epoxide hydrolase mRNA. Pickett CB, et al. **Proc Natl Acad Sci USA** 1981 Feb;78(2):893-7

Critical periods for diphenylhydantoin and phenobarbital administration during gestation. Gauron EF, et al. **Psychol Rep** 1980 Dec; 47(3 Pt 2):1163-6

Cholesterol HDL in phenobarbital-treated male and female Wistar rats. Dessi S, et al. **Res Commun Chem Pathol Pharmacol** 1981 Feb; 31(2):375-8

Substrate-labeled fluorescent immunoassay for phenobarbital. Krausz LM, et al. **Ther Drug Monit** 1980;2(3):261-72

[Nutritional lipidic factors of enzymatic phenobarbital induction in the rat. Effects of quantitative and qualitative composition of dietary lipids (author's transl)] Mounié J, et al. **J Pharmacol** 1981 Jan-Mar; 12(1):3-14 (Eng. Abstr.) (Fre)

[Acute cotrimoxazole-induced thrombocytopenia, facilitating role of phenobarbital (author's transl)] Thorel JB, et al. **Sem Hop Paris** 1981 May 8-15;57(17-18):914-5 (Eng. Abstr.) (Fre)

[The effect of phenobarbital on anti-mitotic activity of vincristine and colchicine. Experimental study] Lambertini F, et al. **Arch Sci Med (Torino)** 1980 Jul-Sep;137(3):405-10 (Eng. Abstr.) (Ita)

[Effect of phenobarbital on hepatic glutathione and GSH-S transferase in the rat] Dore M, et al. **Boll Soc Ital Biol Sper** 1980 Nov 15; 56(21):2212-7 (Eng. Abstr.) (Ita)

[Metabolism of lipid-carrying proteins of rat liver in normal rats and after phenobarbital injection] Gapparov MM, et al. **Biokhimiia** 1980 Oct; 45(10):1744-8 (Eng. Abstr.) (Rus)

PHENOTHIAZINE TRANQUILIZERS

Outcome and risks of ultra-long-term treatment with an oral neuroleptic drug. Relationship between perazine serum levels and clinical variables in schizophrenic outpatients. Pietzcker A, et al. **Arch Psychiatr Nervenkr** 1981;229(4):315-29

Photoaffinity labeling of calmodulin by phenothiazine antipsychotics. Prozialeck WC, et al. **Mol Pharmacol** 1981 Mar;19(2):264-9

PHENOTHIAZINES

Thionine-Feulgen Congo Red — a new staining technique for automated cytology. Oud PS, et al. **Acta Histochem [Suppl] (Jena)** 1981; 24:199-206

Phenothiazine antagonism of calmodulin: a structurally-nonspecific interaction. Roufogalis BD. **Biochem Biophys Res Commun** 1981 Feb 12;98(3):607-13

Phenothiazines as reagents for the detection of faecal occult blood. Ahmed SA, et al. **Clin Chim Acta** 1981 Apr 9;111(2-3):275-8

Influence of phenothiazines or reserpine on the formation of 14C-glycine from U-14C-serine. Gründig E, et al. **Enzyme** 1981;26(1):43-8

Thermodynamics of partitioning and efflux of phenothiazines from liposomes. Ahmed M, et al. **J Membr Biol** 1981 Feb 28;58(3):181-9

High-performance liquid chromatographic determination of ethmozin in plasma. Whitney CC, et al. **J Pharm Sci** 1981 Apr;70(4):462-3

[Effect of indomethacin and nonachlazine on myocardial and cerebral tyrosine hydroxylase activity in rats] Mineeva MF, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):181-4 (Eng. Abstr.) (Rus)

PHENOXYBENZAMINE

Inhibition of renin secretion by intrarenal alpha-adrenoceptor blockade. Blair ML. **Am J Physiol** 1981 Jun;240(6):E682-8

Effect of adrenoceptor blocker and MAOI on postcoital utero-oviductal contractility, sperm transport, and sperm attachment to eggs in rabbits. Marsafy YM, et al. **Arch Androl** 1981 Jun;6(4):307-16

alpha-Difluoromethylornithine (alpha DFMO) and phenoxybenzamine hydrochloride in the treatment of chronic non-suppurative prostatitis. Dunzendorfer U. **Arzneimittelforsch** 1981;31(2):382-5

The role of calcium in the effects of noradrenaline and phenoxybenzamine on adrenergic transmitter release from atria: no support for negative feedback of release. Kalsner S. **Br J Pharmacol** 1981 Jun;73(2):363-71

Reactivation by cysteamine of vascular alpha adrenoceptors blocked by the tetramine disulfide benextramine and interaction of benextramine with phenoxybenzamine. Brasili L, et al. **Can J Physiol Pharmacol** 1980 Dec;58(12):1490-3

The effect of phenoxybenzamine on the relationship between glycerol release and cyclic AMP levels in the presence of insulin in epinephrine-stimulated rat adipocytes. Wong EH, et al. **FEBS Lett** 1981 May 18;127(2):217-20

Effects of phenoxybenzamine on bladder neck opening. Waterfall NB, et al. **J R Soc Med** 1980 May;73(5):345-7

Acceleration of beta-receptor desensitization in combined administration of antidepressants and phenoxybenzamine. Crews FT, et al. **Nature** 1981 Apr 30;290(5809):787-9

Treatment with trazodone plus phenoxybenzamine accelerates development of decreased type 2 serotonin binding in rat cortex. Taylor DP, et al. **Neuropharmacology** 1981 May;20(5):513-6

Phenoxybenzamine and bromocriptine attenuate need for REM sleep in rats. Radulovacki M, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):371-5

Phenoxybenzamine for benign prostatic obstruction. Review of 200 cases. Caine M, et al. **Urology** 1981 Jun;17(6):542-6

[Use of drugs to encourage emptying of neo-bladders] Perales L, et al. **Actas Urol Esp** 1981 Jan-Feb;5(1):59-62 (Eng. Abstr.) (Spa)

PHENYLALANINE

Use of aromatic amino acids as monitors of protein turnover. Williams IH, et al. **Am J Physiol** 1981 Jun;240(6):E677-81

Cross-tolerance between D-amino acids and morphine in mice. Filibeck U, et al. **Brain Res** 1981 May 11;212(1):227-9

[Phenylalanine burden in endogenous psychoses] Uebelhack R, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1980 Oct;32(10):631-3 (Ger)

[Uptake of phenylalanine and tyrosine in the lymphocytes of uremic patients] Esposito R, et al. **Minerva Nefrol** 1980 Jul-Sep;27(3):417-9 (Eng. Abstr.) (Ita)

PHENYLPROPANOLAMINE

Effect of norephedrine locally applied to the vas deferens on semen quality of rabbits. Ratnasooriya WD, et al. **Indian J Exp Biol** 1981 Jan;19(1):20-5

Combined treatment with estriol and alpha-adrenergic stimulation in elderly female patients with urinary incontinence. A pilot study. Beisland HO, et al. **J Oslo City Hosp** 1981 Mar;31(3):39-42

Sustained-release drug delivery system I: Coated ion-exchange resin system for phenylpropanolamine and other drugs. Raghunathan Y, et al. **J Pharm Sci** 1981 Apr;70(4):379-84

Effects of amphetamine and phenylpropanolamine on food intake in rats with ventromedial hypothalamic or dorsolateral tegmental damage. Wellman PJ, et al. **Physiol Behav** 1980 Dec;25(6):819-27

PHENYTOIN

Antigranulocyte antibodies and deranged immune function associated with phenytoin-induced serum sickness. Menitove JE, et al. **Am J Hematol** 1981;10(3):277-84

Phenytoin sodium solubility in three intravenous solutions. Pfeifle CE, et al. **Am J Hosp Pharm** 1981 Mar;38(3):358-62

Prediction of phenytoin dosage in relation to the variability of phenytoin plasma concentration. Van der Velde EA, et al. **Br J Clin Pharmacol** 1981 Jan;11(1):41-52

Effects of phenytoin on pyramidal neurons of the rat hippocampus. Hershkowitz N, et al. **Brain Res** 1981 Mar 16;208(2):487-92

Saturable binding of [3H]phenytoin to rat brain membrane fraction. Burnham WM, et al. **Can J Physiol Pharmacol** 1981 Apr;59(4):402-7

Metabolite interference in homogeneous enzyme immunoassay of phenytoin [letter] Aldwin L, et al. **Clin Chem** 1981 May;27(5):770-1

Effect of trifluoperazine, D600, and phenytoin on depolarization- and thyrotropin-releasing hormone-induced thyrotropin release from rat pituitary tissue. Fleckman A, et al. **Endocrinology** 1981 Jun;108(6):2072-7

New standards for phenytoin products. **FDA Drug Bull** 1981 Mar;11(1):4

Purification of phenytoin-binding site from the brain. Imazawa M, et al. **Folia Psychiatr Neurol Jpn** 1980;34(3):362

Modification of glybenclamide hypoglycaemia by phenytoin in rabbits. Singh RC, et al. **Indian J Exp Biol** 1981 Jan;19(1):54-6

Bioavailability in humans of solid dosage forms of phenytoin marketed in India. Baichwal AR, et al. **Indian J Med Res** 1980 Dec;72:916-9

In vivo and in vitro availability of commercial phenytoin formulations containing phenobarbitone. Shukla UA, et al. **Indian J Med Res** 1980 Dec;72:910-5

The effects of phenytoin on phenobarbitone and primidone metabolism. Lambie DG, et al. **J Neurol Neurosurg Psychiatry** 1981 Feb;44(2):148-51

Interactions among chloramphenicol, phenytoin, and phenobarbital in a pediatric patient. Powell DA, et al. **J Pediatr** 1981 Jun;98(6):1001-3

Prediction of phenytoin dosage requirements [letter] Sanders SW. **J Pediatr** 1981 May;98(5):856-7

Anticonvulsant potency of two deuterated analogues of phenytoin: 'DPH-5d and DPH-d5'. Dumont P, et al. **J Pharm Belg** 1981 Jan-Feb;36(1):21-6

Diphenylhydantoin enhances early adaptation in Aplysia giant neurons. Lewis DV Jr, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):41-5

Evidence for a synergistic interaction between phenytoin and phenobarbital in experimental animals. Masuda Y, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):805-11

Folic acid and phenytoin hyperplasia [letter] Inoue F, et al. **Lancet** 1981 Jul 11;2(8237):86

Separation of phenytoin and its metabolites by high-performance liquid chromatography. Chow SA, et al. **Life Sci** 1980 Dec 22-29;27(25-26):2477-82

Excessive frequency of phenytoin dosage [letter] Lane MJ, et al. **Med J Aust** 1981 Feb 21;1(4):191-2

Acute effects of phenytoin on peripheral nerve function in the rat. Marcus DJ, et al. **Muscle Nerve** 1981 Jan-Feb;4(1):48-50

Intravenous valproate: effects on plasma and saliva phenytoin levels. Pisani FD, et al. **Neurology (NY)** 1981 Apr;31(4):467-70

Phenytoin: plasma levels and behavioral changes associated with suppression of auditory evoked potentials in the cat. Faingold CL, et al. **Neuropharmacology** 1981 May;20(5):445-9

Effects of phenytoin on mouse cerebellar 5-hydroxytryptamine and norepinephrine. Fry BW, et al. **Neuropharmacology** 1981 Jun;20(6):623-5

Critical periods for diphenylhydantoin and phenobarbital administration during gestation. Gauron EF, et al. **Psychol Rep** 1980 Dec;47(3 Pt 2):1163-6

Maternal hyperoxia greatly reduces the incidence of phenytoin-induced cleft lip and palate in A/J mice. Millicovsky G, et al. **Science** 1981 May 8;212(4495):671-2

A comparison of plasma phenytoin level determinations by EMIT and gas-liquid chromatography in patients with renal insufficiency. Nandedkar AK, et al. **Ther Drug Monit** 1980;2(4):427-30

The effect of diethylstilbestrol treatment on the metabolism and biliary excretion of [14C]phenytoin in the isolated perfused rat liver. Montgomery C, et al. **Toxicol Appl Pharmacol** 1981 May;58(3):510-9

[Protection of the myocardium and coronary artery circulation (5)] Hirano T. **Kokyu To Junkan** 1980 Oct;28(10):1102 (Jpn)

PHOBIC DISORDERS

The treatment of phobic anxiety by zimelidine. Evans L, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):342-5

A pilot study of the effect of the 5-HT-uptake inhibitor, zimelidine, on phobic anxiety. Koczkas S, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):328-41

Differential diagnosis and treatment of panic attacks and phobic states. Liebowitz MR, et al. **Annu Rev Med** 1981;32:583-99 (46 ref.)

Exposure treatments for focal phobias. A review. Linden W. **Arch Gen Psychiatry** 1981 Jul;38(7):769-75 (49 ref.)

Phenelzine and exposure in the treatment of phobias. Solyom C, et al. **Biol Psychiatry** 1981 Mar;16(3):239-47

Agoraphobia: the 'what if' syndrome. Fier M. **J Med Soc NJ** 1981 Apr;78(4):286-8

Psychotropic drugs and behaviour therapy. Stern R. **Practitioner** 1981 Jan;225(1351):21-5

PHYSOSTIGMINE

[Effect of cholinergic factors on the state of erythrocyte membrane proteins of animals] Savina LS, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):153-5 (Eng. Abstr.) (Rus)

PILOCARPINE

Effects of cholinergic stimulation on levels and fatty acid composition of diacylglycerols in mouse pancreas. Banschbach MW, et al. **Biochim Biophys Acta** 1981 Jan 26;663(1):34–45

Effects of pilocarpine and paracentesis on occluding junctions between the nonpigmented ciliary epithelial cells. Ohnishi Y, et al. **Exp Eye Res** 1981 May;32(5):635–47

Effect of drugs interacting with adrenergic mechanisms and of adrenalectomy on pilocarpine-induced salivation in mice. Jha RJ, et al. **Indian J Med Res** 1980 Dec;72:923–6

Analysis of pilocarpine and isopilocarpine in ophthalmic solutions by normal-phase high-performance liquid chromatography. Dunn DL, et al. **J Pharm Sci** 1981 Apr;70(4):446–9

Quantitative determination of pilocarpine, isopilocarpine, pilocarpic acid, and isopilocarpic acid in clinical ophthalmic pilocarpine formulations by reversed-phase liquid chromatography. Noordam A, et al. **J Pharm Sci** 1981 Jan;70(1):96–7

[Stability and determination of pilocarpine in eyedrops] Jacob M, et al. **Pharm Acta Helv** 1981;56(2):59–63 (Fre)

[Effects of pilocarpine and carteolol, a new beta-adrenergic blocking agent on human aqueous humor dynamics (author's transl)] Araie M, et al. **Nippon Ganka Gakkai Zasshi** 1980 Dec 10;84(12):2085–91 (Eng. Abstr.) (Jpn)

PITUITARY HORMONE RELEASING HORMONES

Effect of calcium and potassium on basal and gonadotrophin-releasing hormone (GnRH) stimulated release of luteinizing hormone (LH). Zolman JC, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):26–32

Ovarian response to gonadotropin-releasing hormone in postpartum dairy cows. Garverick HA, et al. **Am J Vet Res** 1980 Oct;41(10):1582–5

Immunohistochemical localization of gonadotropin-releasing hormone (GnRH) in the brain and infundibulum of the sheep. Dees WL, et al. **Cell Tissue Res** 1981;215(1):181–91

Degradation of gonadotropin-releasing hormone by anterior pituitary enzymes. Hazum E, et al. **FEBS Lett** 1981 May 18;127(2):273–6

Effects of neonatal administration of gonadotropins-releasing hormone (Gn-RH) on the testis of mice. Unnithan RR, et al. **Indian J Exp Biol** 1981 Jan;19(1):12–5

[Trials to induce ovulation with Berlin-Chemie Gn-RH vet. in prepuberal gilts] Brüssow KP, et al. **Arch Exp Veterinaermed** 1981;35(2):285–90 (Eng. Abstr.) (Ger)

PITUITARY HORMONES

Hypothalamic hypophysiotropic hormones and neurotransmitter regulation: current views. Meites J, et al. **Annu Rev Pharmacol Toxicol** 1981;21:295–322 (160 ref.)

Specific stimulation of steroidogenesis in rat adrenal zona glomerulosa cells by pituitary peptides. Vinson GP, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):65–72

Regulation of tryptophan-niacin metabolism by hormones. Sanada H, et al. **J Nutr Sci Vitaminol (Tokyo)** 1980;26(6):617–27

PITUITARY HORMONES, ANTERIOR

New perspectives in neuropeptides. Biosynthesis from large precursors. The pro-opio-melanocortin model in the pars intermedia. Chrétien M, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):699–713

Concentrations of pituitary, gonadal and adrenal hormones in serum of laying and broody white rock hens (Gallus domesticus). Bedrak E, et al. **J Endocrinol** 1981 May;89(2):197–204

Serum concentrations of prolactin, luteinizing hormone, growth hormone, corticosterone, progesterone, testosterone and oestradiol in relation to broodiness in domestic turkeys (Meleagris gallopavo). Harvey S, et al. **J Endocrinol** 1981 May;89(2):187–95

Chemistry and biosynthesis of pro-opiomelanocortin. ACTH, MSH's, endorphins and their related peptides. Chrétien M, et al. **Mol Cell Biochem** 1981 Jan 28;34(2):101–27 (232 ref.)

Characterisation of the pro opiocortin family of peptides in human cerebrospinal fluid McLoughlin L, et al. **Neuroendocrinology** 1981 Apr;32(4):209–12

Opiocortin peptides: localization, source and avenues of transport. de Kloet ER, et al. **Pharmacol Ther** 1981;12(2):321–51 (193 ref.)

[Different effects of tricyclic (clomipramine and amitriptyline) and tetracyclic (maprotiline) antidepressors on the release of thyroid stimulating hormone, prolactin and growth hormone to thyrostimulating releasing hormone in patients with psychoaffective disorders (author's transl)] Schlienger JL, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):584–99 (Eng. Abstr.) (Fre)

PRAZEPAM

Concentrations of N-descyclopropylmethylprazepam in whole-blood, plasma, and milk after administration of prazepam to humans. Brodie RR, et al. **Biopharm Drug Dispos** 1981 Jan-Mar;2(1):59–68

PREDNISONE

A study on the release of prednisone from new ointment bases containing various additives. Attia MA, et al. **Pharmazie** 1981;36(1):21–3

PROBLEM SOLVING

Role of the neostriatal dopaminergic activity in sequencing and selecting behavioural strategies: facilitation of processes involved in selecting the best strategy in a stressful situation. Cools AR. **Behav Brain Res** 1980 Oct;1(5):361–78

PROGESTERONE

Influence of phenobarbital, chlorpromazine, progesterone and phenylbutazone on the biliary cholesterol excretion in rats. Barth A, et al. **Acta Biol Med Ger** 1980;39(11-12):1217–26

Effects of ovarian steroids and pregnancy on adrenergic nerves of uterus and oviduct. Marshall JM. **Am J Physiol** 1981 May;240(5):C165–74 (83 ref.)

Negative feedback effects of progesterone correlated with changes in hypothalamic norepinephrine and dopamine turnover rates, median eminence luteinizing hormone-releasing hormone, and peripheral plasma gonadotropins. Rance N, et al. **Endocrinology** 1981 Jun;108(6):2194–9

Effects of estradiol and progesterone on catecholamine turnover rates in discrete hypothalamic regions in ovariectomized rats. Wise PM, et al. **Endocrinology** 1981 Jun;108(6):2186–93

Deoxycorticosterone biosynthesis from progesterone in kidney tissue of the human fetus. Winkel CA, et al. **J Clin Endocrinol Metab** 1981 Jul;53(1):10–5

Regulation of Ca2+ and cyclic AMP during the first meiotic division in amphibian oocytes by progesterone. Kostellow AB, et al. **J Cyclic Nucleotide Res** 1980;6(5):347–58

Inhibition of HCG-induced cyclic AMP accumulation and steroidogenesis in rat luteal cells by an LHRH agonist. Massicotte J, et al. **J Steroid Biochem** 1981 Mar;14(3):239–42

Effect of progesterone therapy on the responses of the isolated rat stomach fundus strip preparations to 5-hydroxytryptamine and acetylcholine. Qayum A, et al. **JPMA** 1981 Apr;31(4):84–8

Adrenal steroids and extinction behavior: antagonism by progesterone, deoxycorticosterone and dexamethasone of a specific effect of corticosterone. Bohus B, et al. **Life Sci** 1981 Jan 26;28(4):433–40

A dopamine agonist stimulates progesterone secretion from adrenal gland. Kalra SP, et al. **Life Sci** 1981 Mar 30;28(13):1467–9

Deoxycorticosterone biosynthesis in human kidney: potential for formation of a potent mineralocorticosteroid in its site of action. Winkel CA, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7069–73

[Induction of lactation in cattle after short-term hormonal treatment] Manunta G, et al. **Boll Soc Ital Biol Sper** 1981 Jan 30;57(2):172–8 (Eng. Abstr.) (Ita)

PROLACTIN

Serum prolactin and thyrotrophin responses to thyrotrophin-releasing hormone at different times of the day in normal women. Pérez-López FR, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):7–11

The effect of dopamine on prolactin cells in vivo. Wurchol JB, et al. **Acta Med Pol** 1980;21(4):403–4

Influence of estrogens on tuberoinfundibular and striatal dopaminergic systems in the rat. Labrie F, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):658–73

Haloperidol and droperidol treatment in schizophrenics. Clinical application of the 'prolactin-model'. Langer G, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):574–83

Effect of antidepressants, lithium and electroconvulsive treatment on rat serum prolactin levels. Meltzer HY, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):100–21

Immunoreactive endorphin peptides and prolactin in umbilical vein and maternal blood. Kimball CD, et al. **Am J Obstet Gynecol** 1981 May 15;140(2):157–64

Resumption of prolactin secretion after dopaminergic inhibition: differential effects of dopamine and its agonists. Woolf PD. **Am J Physiol** 1981 Jun;240(6):E700–4

The effect of amoxapine and imipramine on serum prolactin levels. Cooper DS, et al. **Arch Intern Med** 1981 Jul;141(8):1023–5

Exaggerated hyperprolactinemia in response to thiothixene [letter] Ash PR, et al. **Arch Neurol** 1981 Aug;38(8):534–5

Paradoxical effects of D-Trp6-LHRH in immature female rats correlated with changes in ACTH, prolactin, and corticosterone levels. Nekola MV, et al. **Biol Reprod** 1981 Apr;24(3):505–11

Role of the ovary in controlling luteinizing hormone, follicle stimulating hormone, and prolactin secretion during and after lactation in pigs. Stevenson JS, et al. **Biol Reprod** 1981 Mar;24(2):341–53

Inhibition of LH and prolactin release in the cycling rat following inhibition of dopamine-beta-hydroxylase. Voogt JL, et al. **Brain Res** 1981 Mar 30;209(2):411-9

Pituitary function in normoprolactinaemic infertile men receiving bromocriptine. Glatthaar C, et al. **Clin Endocrinol (Oxf)** 1980 Nov; 13(5):455-9

Two new dopamine agonists that are long acting in vivo but short acting in vitro. Grossman A, et al. **Clin Endocrinol (Oxf)** 1980 Dec; 13(6):595-9

Effect of propranolol treatment on serum prolactin level in schizophrenic patients. Elizur A, et al. **Commun Psychopharmacol** 1980;4(3):203-6

Changes in ovarian 3 alpha-androstanediol response to human chorionic gonadotropin during puberty in the rat: modulatory role of prolactin. Advis JP, et al. **Endocrinology** 1981 Jul;109(1):223-8

Prolactin regulation of cytological differentiation of mammary epithelial cells in periparturient cows. Akers RM, et al. **Endocrinology** 1981 Jul; 109(1):31-40

Prolactin regulation of milk secretion and biochemical differentiation of mammary epithelial cells in periparturient cows. Akers RM, et al. **Endocrinology** 1981 Jul;109(1):23-30

A serotonergic mechanism of the prolactin-stimulating action of metoclopramide. Fang VS, et al. **Endocrinology** 1981 May; 108(5):1622-7

Hormonal control of growth in the infant rat. Glasscock GF, et al. **Endocrinology** 1981 Jul;109(1):176-84

Dopamine in hypophysial portal plasma and prolactin in systemic plasma of rats treated with 5-hydroxytryptamine. Pilotte NS, et al. **Endocrinology** 1981 Jun;108(6):2137-41

The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone-releasing hormone and the effect of prolactin on catecholamine turnover. Selmanoff M. **Endocrinology** 1981 May;108(5):1716-22

Comparison of acute effects of dynorphin and beta-endorphin on prolactin release in the rat. Van Vugt DA, et al. **Endocrinology** 1981 May; 108(5):2017-8

Effects of prolactin and bromocriptine on the luteal phase in infertile women. Fredricsson B, et al. **Eur J Obstet Gynaecol Reprod Biol** 1981 Apr;11(5):319-33

Possible role of prolactin in the modification of medial basal hypothalamic glutamic acid decarboxylase activity. Prato A, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):169-72

Effect of apomorphine hydrochloride administration on serum concentrations of prolactin and growth hormone in cattle. Gorewit RC. **Experientia** 1981 Feb 15;37(2):204-6

Effects of hyperprolactinemia and bromocriptine on the human endometrium. Nunley WC Jr, et al. **Fertil Steril** 1981 Apr; 35(4):479-80

Prolactin inhibits the induction of its own renal receptors in Rana catesbeiana tadpoles. White BA, et al. **Gen Comp Endocrinol** 1981 Jan; 43(1):30-8

Cell population kinetics in tadpole limb epidermis during thyroxine-induced, spontaneous, and prolactin-inhibited metamorphosis. Wright ML, et al. **Gen Comp Endocrinol** 1981 Apr; 43(4):451-61

Ergot drugs suppress plasma prolactin and lactation but not aggression in parturient mice. Mann M, et al. **Horm Behav** 1980 Dec; 14(4):319-28

Growth hormone, prolactin, and growth responses in hyperkinetic males treated with d-amphetamine. Greenhill LL, et al. **J Am Acad Child Psychiatry** 1981 Winter;20(1):84-103

Regulation of pituitary function and prolactin production in the GH4 cell line by vitamin D. Murdoch GH, et al. **J Biol Chem** 1981 Apr 25;256(8):4050-3

Diurnal rhythm of plasma immunoreactive beta-endorphin and its relationship to sleep stages and plasma rhythms of cortisol and prolactin. Dent RR, et al. **J Clin Endocrinol Metab** 1981 May;52(5):942-7

The effect of histamine and H1 and H2 receptors on prolactin and luteinizing hormone release in humans: sex differences and the role of stress. Pontiroli AE, et al. **J Clin Endocrinol Metab** 1981 May; 52(5):924-8

Thyrotropin-releasing hormone stimulation of prolactin release from clonal rat pituitary cells: evidence for action independent of extracellular calcium. Gershengorn MC, et al. **J Clin Invest** 1981 Jun; 67(6):1769-76

Partial remission of hyperprolactinemic amenorrhea after bromocriptine-induced pregnancy. Campagnoli C, et al. **J Endocrinol Invest** 1981 Jan-Mar;4(1):85-91

Serum prolactin concentrations in mangabey (Cercocebus atys lunulatus) and patas (Erythrocebus patas) monkeys in response to stress, ketamine, TRH, sulpiride and levodopa. Aidara D, et al. **J Reprod Fertil** 1981 May;62(1):165-72

Autonomous prolactin secretion in schizophrenic male on long-term neuroleptic therapy [letter] Semple CG, et al. **Lancet** 1981 Jul 11; 2(8237):103

Slow decline of plasma drug and prolactin levels after discontinuation of chronic treatment with depot neuroleptics [letter] Wistedt B, et al. **Lancet** 1981 May 23;1(8230):1163

Differential effects of cannabinoid exposure and stress on plasma prolactin, growth hormone and corticosterone levels in male mice. Dalterio SL, et al. **Life Sci** 1981 Feb 16;28(7):761-6

Thyroid hormones are required for daily rhythms of plasma corticosterone and prolactin concentration. Ottenweller JE, et al. **Life Sci** 1981 Mar 2;28(9):1033-40

Effect of prolactin and prostaglandins on the stimulation of prolactin binding sites in the male rat liver. Barkey RJ, et al. **Mol Cell Endocrinol** 1981 Feb;21(2):129-38

Dopaminergic control of prolactin mRNA accumulation in the pituitary of the male rat. Brocas H, et al. **Mol Cell Endocrinol** 1981 Apr; 22(1):25-30

Prolactin and the regulation of adipose-tissue metabolism during lactation in rats. Flint DJ, et al. **Mol Cell Endocrinol** 1981 May;22(2):265-75

Stimulation of prolactin secretion by neuroleptics in rats with medial basal hypothalamic lesions. Cheung CY, et al. **Neuroendocrinology** 1981 Jun; 32(6):370-4

Dopamine levels in hypophysial stalk plasma and prolactin levels in peripheral plasma of the lactating rat: effects of a simulated suckling stimulus. de Greef WJ, et al. **Neuroendocrinology** 1981 Apr; 32(4):229-33

GABA and muscimol inhibit the release of prolactin from dispersed rat anterior pituitary cells. Grossman A, et al. **Neuroendocrinology** 1981 Mar;32(3):145-9

Effects of the interaction between methysergide and clonidine on growth hormone and prolactin secretion in normal man. Agnati LF, et al. **Neurosci Lett** 1981 Feb 6;21(3):333-8

Experimental hyperprolactinemia and hypoprolactinemia and human chorionic gonadotropin during early pregnancy. Viinikka L, et al. **Obstet Gynecol** 1981 Apr;57(4):441-3

Interaction of morphine with the cholinergic system on prolactin release. Fanjul LF, et al. **Proc Soc Exp Biol Med** 1981 Apr;166(4):542-5

Differential prolactin responses to haloperidol and TRH in normal adult men. Hays SE, et al. **Psychoneuroendocrinology** 1981;6(1):45-52

Clozapine: plasma levels and prolactin response. Kane JM, et al. **Psychopharmacology (Berlin)** 1981;73(2):184-7

Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge. Kolakowska T, et al. **Psychopharmacology (Berlin)** 1981;72(3):283-5

Effect of 5,7-dihydroxytryptamine on serotonergic control of prolactin secretion and behavior in rats. Kuhn CM, et al. **Psychopharmacology (Berlin)** 1981;73(2):188-93

LH and prolactin in estrogenized female rats: response to LHRH. Vaticón MD, et al. **Rev Esp Fisiol** 1980 Dec;36(4):371-6

[Comparative evolution of prolactin plasma levels during antidepressant treatment (author's transl)] Vandel B, et al. **Therapie** 1981 Jan-Feb; 36(1):87-94 (Eng. Abstr.) (Fre)

[Evaluation of motor behavior in conditions of hyperprolactinemia] Rampello L, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):297-301 (Eng. Abstr.) (Ita)

[Role of the prostaglandin system in the monoaminergic control of prolactin release in the rat] Costa G, et al. **Boll Soc Ital Biol Sper** 1979 Aug 15;55(15):1492-7 (Eng. Abstr.) (Ita)

[Clinical significance of prolactin in amenorrheas] Garzarelli S, et al. **Minerva Ginecol** 1981 Apr;33(4):315-20 (Eng. Abstr.) (Ita)

[Use of dopaminergic drugs (pyridoxine, 2-bromo-alpha-ergocriptine, piribedil) in blocking lactation] Lo Dico G, et al. **Minerva Ginecol** 1980 Sep;32(9):771-9 (Eng. Abstr.) (Ita)

[A study on the significance of bromocriptine (CB-154) administration in normoprolactinemic anovulatory women (author's transl)] Ishimaru T, et al. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Oct; 32(10):1583-90 (Eng. Abstr.) (Jpn)

[Influences of hypothalamus prolactin inhibiting factor and releasing factors and pineal gland on pituitary prolactin secreting functions (author's transl)] Takahashi K, et al. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Sep;32(9):1249-56 (Jpn)

[Prolactin secretion during normal pregnancy and puerperium, particularly with regard to nursing (author's transl)] Wada Y. **Nippon Sanka Fujinka Gakkai Zasshi** 1980 Jul;32(7):891-8 (Eng. Abstr.) (Jpn)

[Adrenal cortical androgen function in women suffering from sterility and hyperprolactinemia] Pobedinskii NM, et al. **Akush Ginekol (Mosk)** 1981 Feb;(2):10-2 (Eng. Abstr.) (Rus)

[Prolactin secretion inhibition as affected by leucine enkephalin] Iudaev NA, et al. **Dokl Akad Nauk SSSR** 1981;256(2):500-2 (Rus)

PROMAZINE

The metabolism of promazine and acetylpromazine in the horse. Dewey EA, et al. **Drug Metab Dispos** 1981 Jan-Feb;9(1):30-6

PROMETHAZINE

A comparative study of the interaction of chlorpromazine, trifluoperazine, and promethazine with mouse brain tubulin. Rao AG, et al. **Mol Pharmacol** 1981 Mar;19(2):295-301

PROPANEDIOLS

Toxicological assessment of heat transfer fluids proposed for use in solar energy applications, II. Marshall TC, et al. **Toxicol Appl Pharmacol** 1981 Mar 30;58(1):31–8

PROPRANOLOL

DL-propranolol and chlorpromazine following admission for schizophrenia. A controlled comparison. Yorkston NJ, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):13–27

Propranolol: the preferred palliation for tetralogy of Fallot. Garson A Jr, et al. **Am J Cardiol** 1981 May;47(5):1098–104

Shortened platelet survival time and enhanced heart rate responses after abrupt withdrawal of propranolol from normal subjects. Goldstein RE, et al. **Am J Cardiol** 1981 May;47(5):1115–22

Treatment of diazepam withdrawal syndrome with propranolol. Abernethy DR, et al. **Ann Intern Med** 1981 Mar;94(3):354–5

Antagonism of calmodulin by local anesthetics, mepacrine, and propranolol. Volpi M, et al. **Ann NY Acad Sci** 1980;356:441–2

Effect of adrenoceptor blocker and MAOI on postcoital utero-oviductal contractility, sperm transport, and sperm attachment to eggs in rabbits. Marsafy YM, et al. **Arch Androl** 1981 Jun;6(4):307–16

Bioavailability of propranolol in the dog. Tse FL, et al. **Arch Int Pharmacodyn Ther** 1980 Dec;248(2):180–9

The effect of propranolol on the osmotic fragility of red cells and liposomes and the influence of the drug on glycerol transport across the membrane of red cells. Surewicz KW, et al. **Biochem Pharmacol** 1981 Apr;30(8):839–42

Interaction of propranolol with model phospholipid membranes. Monolayer, spin label and fluorescent spectroscopy studies. Surewicz WK, et al. **Biochim Biophys Acta** 1981 May 6;643(2):387–97

Bioavailability of sustained release propranolol formulations. McAinsh J, et al. **Biopharm Drug Dispos** 1981 Jan–Mar;2(1):39–48

A propranolol radioimmunoassay and its use in the study of its pharmacokinetics following low doses. Mould GP, et al. **Biopharm Drug Dispos** 1981 Jan–Mar;2(1):49–57

Inhibition of the plasma cholinesterase variants by propranolol. Whittaker M, et al. **Br J Anaesth** 1981 May;53(5):511–6

Inhibitory effects of propranolol on the calcium current of Helix neurones. Akaike N, et al. **Br J Pharmacol** 1981 Jun;73(2):431–4

Inhibition of lymphocyte capping and transformation by propranolol and related compounds. Anderton BH, et al. **Br J Pharmacol** 1981 Jan; 72(1):69–74

Influence of cimetidine on pharmacokinetics of propranolol. Heagerty AM, et al. **Br Med J [Clin Res]** 1981 Jun 13;282(6280):1917–9

Reduction of first-pass hepatic clearance of propranolol by food. McLean AJ, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):31–4

Propranolol and sotalol metabolism after a drinking party. Sotaniemi EA, et al. **Clin Pharmacol Ther** 1981 Jun;29(6):705–10

The effect of prolonged administration of propranolol and timolol on the growth and the heart of growing rabbits. Evemy KL, et al. **Clin Sci** 1981 Jan;60(1):33–40

Effect of propranolol treatment on serum prolactin level in schizophrenic patients. Elizur A, et al. **Commun Psychopharmacol** 1980;4(3):203–6

Propranolol and the respiratory, circulatory, and ECG responses to high altitude. Boutellier U, et al. **Eur J Applied Physiol** 1981;46(2):105–19

Exercise-induced release of pancreatic polypeptide and its inhibition by propranolol: evidence for adrenergic stimulation. Feurle GE, et al. **Eur J Clin Invest** 1980 Jun;10(3):249–51

The effect of a single dose of propranolol on human erythrocytes in vivo. Reinhart W, et al. **Eur J Clin Invest** 1981 Feb;11(1):65–8

Relaxation of isolated dog coronary artery induced by propranolol. Sakanashi M, et al. **Eur J Pharmacol** 1981 Mar 5;70(1):83–5

Effects of DL-propranolol on the thermoregulatory responses of rats at different ambient temperatures. Lin MT, et al. **Experientia** 1981 Apr 15;37(4):370–1

Inhibition of antigen-induced and anti-immunoglobulin-induced capping by hydrocortisone and propranolol. Ashman RF, et al. **Immunopharmacology** 1981 Feb;3(1):41–7

Separation of enantiomeric amines by ion-pair chromatography. Pettersson C, et al. **J Chromatogr** 1981 Jan 16;204:179–83

Chronic dog intestinal loop model for studying drug absorption as exemplified by beta-adrenoreceptor blocking agents, atenolol and propranolol. Taylor DC, et al. **J Pharm Sci** 1981 May;70(5):516–21

Influence of the route of administration on the mean hepatic extraction ratio of propranolol in the rat. Suzuki T, et al. **J Pharmacobiodyn** 1980 Nov;3(11):603–11

Propranolol as cause of watery nasal secretion [letter] Malm L. **Lancet** 1981 May 2;1(8227):1006

Benzodiazepine withdrawal symptoms and propranolol. Tyrer P, et al. **Lancet** 1981 Mar 7;1(8219):520–2

Increased plasma protein binding of propranolol in rabbits with acute renal failure. Fichtl B, et al. **Life Sci** 1981 Jan 5;28(1):31–5

Effects of propranolol on the adenylate cyclase activities in the arteries and ventricle of dog. Murthy VV. **Life Sci** 1980 Dec 22–29; 27(25–26):2645–8

Self-poisoning with propranolol. Tynan RF, et al. **Med J Aust** 1981 Jan 24;1(2):82–3

The inhibition by (+/−)-propranolol of the positive inotropic effects of (+/−)-isoprenaline and (−)-noradrenaline. Competitive antagonism and saturable uptake. Ebner F. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):96–107

Propranolol differentially blocks the methamphetamine-induced depression of tryptophan hydroxylase in various rat brain regions. Bakhit C, et al. **Neurosci Lett** 1981 Apr 9;23(1):99–103

Local anesthetics, mepacrine, and propranolol are antagonists of calmodulin. Volpi M, et al. **Proc Natl Acad Sci USA** 1981 Feb; 78(2):795–9

Dextro-propranolol in schizophrenia. Hirsch SR, et al. **Prog Neuropsychopharmacol** 1980;4(6):633–7

Effects of propranolol on the locomotor stimulation induced by activation of postsynaptic catecholamine receptors. Hallberg H, et al. **Psychopharmacology (Berlin)** 1981;72(3):227–31

The lack of effect of propranolol on the intestinal phase secretion in the dog. Grabner P, et al. **Scand J Gastroenterol** 1981;16(1):65–70

[Beta-adrenergic receptors and paradoxical sleep in the rat] Lanfumey L, et al. **C R Acad Sci [D] (Paris)** 1981 Mar 2;292(9):645–7 (Eng. Abstr.) **(Fre)**

[Possible effects of propranolol on the estrous cycle of the rat] Bruguerolle B, et al. **C R Soc Biol (Paris)** 1981;175(1):87–90 (Eng. Abstr.) **(Fre)**

[Use of the beta receptor blockader propranolol (Obsidan), in oral surgery] Neumann HJ, et al. **Stomatol DDR** 1980 Dec;30(12):908–12 (Eng. Abstr.) **(Ger)**

[Effect of the beta-receptor blockers propranolol and talinolol on glucose-orciprenaline induced insulin secretion, glucose tolerance and the behavior of nonesterified free fatty acids in metabolically normal probands.] Möricke R, et al. **Z Gesamte Inn Med** 1981 Mar; 36(5):263–7 (Eng. Abstr.) **(Ger)**

[Preliminary study of the combined administration of furosemide and propranolol. Evaluation of serum propranolol] Volpe M, et al. **Boll Soc Ital Cardiol** 1978;23(6):1001–5 **(Ita)**

[Behavior of the number of lysosomes in the placenta of pregnant rats subjected to acute stress and previously treated with 1-isopropylamino-3-(1-naphthyloxy)-2-propanol hydrochloride] Kulay MN, et al. **Rev Paul Med** 1980 Nov–Dec;96(5–6):96–9 (Eng. Abstr.) **(Por)**

PROSTAGLANDINS

Effect of prostaglandin synthesis inhibition on the central activity of noradrenaline in rats. Brus R, et al. **Acta Physiol Pol** 1981 Jan–Feb; 32(1):47–51

Evolution of ideas on the role of prostaglandins in inflammation. Grygiewski RJ. **Agents Actions [Suppl]** 1980;7:247–51 (24 ref.)

Effects of cannabinoids and female exposure on the pituitary-testicular axis in mice: possible involvement of prostaglandins. Dalterio S, et al. **Biol Reprod** 1981 Mar;24(2):315–22

Effects of nerve stimulation and of administration of noradrenaline or potassium chloride upon the release of prostaglandins, I2, E2, and F2 alpha from te perfused mesenteric arterial bed of the rabbit. Pipili E, et al. **Br J Pharmacol** 1981 Jan;72(1):89–93

Prostaglandin involvement in contractions evoked in rabbit detrusor by field stimulation and by adenosine 5'-triphosphate. Downie JW, et al. **Can J Physiol Pharmacol** 1981 Mar;59(3):253–60

Pharmacological studies of the involvement of hypothalamic prostaglandins in the regulation of thyrotropin secretion. Wright KC, et al. **Environ Health Perspect** 1981 Apr;38:83–8

Glomerulopressin in dogs' mesenteric blood flow and prostaglandins. del Castillo E, et al. **Horm Metab Res** 1981 Feb;13(2):126–7

Participation of prostaglandins in the vasodepressor effect of substance P. Pals DT, et al. **J Pharm Pharmacol** 1981 Feb;33(2):110–1

Effect of PGD2, PGE2 PGF2 alpha and PGI on blood pressure, heart rate and plasma catecholamine responses to spinal cord stimulation in the rat. Feuerstein G, et al. **Prostaglandins** 1981 Feb;21(2):189–206

6-keto-PGE1 exhibits more potent bronchodilatory activity in the cat than its precursor, PGI2. Spannhake EW, et al. **Prostaglandins** 1981 Feb;21(2):267–75

Influence of prostaglandins on vasoconstrictor responses in the hindquarters vascular bed of the cat. Lippton HL, et al. **Prostaglandins Med** 1981 Feb;6(2):183–202

The mechanism of the inhibitory effect of protease inhibitors on platelet aggregation and cellular synthesis of prostaglandins. I. The effect on the release of arachidonic acid from phospholipids. Kosaki G, et al. **Thromb Res** 1980 Dec 1–15;20(5–6):587–98

[Role of the prostaglandin system in the monoaminergic control of prolactin release in the rat] Costa G, et al. **Boll Soc Ital Biol Sper** 1979 Aug 15;55(15):1492–7 (Eng. Abstr.) **(Ita)**

[Changes in the morphofunctional status of the capillary system of the cerebral cortex in cats exposed to adrenergic stimulation while prostaglandin biosynthesis is inhibited] Gabrielian ES, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):173–5 (Eng. Abstr.) **(Rus)**

[Reactions of an identified edible snail neuron to application of peptides, mediators, prostaglandins, and cyclic nucleotides] Osipovskii SA, et al. **Neirofiziologiia** 1981;13(1):80-7 (Eng. Abstr.) (Rus)

PSYCHIATRIC STATUS RATING SCALES

The Hamilton depression scale. Evaluation of objectivity using logistic models. Bech P, et al. **Acta Psychiatr Scand** 1981 Mar;63(3):290-9

PSYCHIATRY

An interdisciplinary comparison of consultation outcomes. Psychiatry vs cardiology. Popkin MK, et al. **Arch Gen Psychiatry** 1981 Jul; 38(7):821-5

Neuropsychopharmacology research in psychiatry at Yale University. Bowers M Jr, et al. **Psychopharmacol Bull** 1981 Apr;17(2):17-39

Daytime effects of L-tryptophan [proceedings] Spinweber CL. **Psychopharmacol Bull** 1981 Jan;17(1):81-2

PSYCHOLOGY, COMPARATIVE

Comparative psychopharmacology. Lagerspetz KY. **Curr Dev Psychopharmacol** 1981;6:1-43 (182 ref.)

PSYCHOPATHOLOGY

[Documentation of psychopathological data in psychopharmacotherapy] Kühne GE, et al. **Agressologie** 1980;21(A):1-5 (Eng. Abstr.) (Ger)

PSYCHOPHARMACOLOGY

Comparative psychopharmacology. Lagerspetz KY. **Curr Dev Psychopharmacol** 1981;6:1-43 (182 ref.)

The psychopharmacology of aggression and social behavior. Symposium of the International Society for Research on Aggression. July 12, 1980, Groningen, The Netherlands. **Pharmacol Biochem Behav** 1981; 14 Suppl 1:1-124

A simple system for control of the continuous performance test in psychopharmacological research. Aman MC, et al. **Prog Neuropsychopharmacol** 1980;4(6):621-6

Research center reports. Current research activities in India. Bagadia VN. **Psychopharmacol Bull** 1981 Apr;17(2):14-6

Neuropsychopharmacology research in psychiatry at Yale University. Bowers M Jr, et al. **Psychopharmacol Bull** 1981 Apr;17(2):17-39

Department of Health and Human Services regulations affecting psychopharmacology research. Reatig N. **Psychopharmacol Bull** 1981 Apr;17(2):56-65

On the use of repeated measures designs in psychopharmacology. Vitaliano PP, et al. **Psychopharmacology (Berlin)** 1981;72(3):247-9

[2d Czechoslovakian Symposium of Psychopharmacology. Smolenice, 28-30 September 1977] **Agressologie** 1980;21(A):1-69 (Ger)

PSYCHOSES, SUBSTANCE-INDUCED

A primate analogue of amphetamine-induced behaviors in humans. Haber S, et al. **Biol Psychiatry** 1981 Feb;16(2):181-96

Stimulant-induced psychosis: an evaluation of animal methods. Segal DS, et al. **Essays Neurochem Neuropharmacol** 1981;5:95-129 (123 ref.)

PSYCHOTHERAPY

Treatment of the seriously disturbed adolescent. Miller D. **Adolesc Psychiatry** 1980;8:469-81

Psychotherapeutic drug recommendations based on the Mini-Mult. Siddall JW, et al. **Psychol Rep** 1980 Dec;47(3 Pt 2):1283-8

[Cooperation of pharmacotherapy and psychotherapy: an experimental illustration] Caplová T, et al. **Agressologie** 1980;21(A):37-9 (Eng. Abstr.) (Ger)

[Suicide prevention in psychoses and combined pharmacotherapy and psychotherapy] Richter H. **Agressologie** 1980;21(A):41-3 (Ger)

PSYCHOTIC DISORDERS

Antidepressants: old drugs, new uses. Harris E. **Am J Nurs** 1981 Jul; 81(7):1308-9

Antipsychotic medications. Harris E. **Am J Nurs** 1981 Jul; 81(7):1316-23

Auditory brain stem evoked responses in hospitalized patients undergoing drug treatment or ECT. Small JG, et al. **Biol Psychiatry** 1981 Mar; 16(3):287-90

Clinical processes and central dopaminergic activity in psychotic disorders. Bowers MB Jr, et al. **Commun Psychopharmacol** 1980; 4(3):177-83

The effects of neuroleptic drugs on the social interactions of hospitalized psychotic patients. Rosen AJ, et al. **J Nerv Ment Dis** 1981 Apr; 169(4):240-3

Classification of endorphins/enkephalins in brain physiology and pathology (based on EEG and clinical study of synthetically-modified methionine-enkephalin). Roubicek J, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):507-18

A symptom profile analysis of antipsychotic drug treatment: nonparametric multidimensional technique. Shalif I, et al. **Psychiatry Res** 1981 Feb;4(1):1-12

The pharmacological treatment of schizoaffective disorder-depressed: a review of the literature [proceedings] Spiker DG. **Psychopharmacol Bull** 1981 Jan;17(1):75-8

Concentrations of chlorpromazine and two of its active metabolites in plasma and cerebrospinal fluid of psychotic patients treated with fixed drug doses. Wode-Helgodt B, et al. **Psychopharmacology (Berlin)** 1981; 73(1):55-62

[Suicide prevention in psychoses and combined pharmacotherapy and psychotherapy] Richter H. **Agressologie** 1980;21(A):41-3 (Ger)

[Pharmacological treatment of psychiatric emergencies in general practice (author's transl)] Wildbolz A. **Praxis** 1981 Feb 3;70(6):211-4 (Eng. Abstr.) (Ger)

[Psychopathologic aspects of the course of idiopathic psychoses] Janzarik W. **Psychiatr Clin (Basel)** 1980;13(3-4):139-49 (Eng. Abstr.) (Ger)

[Phenylalanine burden in endogenous psychoses] Uebelhack R, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1980 Oct;32(10):631-3 (Ger)

QUINIDINE

Effects of chronic oral quinidine on left ventricular performance. O'Rourke RA, et al. **Am Heart J** 1981 Jun;101(6):769-73

Effect of quinidine on positive inotropic action of digoxin. Williams JF Jr, et al. **Am J Cardiol** 1981 May;47(5):1052-5

The digoxin-quinidine interaction: serum protein binding unlikely to be involved. Fichtl B, et al. **Br J Clin Pharmacol** 1981 Jan;11(1):94-6

Quinidine determination in serum: enzyme immunoassay (EIA) V HPLC [letter] Ha HR, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):312-4

The effect of quinidine and its metabolites on the electrocardiogram and systolic time intervals: concentration--effect relationships. Holford NH, et al. **Br J Clin Pharmacol** 1981 Feb;11(2):187-95

Pharmacokinetics of digoxin in patients subjected to the quinidine-digoxin interaction. Schenck-Gustafsson K, et al. **Br J Clin Pharmacol** 1981 Feb;11(2):181-6

Electrophysiological effects of the optical isomers of disopyramide and quinidine in the dog. Dependence on stereochemistry. Mirro MJ, et al. **Circ Res** 1981 Jun;48(6 Pt 1):867-74

Effects of contact with vacutainer tube stoppers on the estimation of quinidine in serum and plasma. Ooi DS, et al. **Clin Biochem** 1980 Dec; 13(6):297-300

Serum quinidine concentrations as measured by direct fluorometry, double-extraction fluorometry, and enzyme immunoassay [letter] Batra KK, et al. **Clin Chem** 1981 May;27(5):780-1

Decreased quinidine plasma protein binding during hemodialysis. Kessler KM, et al. **Clin Pharmacol Ther** 1981 Jul;30(1):121-6

Comparison of an enzyme immunoassay and a high performance liquid chromatographic method for quantitation of quinidine in serum. Dextraze PG, et al. **Clin Toxicol** 1981;18(3):291-7

Bioavailability of 11 quinidine formulations adn pharmacokinetic variation in humans. McGilveray IJ, et al. **J Pharm Sci** 1981 May;70(5):524-9

Effects of quinidine on the cardiac-glycoside sensitivity of guinea-pig and rat heart. Kim DH, et al. **J Pharmacol Exp Ther** 1981 Jun; 217(3):559-65

Interactions between quinidine and cardiac glycosides involving mutual binding sites in the guinea pig. Kim DH, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):108-14

Quinidine-rifampin interaction. Twum-Barima Y, et al. **N Engl J Med** 1981 Jun 11;304(24):1466-9

Sodium current depression by lidocaine and quinidine in isolated ventricular cells. Lee KS, et al. **Nature** 1981 May 28; 291(5813):325-7

Quinidine-induced thrombocytopenia. Clark MJ, et al. **Oral Surg** 1981 May;51(5):478-80

The effect of Craviten, a new antiarrhythmic drug, its 2R, 2'R isomer, quinidine and procaine amide on human platelet aggregation. Kędryna T, et al. **Pol J Pharmacol Pharm** 1980 Nov-Dec;32(6):883-8

Digitalis-quinidine interaction [editorial] **S Afr Med J** 1981 May 9; 59(20):695

Digitoxin-quinidine interaction: potentiation during administration of cimetidine. Polish LB, et al. **South Med J** 1981 May;74(5):633-4

[Digitalis and quinidine] Amlie JP. **Tidsskr Nor Laegeforen** 1981 Apr; 101(11):655-7 (Nor)

REACTION TIME

Selective effects of barbiturate and amphetamine on information processing and response execution. Frowein HW. **Acta Psychol (Amst)** 1981 Feb;47(2):105-15

Effect of lithium on reaction time—a study of diurnal variations. Elsass P, et al. **Psychopharmacology (Berlin)** 1981;72(3):279-82

RECEPTORS, ADRENERGIC

Differential beta-adrenergic sensitivity of atrial tissue assessed by chronotropic and inotropic responses to several sympathomimetic amines. Marquez MT, et al. **Acta Physiol Lat Am** 1978; 28(4-5):193-9

Central pre- and postsynaptic monoamine receptors in antidepressant therapy. Svensson TH, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):67-78

Inhibition of renin secretion by intrarenal alpha-adrenoceptor blockade. Blair ML. **Am J Physiol** 1981 Jun;240(6):E682-8

Antidepressants and alpha 2-adrenergic autoreceptor desensitization. Siever LJ, et al. **Am J Psychiatry** 1981 May;138(5):681-2

Receptors, adenylate cyclase, depression, and lithium. Belmaker RH. **Biol Psychiatry** 1981 Apr;16(4):333-50

Type of adrenoceptors involved in induction by adrenaline of hepatic alkaline phosphatase in mice in vivo. Mary PL, et al. **Br J Pharmacol** 1981 Jan;72(1):8-9

Characteristics of the beta 1-and beta 2-adrenergic-sensitive adenylate cyclases in glial cell primary cultures and their comparison with beta 2-adrenergic-sensitive adenylate cyclase of meningeal cells. Ebersolt C, et al. **Brain Res** 1981 May 25;213(1):151-61

Noradrenergic responses in rat hippocampus: evidence for medication by alpha and beta receptors in the in vitro slice. Mueller AL, et al. **Brain Res** 1981 Jun 9;214(1):113-26

alpha 2-Adrenoreceptors in rat brain are decreased after long-term tricyclic antidepressant drug treatment. Smith CB, et al. **Brain Res** 1981 Apr 6;210(1-2):413-8

Reactivation by cysteamine of vascular alpha adrenoceptors blocked by the tetramine disulfide benextramine and interaction of benextramine with phenoxybenzamine. Brasili L, et al. **Can J Physiol Pharmacol** 1980 Dec;58(12):1490-3

Mianserin: direct activation of brain norepinephrine neurons by blocking alpha 2-receptors. Engberg G, et al. **Commun Psychopharmacol** 1980; 4(3):233-9

Stimulation of beta 2-adrenergic responsiveness by follicle-stimulating hormone in rat granulosa cells in vitro and in vivo. Adashi EY, et al. **Endocrinology** 1981 Jun;108(6):2170-8

The role of hypothalamic adrenergic receptors in preventing testosterone-induced androgenization in the female rat brain. Raum WJ, et al. **Endocrinology** 1981 Jul;109(1):273-8

Reversal of noradrenaline denervation-induced increase of beta-adrenoreceptor binding in rat neocortex by noradrenaline infusion. Biswas B, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):341-6

Supersensitivity of central noradrenergic presynaptic autoreceptors following chronic treatment with the antidepressant mianserin. Cerrito F, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):425-6

Involvement of both dopaminergic and alpha-adrenergic receptors in the hypomotility induced by dibenzoyl-6,7-ADTN. Sumners C, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):541-50

Inhibition of phenylephrine-stimulated gluconeogenesis by chlorpromazine is mediated by alpha-adrenergic receptors. Tilley L, et al. **FEBS Lett** 1981 Apr 20;126(2):313-7

Thyroid hormone effects on beta-adrenergic receptors in isolated fat cells in rats. Pfeifle B, et al. **Horm Metab Res** 1981 Apr;13(4):218-21

Regulation of human leukocyte beta receptors by endogenous catecholamines: relationship of leukocyte beta receptor density to the cardiac sensitivity to isoproterenol. Fraser J, et al. **J Clin Invest** 1981 Jun;67(6):1777-84

Selectivity of dobutamine for adrenergic receptor subtypes: in vitro analysis by radioligand binding. Williams RS, et al. **J Clin Invest** 1981 Jun;67(6):1703-11

Individually reared rats: alteration in noradrenergic brain functions. Kraeuchi K, et al. **J Neural Transm** 1981;50(2-4):103-12

Affinity of butriptyline and other tricyclic antidepressants for alpha-adrenoceptor binding sites in rat brain. Pugsley TA, et al. **J Pharm Pharmacol** 1981 Feb;33(2):113-5

Effects of chronic reserpine administration on beta adrenergic receptors, adenylate cyclase and phosphodiesterase of the rat submandibular gland. Bylund DB, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):134-41

Comparison of the receptors mediating the catecholamine hyperpolarization and slow inhibitory postsynaptic potential in sympathetic ganglia. Cole AE, et al. **J Pharmacol Exp Ther** 1981 May; 217(2):440-4

Prenatal exposure to imipramine alters early behavioral development and beta adrenergic receptors in rats. Jason KM, et al. **J Pharmacol Exp Ther** 1981 May;217(2):461-6

DPI, a supposed selective agonist of inhibitory dopamine receptors, strongly increases rat diuresis through alpha-adrenergic receptor activation. Baggio G, et al. **Life Sci** 1981 Mar 30;28(13):1449-56

II. Beta-adrenergic receptors and catecholamine sensitive adenylate cyclase in the developing rat lung. Whitsett JA, et al. **Life Sci** 1981 Jan 26;28(4):339-45

Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 3. Modified binding properties of beta-adrenoreceptor and its decreased coupling efficiency for adenylate cyclase. Fan CC, et al. **Mol Cell Biochem** 1981 Jan 20;34(1):51-8

Subsensitivity of the beta-adrenergic receptor-linked adenylate cyclase system of rat pineal gland following repeated treatment with desmethylimipramine and nialamide. Moyer JA, et al. **Mol Pharmacol** 1981 Mar;19(2):187-93

Acceleration of beta-receptor desensitization in combined administration of antidepressants and phenoxybenzamine. Crews FT, et al. **Nature** 1981 Apr 30;290(5809):787-9

A pharmacological method to estimate the pKi of competitive inhibitors of agonist uptake processes in isolated tissues. Kenakin TP. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):89-95

Effects of some membrane perturbers on alpha 1-adrenergic receptor binding. Ciofalo FR. **Neurosci Lett** 1981 Feb 6;21(3):313-8

Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors. Tang SW, et al. **Psychiatry Res** 1981 Apr;4(2):129-38

Drug regimens facilitating aggression: behavior, amine, and receptor alterations [proceedings] Eichelman B. **Psychopharmacol Bull** 1981 Jan; 17(1):58-60

Effects of propranolol on the locomotor stimulation induced by activation of postsynaptic catecholamine receptors. Hallberg H, et al. **Psychopharmacology (Berlin)** 1981;73(3):227-31

Electrophysiological changes at a central noradrenergic synapse during thallium toxicosis. Marwaha J, et al. **Toxicol Appl Pharmacol** 1980 Dec; 56(3):345-52

[Beta-adrenergic receptors and paradoxical sleep in the rat] Lanfumey L, et al. **C R Acad Sci [D] (Paris)** 1981 Mar 2;292(9):645-7 (Eng. Abstr.) (Fre)

RECEPTORS, CHOLINERGIC

Correlation between cholinergic histamine release and quinuclidinyl-benzilate ([3H]-QNB) binding in mast cell membranes. Masini E, et al. **Agents Actions** 1981 Apr;11(1-2):55-9

Reconstitution of acetylcholine receptor function using purified receptor protein. Wu WC, et al. **Biochemistry** 1981 Feb 17;20(4):[illegible]94-701

A comparison of stereospecificity at central and peripheral 'muscarine-sensitive' acetylcholine receptors: observations with the enantiomeric forms of procyclidine and tricyclamol. Barlow RB, et al. **Br J Pharmacol** 1981 Feb;72(2):277-80

5-hydroxytryptamine controls ACh-receptor sensitivity of bullfrog sympathetic ganglion cells. Akasu T, et al. **Brain Res** 1981 Apr 27; 211(1):217-20

Maintenance and dissolution of acetylcholine receptor clusters in the embryonic muscle cell membrane. Orida N, et al. **Brain Res** 1981 Apr; 227(2):293-8

Potentiation and inhibition of nicotinic effects on striated muscle by the tetramine disulfide benextramine. Benfey BG, et al. **Can J Physiol Pharmacol** 1980 Aug;58(8):984-8

Reflexly induced inhibition of catecholamine release through a peripheral muscarinic mechanism. Lavallée M, et al. **Can J Physiol Pharmacol** 1980 Nov;58(11):1334-41

Baclofen modifies via the release of monoamines the synaptic depression, frequency facilitation, and posttetanic potentiation observed at an identified cholinergic synapse of Aplysia californica. Philippe E, et al. **Can J Physiol Pharmacol** 1981 Mar;59(3):244-52

Altered ontogenesis of muscarinic cholinergic receptor in mouse brain: effect of L-thyroxine and betamethasone. Ben-Baruch G, et al. **Endocrinology** 1981 Jul;109(1):235-9

Secoverine selectively antagonizes muscarinic effects in various in vivo preparations. Zwagemakers JM, et al. **Eur J Pharmacol** 1981 Apr 24; 71(1):165-8

Stabilization of acetylcholine receptor channels by lipids in cholate solution and during reconstitution in vesicles. Anholt R, et al. **J Biol Chem** 1981 May 10;256(9):4377-87

Acetylcholine receptor kinetics. Adams PR. **J Membr Biol** 1981 Feb 26; 58(3):161-74 (132 ref.)

Acetylcholine receptor-controlled ion flux in electroplax membrane vesicles: identification and characterization of membrane properties that affect ion flux measurements. Kim PS, et al. **J Membr Biol** 1981 Feb 28;58(3):203-11

Molecular requirements of the active site of cholinergic receptors XV: Synthesis and biological activity of 2,3-dehydrodeoxamuscarone and 2,3-dehydrodeoxamuscarines. Angeli P, et al. **J Pharm Sci** 1981 May; 70(5):489-92

An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment. Koide T, et al. **Life Sci** 1981 Mar 9;28(10):1139-45

The identification of an invertebrate acetylcholine receptor. Thomas WE, et al. **Life Sci** 1981 Mar 2;28(9):965-71 (42 ref.)

Does rigidity in structure of muscarinic agonists and antagonists reflect drug specificity? Fisher A, et al. **Monogr Neural Sci** 1980;7:41-54

Pre- and postsynaptic effects of muscarinic agonists in the guinea-pig ileum. Kilbinger H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):259-66

Choline inhibits acetylcholine release via presynaptic muscarine receptors. Kilbinger H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):131-4

Comparison of the antimuscarinic activity of mianserin and amitriptyline in the cat superior cervical ganglion. Kwok YH, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr;316(2):161-4

The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Yamada K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):155-60

Circadian acetylcholine receptor rhythm in rat brain and its modification by imipramine. Kafka MS, et al. **Neuropharmacology** 1981 May; 20(5):421-5

The time course of the muscarinic response to ionophoretic acetylcholine application to the S-A node of the rabbit heart. Osterrieder W, et al. **Pfluegers Arch** 1981 Mar;389(3):283-91

[3H]Phencyclidine: a probe for the ionic channel of the nicotinic receptor. Eldefrawi ME, et al. **Proc Natl Acad Sci USA** 1980 Dec; 77(12):7458-62

Pirenzepine--a ligand with original binding properties to muscarinic receptors. Birdsall NJ, et al. **Scand J Gastroenterol [Suppl]** 1980; 15(66):1-4

RECEPTORS, DOPAMINE

Electroconvulsive therapy and receptor sensitivity. Modigh K, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):91-9

The relationship between loss of dopamine nerve terminals, striatal [3H]spiroperidol binding and rotational behavior in unilaterally 6-hydroxydopamine-lesioned rats. Heikkila RE, et al. **Brain Res** 1981 May 4;211(2):285-92

Dopamine receptor changes following destruction of the nigrostriatal pathway: lack of a relationship to rotational behavior. Staunton DA, et al. **Brain Res** 1981 May 4;211(2):315-27

A dopaminergic binding site in the high speed supernatant of steer anterior pituitary homogenates. Kerdelhue B, et al. **Endocrinology** 1981 Jul; 109(1):307-9

Solubilization of neuroleptic/dopamine receptors of human brain striatum. Davis A, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):321-9

Kainate lesion dissociates striatal dopamine receptor radioligand binding sites. Leff S, et al. **Eur J Pharmacol** 1981 Mar 5;70(1):71-5

Involvement of both dopaminergic and alpha-adrenergic receptors in the hypomotility induced by dibenzoyl-6,7-ADTN. Sumners C, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):541-50

D2- but not D3-dopamine receptors detected in the anterior pituitary. Titeler M, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):143-6

A comparison of dopamine receptor blocking assay with plasma drug levels of haloperidol in schizophrenic patients. Kurland AA, et al. **J Clin Pharmacol** 1981 Jan;21(1):42-7

Prolonged dopamine receptor blockade in rats after termination of long-term depot fluphenazine [letter] Waddington JL, et al. **Lancet** 1981 Jun 20;1(8234):1375-6

Dopamine receptors in rat frontal cortex: pharmacological properties in vivo and in vitro. Bacopoulos NG, et al. **Life Sci** 1980 Dec 22-29; 27(25-26):2489-94

DPI, a supposed selective agonist of inhibitory dopamine receptors, strongly increases rat diuresis through alpha-adrenergic receptor activation. Baggio G, et al. **Life Sci** 1981 Mar 30;28(13):1449-56

Neostriatal dopamine receptor loss and behavioral deficits in the senescent rat. Cubells JF, et al. **Life Sci** 1981 Mar 16;28(11):1215-8

3-PPP, a new centrally acting DA-receptor agonist with selectivity for autoreceptors. Hjorth S, et al. **Life Sci** 1981 Mar 16;28(11):1225-38

An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment. Koide T, et al. **Life Sci** 1981 Mar 9;28(10):1139-45

Chronic neuroleptic treatment specifically alters the number of dopamine receptors in rat brain. Theodorou A, et al. **Life Sci** 1981 Apr 6; 28(14):1621-7

Mesocortical dopamine neurons. Lack of autoreceptors modulating dopamine synthesis. Bannon MJ, et al. **Mol Pharmacol** 1981 Mar; 19(2):270-5

The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Yamada K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):155-60

Response of striatonigral substance P systems to a dopamine receptor agonist and antagonist. Hanson G, et al. **Neuropharmacology** 1981 Jun; 20(6):541-8

Blink rates and receptor supersensitivity. Karson CN, et al. **Neuropharmacology** 1981 Jan;20(1):91-3

Binding of [3H]sulpiride to purified rat striatal synaptic membranes. Woodruff GN, et al. **Neuroscience** 1981;6(3):407-10

Evidence for dopamine mediation of submissive gestures in the stumptail macaque monkey. Schlemmer RF Jr, et al. **Pharmacol Biochem Behav** 1981;14 Suppl 1:95-102

Tonic immobility in domestic fowl: possible interaction of serotonergic and dopaminergic mechanisms. Wallnau LB, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):469-73

Resolution of dopamine and serotonin receptor components of [3H]spiperone binding to rat brain regions. List SJ, et al. **Proc Natl Acad Sci USA** 1981 Apr;78(4):2620-4

Repeated antidepressant treatments induce a long-lasting dopamine autoreceptor subsensitivity: is daily treatment necessary for clinical efficacy? [proceedings] Antelman SM, et al. **Psychopharmacol Bull** 1981 Jan;17(1):92-4

Long-term d-amphetamine in rats: lack of change in post-synaptic dopamine receptor sensitivity. Jackson DM, et al. **Psychopharmacology (Berlin)** 1981;73(3):276-80

The effects of electroconvulsive shock on the discriminative stimulus properties of d-amphetamine and apomorphine: evidence for dopamine receptor alteration subsequent ECS. White DK, et al. **Psychopharmacology (Berlin)** 1981;73(3):211-4

The effects of acrylamide treatment upon the dopamine receptor. Agrawal AK, et al. **Toxicol Appl Pharmacol** 1981 Mar 30;58(1):89-99

Effects of acrylamide given during gestation on dopamine receptor binding in rat pups. Agrawal AK, et al. **Toxicol Lett** 1981 Jan; 7(3):233-8

3,4,3',4'-Tetrachlorobiphenyl given to mice prenatally produces long-term decreases in striatal dopamine and receptor binding sites in the caudate nucleus. Agrawal AK, et al. **Toxicol Lett** 1981 Mar; 7(6):417-24

[Neurophysiologic and pharmacologic evidence of autoregulationin the nigrostriatal system] Arushanian EB, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):133-6 (Eng. Abstr.) **(Rus)**

RECEPTORS, DRUG

Receptor adaptations to centrally acting drugs. Creese I, et al. **Annu Rev Pharmacol Toxicol** 1981;21:357-91 (235 ref.)

The benzodiazepine--GABA--chloride ionophore receptor complex: common site of minor tranquilizer action. Paul SM, et al. **Biol Psychiatry** 1981 Mar;16(3):213-29

Kainic acid-induced lesion of rat retina: differential effect on cyclic GMP and benzodiazepine and GABA receptors. Guarneri P, et al. **Brain Res** 1981 Mar 23;209(1):216-20

The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures. Shibla DB, et al. **Brain Res** 1981 Apr 6;210(1-2):471-4

gamma-Aminobutyric acid regulation of the benzodiazepine receptor: biochemical evidence for pharmacologically different effects of benzodiazepines and propyl beta-carboline-3-carboxylate. Ehlert FJ, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):593-5

Increase of benzodiazepine binding to the membranes isolated in the presence of diazepam. Korneyev AY, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):127-30

Tolerance during chronic benzodiazepine treatment associated with decreased receptor binding. Rosenberg HC, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):453-60

Specific high-affinity saturable binding of [3H] R05-4864 to benzodiazepine binding sites in the rat cerebral cortex. Schoemaker H, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):173-5

Molecular sizes of benzodiazepine receptors and the interacting GABA receptors in the membrane are identical. Chang LR, et al. **FEBS Lett** 1981 Apr 20;126(2):309-12

Purification of phenytoin-binding site from the brain. Imazawa M, et al. **Folia Psychiatr Neurol Jpn** 1980;34(3):362

Effect of picrotoxin on benzodiazepine receptors and GABA receptors with reference to the effect of Cl- ion. Fujimoto M, et al. **Life Sci** 1981 Feb 23;28(8):895-901

Modulation by picrotoxin and IPTBO of 3H-flunitrazepam binding to the GABA/benzodiazepine receptor complex of rat cerebellum. Karobath M, et al. **Life Sci** 1981 Jan 19;28(3):307-13

Multiple benzodiazepine receptors: evidence of dissociation between anticonflict and anticonvulsant properties by PK 8165 and PK 9084 (two quinoline derivatives). Le Fur G, et al. **Life Sci** 1981 Mar 30; 28(13):1439-48

Do benzodiazepines bind at adenosine uptake sites in CNS? Wu PH, et al. **Life Sci** 1981 Mar 2;28(9):1023-31

Benzodiazepine receptor: heterogeneity in rabbit brain. Yokoi I, et al. **Life Sci** 1981 Apr 6;28(14):1591-5

Increase in 3H-flunitrazepam binding in vitro and in vivo to rat brain benzodiazepine receptors by tofizopam, a 3,4-benzo-diazepine. Saano V, et al. **Pharmacol Res Commun** 1981 Jan;13(1):75-85

gamma-Aminobutyric acid and benzodiazepine receptors: copurification and characterization. Gavish M, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1939-42

Autoradiographic localization of benzodiazepine receptors in immunocytochemically identified gamma-aminobutyrergic synapses. Möhler H, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1935-8

Localized binding of [3H]muscimol to synapses in chicken retina. Yazulla S, et al. **Proc Natl Acad Sci USA** 1981 Jan;78(1):643-7

RECEPTORS, ENDORPHIN

Proposals for conformation of enkephalins related to opiate mu-pharmacophore. Maigret B, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):267-74

ACTH1-24 blocks opiate - induced analgesia in the rat. Smock T, et al. **Brain Res** 1981 May 11;212(1):202-6

The interaction of N alpha-alkylenkephalins with opiate receptors.

Tissue-dependent shifts in the opiate activity of methionine-enkephalin following N alpha-alkylation. Summers MC, et al. **J Biol Chem** 1981 May 25;256(10):4951-6

Comparative study on the effect of morphine and the opioid-like peptides in the vas deferens of rodents: species and strain differences, evidence for multiple opiate receptors. Huidobro-Toro JP, et al. **Life Sci** 1981 Mar 23;28(12):1331-6

Affinity of beta-carbolines on rat brain benzodiazepine and opiate binding sites. Airaksinen MM, et al. **Med Biol** 1980 Dec;58(6):341-4

Opiate receptors modulate LHRH and SRIF release from mediobasal hypothalamic neurons. Drouva SV, et al. **Neuroendocrinology** 1981 Mar; 32(3):163-7

A cyclic enkephalin analog with high in vitro opiate activity. DiMaio J, et al. **Proc Natl Acad Sci USA** 1980 Dec;77(12):7162-6

RECEPTORS, HORMONE

Changes of receptor cooperation in Tetrahymena by re-exposure to hormones. Csaba G, et al. **Acta Biol Acad Sci Hung** 1980; 31(1-3):43-7

Mucosal gastrin receptor. VI. Induction by corticosterone in newborn rats. Peitsch W, et al. **Am J Physiol** 1981 Jun;240(6):G442-9

Human placental receptors for luteinizing hormone releasing hormone. Currie AJ, et al. **Biochem Biophys Res Commun** 1981 Mar 16; 99(1):332-8

GABA receptor pharmacology. Functional considerations. Enna SJ. **Biochem Pharmacol** 1981 May 1;30(9):907-13

The benzodiazepine--GABA--chloride ionophore receptor complex: common site of minor tranquilizer action. Paul SM, et al. **Biol Psychiatry** 1981 Mar;16(3):213-29

Relationship between the presence of dopaminergic neurons and GABA receptors in substantia nigra: effects of lesions. Gale K. **Brain Res** 1981 Apr 6;210(1-2):401-6

Kainic acid-induced lesion of rat retina: differential effect on cyclic GMP and benzodiazepine and GABA receptors. Guarneri P, et al. **Brain Res** 1981 Mar 23;209(1):216-20

Heterogeneous depression of glucose utilization in the caudate nucleus by GABA agonists. Kelly PA, et al. **Brain Res** 1981 Mar 30; 209(2):458-63

Effects of halopemide on GABA receptor binding, uptake and release. Loonen AJ, et al. **Brain Res** 1981 Apr 6;210(1-2):485-92

Neurotensin receptor localization by light microscopic autoradiography in rat brain. Young WS 3d, et al. **Brain Res** 1981 Feb 16; 206(2):273-85

A simple, inexpensive filtration device suitable for neurotransmitter receptor binding studies in brain tissue. Wilkinson M, et al. **Can J Physiol Pharmacol** 1981 May;59(5):504-6

Binding characteristics of gonadotropin-releasing hormone receptors throughout the estrous cycle of the hamster. Adams TE, et al. **Endocrinology** 1981 Jun;108(6):2245-53

Pituitary and gonadal gonadotropin-releasing hormone receptors during sexual maturation in the rat. Dalkin AC, et al. **Endocrinology** 1981 May; 108(5):1658-64

Dissociated changes of pituitary luteinizing hormone-releasing hormone (LHRH) receptors and responsiveness to the neurohormone induced by 17 beta-estradiol and LHRH in vivo in the rat. Ferland L, et al. **Endocrinology** 1981 Jul;109(1):87-93

Regulation of adrenal and testicular prolactin receptors by adrenocorticotropin and luteinizing hormone. Katikineni M, et al. **Endocrinology** 1981 Jun;108(6):2367-74

Effects of antidepressant drugs on different receptors in the brain. Hall H, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):393-407

Prolactin inhibits the induction of its own renal receptors in Rana catesbeiana tadpoles. White BA, et al. **Gen Comp Endocrinol** 1981 Jan; 43(1):30-8

Benzodiazepines, barbiturates and baclofen interaction within the GABA-receptors. Azanza MJ. **Gen Pharmacol** 1981;12(3):123-8 (20 ref.)

Absence of LH-RH binding sites in corpora lutea from rhesus monkeys (Macacca mulatta). Asch RH, et al. **J Clin Endocrinol Metab** 1981 Jul; 53(1):215-17

Effect of picrotoxin on benzodiazepine receptors and GABA receptors with reference to the effect of Cl- ion. Fujimoto M, et al. **Life Sci** 1981 Feb 23;28(8):895-901

Effect of prolactin and prostaglandins on the stimulation of prolactin binding sites in the male rat liver. Barkey RJ, et al. **Mol Cell Endocrinol** 1981 Feb;21(2):129-38

Sertoli-Leydig cell communication via an LHRH-like factor. Sharpe RM, et al. **Nature** 1981 Apr 30;290(5809):785-7

Preparation of 3H-[3-M3-His2]TRH as an improved ligand for TRH receptors. Taylor RL, et al. **Neuroendocrinology** 1981 May; 32(5):310-6

Effects of anticonvulsants on excitability and GABA sensitivity of cat dorsal root ganglion cells. Gallagher JP, et al. **Neuropharmacology** 1981 May;20(5):427-33

Pentobarbitone slows the dissociation of GABA from rat brain synaptosomal binding sites. Willow M, et al. **Neurosci Lett** 1981 Apr 9;23(1):71-4

Neurotransmitter receptors in brain regions of acrylamide- treated rats. I: Effects of a single exposure to acrylamide. Agrawal AK, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):527-31

Neurotransmitter receptors in brain regions of acrylamide- treated rats. II: Effects of extended exposure to acrylamide. Bondy SC, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):533-7

gamma-Aminobutyric acid and benzodiazepine receptors: copurification and characterization. Gavish M, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1939-42

[Regulation of genetic activity by thyroid hormones. II. Specificity of interaction of cytoplasmic thyroxine receptor isolated from human embryonal fibroblasts and HeLa cells with DNA] Abdukarimov A, et al. **Probl Endokrinol (Mosk)** 1981 Mar-Apr;27(2):66-70 (Eng. Abstr.) **(Rus)**

[Regulation of genetic activity by thyroid hormones. Effect of purified cytoplasmic hormone-receptor complex on the chromatin template activity] Abdukarimov A, et al. **Probl Endokrinol (Mosk)** 1981 Jan-Feb; 27(1):50-3 (Eng. Abstr.) **(Rus)**

RECEPTORS, SEROTONIN

Central pre- and postsynaptic monoamine receptors in antidepressant therapy. Svensson TH, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):67-78

5-Hydroxytryptamine induces relaxation of goat pulmonary veins: evidence for the noninvolvement of M and D-tryptamine receptors. Chand N. **Br J Pharmacol** 1981 Feb;72(2):233-7

Synaptic remodeling of serotonin axon terminals in rat agranular cerebellum. Beaudet A, et al. **Brain Res** 1981 Feb 16;206(2):305-29

Serotonin-receptor-mediated modulation of Ca2+-dependent 5-hydroxytryptamine release from neurones of the rat brain cortex. Göthert M. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov; 314(3):223-30

The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Yamada K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Apr; 316(2):155-60

Treatment with trazodone plus phenoxybenzamine accelerates development of decreased type 2 serotonin binding in rat cortex. Taylor DP, et al. **Neuropharmacology** 1981 May;20(5):513-6

Antidepressants and serotonin neurons of the raphe. Constantinidis J, et al. **Neuropsychobiology** 1981;7(3):113-21

DOM and related 2,5-dimethoxy-4-alkylphenylisopropylamines: behavioral and serotonin receptor properties. Glennon RA, et al. **Pharmacol Biochem Behav** 1981 Mar;14(3):287-92

The effects of tryptophan and manipulations of serotonergic receptors on tonic immobility in chickens. Wallnau LB, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):463-8

Tonic immobility in domestic fowl: possible interaction of serotonergic and dopaminergic mechanisms. Wallnau LB, et al. **Pharmacol Biochem Behav** 1981 Apr;14(4):469-73

Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. Heron DS, et al. **Proc Natl Acad Sci USA** 1980 Dec; 77(12):7463-7

Resolution of dopamine and serotonin receptor components of [3H]spiperone binding to rat brain regions. List SJ, et al. **Proc Natl Acad Sci USA** 1981 Apr;78(4):2620-4

Evidence that it is possible to cause anorexia by increasing release and/or directly stimulating postsynaptic serotonin receptors in the brain. Samanin R, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):363-9

Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors. Tang SW, et al. **Psychiatry Res** 1981 Apr;4(2):129-38

Effect of 5,7-dihydroxytryptamine on serotonergic control of prolactin secretion and behavior in rats. Kuhn CM, et al. **Psychopharmacology (Berlin)** 1981;73(2):188-93

Two distinct central serotonin receptors with different physiological functions. Peroutka SJ, et al. **Science** 1981 May 15;212(4496):827-9

[Interaction of indoleamines with serotonergic receptors of brain synaptosomes] Uzbekov MG, et al. **Biokhimiia** 1980 Jan;45(1):109-12 (Eng. Abstr.) **(Rus)**

REFLEX

Sensitization of the perioral biting reflex by intranigral GABA agonist after detelencephalization. Weizl H, et al. **Neurosci Lett** 1981 Feb 6; 21(3):351-4

[Studies on voiding mechanism. 2. The effects of urethral distension on the vesical contraction reflex: neuropharmacological and neurophysiological aspects (author's transl)] Bekku T. **Nippon Hinyokika Gakkai Zasshi** 1980 Dec;71(12):1456-71 (Eng. Abstr.) **(Jpn)**

REINFORCEMENT (PSYCHOLOGY)

Fixed-ratio responding under second-order schedules of food presentation or cocaine injection. Goldberg SR, et al. **J Pharmacol Exp Ther** 1981

Jul;218(1):271-81

Comparison of discriminative and reinforcing effects of ketamine and related compounds in the rhesus monkey. Young AM, et al. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(34):173-9

Dopaminergic mediation of reward: evidence gained using a natural reinforcer in a behavioral contrast paradigm. Royall DR, et al. **Neurosci Lett** 1981 Jan 20;21(2):223-9

Effects of chlorpromazine on food-maintained and observing behavior. Dearing ME, et al. **Psychopharmacology (Berlin)** 1981;73(3):281-5

The partial reinforcement extinction effect after treatment with chlordiazepoxide. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 73(3):269-75

REINFORCEMENT SCHEDULE

Effects of diazepam on schedule-controlled and schedule-induced behavior under signaled and unsignaled shock. Hymowitz N. **J Exp Anal Behav** 1981 Jul;36(1):119-32

The pituitary-adrenal response to 'minimized' schedule-induced drinking. Brett LP, et al. **Physiol Behav** 1981 Feb;26(2):153-8

RESERPINE

Terminals of reserpine-sensitive vasopressin-neurophysin neurons in the external layer of the rat median eminence. Seybold V, et al. **Endocrinology** 1981 May;108(5).1803-9

Influence of phenothiazines or reserpine on the formation of 14C-glycine from U-14C-serine. Gründig E, et al. **Enzyme** 1981;26(1):43-8

Role of monoamines in behavior of reserpinized rats given tranylcypromine stereoisomers. Smith DF. **J Neural Transm** 1981; 50(2-4):193-200

Chronic reserpine treatment alters sensitivity and membrane potential of the rabbit saphenous artery. Abel PW, et al. **J Pharmacol Exp Ther** 1981 May;217(2):430-9

Effects of chronic reserpine administration on beta adrenergic receptors, adenylate cyclase and phosphodiesterase of the rat submandibular gland. Bylund DB, et al. **J Pharmacol Exp Ther** 1981 Jul;218(1):134-41

Effects of reserpine on monoamines and intestinal transit in the rat. Stewart JJ, et al. **J Pharmacol Exp Ther** 1981 May;217(2):357-62

Reserpine increases opiate-like peptide content and tyrosine hydroxylase activity in adrenal medullary chromaffin cells in culture. Wilson SP, et al. **Neuroscience** 1981;6(1):71-9

Effect of 5-hydroxytryptamine on isolated aortic strip preparations obtained from untreated and reserpine treated rabbits. Tayyaba B, et al. **Planta Med** 1981 Mar;41(3):295-7

[Effect of reserpine on monoamine uptake by rat brain synaptosomes] Blaschke M, et al. **Acta Biol Med Ger** 1980;39(11-12):1205-12 (Eng. Abstr.) **(Ger)**

[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Initial results] Di Giorgio RM, et al. **Acta Neurol (Napoli)** 1981 Feb;36(1):302-4 (Eng. Abstr.) **(Ita)**

[Hormonal induction of lactation after short-term treatment in sheep. III.] Manunta G, et al. **Boll Soc Ital Biol Sper** 1981 Jan 30;57(2):165-71 (Eng. Abstr.) **(Ita)**

[Induction of lactation in cattle after short-term hormonal treatment] Manunta G, et al. **Boll Soc Ital Biol Sper** 1981 Jan 30;57(2):172-8 (Eng. Abstr.) **(Ita)**

[The effect of reserpine on the morphine abstinence syndrome in mice (author's transl)] Kruszewska A, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979;34:133-9 **(Pol)**

[Effect of reserpine on O- and N-demethylase activity in the liver of rats (author's transl)] Božeková L, et al. **Bratisl Lek Listy** 1981 Feb; 75(2):161-6 (Eng. Abstr.) **(Slo)**

RUBIDIUM

Is ouabain-sensitive rubidium or potassium uptake a measure of sodium pump activity in isolated cardiac muscle? Akera T, et al. **Biochim Biophys Acta** 1981 Feb 6;640(3):779-90

Relationship between the positive inotropic effect of ouabain and its inhibitory effects on Na+, K+ -ATPase and active transport of Rb+ in the dog heart. Rhee HM, et al. **Eur J Pharmacol** 1981 Mar 26; 70(3):273-8

Further studies on the precipitative freeze dissolution technique for the localization of inorganic ions. Van Iren F, et al. **Histochemistry** 1981; 71(2):195-201

Sodium and rubidium uptake in cells transformed by Rous sarcoma virus. Bader JP, et al. **J Cell Physiol** 1981 Feb;106(2):235-43

The effect of pH on 86Rubidium efflux from pancreatic islet cells. Henquin JC. **Mol Cell Endocrinol** 1981 Feb;21(2):119-28

K+ channels close more slowly in the presence of external K+ and Rb+. Swenson RP Jr, et al. **Nature** 1981 Jun 4;291(5814):427-9

SCHIZOPHRENIA

Haloperidol and droperidol treatment in schizophrenics. Clinical application of the 'prolactin-model'. Langer G, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):574-83

Late (4-8 years) outcome of treatment with megadoses of fluphenazine enanthate in drug-refractory schizophrenics. Dencker SJ, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):1-12

DL-propranolol and chlorpromazine following admission for schizophrenia. A controlled comparison. Yorkston NJ, et al. **Acta Psychiatr Scand** 1981 Jan;63(1):13-27

The need for long-term neuroleptic treatment in schizophrenia. Dencker SJ. **Acta Psychiatr Scand [Suppl]** 1981;63(291):29-43

The role of neuroleptics in an integrated treatment program for chronic schizophrenics. Gottfries I, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(291):44-55

High doses of clorotepin in chronic schizophrenia (preliminary report). Bastecký J, et al. **Agressologie** 1980;21(A):31-5

Neuroleptic-induced decrease in platelet MAO activity of schizophrenic patients. Chojnacki M, et al. **Am J Psychiatry** 1981 Jun; 138(6):838-40

Attitudes toward medication change among chronically impaired psychiatric patients. Lesser IM, et al. **Am J Psychiatry** 1981 Jun; 138(6):801-3

Dialysis for schizophrenia: an uncontrolled study of 11 patients. Scheiber SC, et al. **Am J Psychiatry** 1981 May;138(5):662-5

Increased whole blood serotonin concentrations in chronic schizophrenic patients. DeLisi LE, et al. **Arch Gen Psychiatry** 1981 Jun; 38(6):647-50

Blood tryptophan metabolism in chronic schizophrenics. Freedman DX, et al. **Arch Gen Psychiatry** 1981 Jun;38(6):655-9

Relapse in schizophrenia [letter] Goldhamer P. **Arch Gen Psychiatry** 1981 Jul;38(7):842-3

Schizophrenia. A follow-up study of the results of five forms of treatment. May PR, et al. **Arch Gen Psychiatry** 1981 Jul;38(7):776-84

Brain monoamine oxidase activity in schizophrenics and controls. Reveley MA, et al. **Arch Gen Psychiatry** 1981 Jun;38(6):663-5

Outcome and risks of ultra-long-term treatment with an oral neuroleptic drug. Relationship between perazine serum levels and clinical variables in schizophrenic outpatients. Pietzcker A, et al. **Arch Psychiatr Nervenkr** 1981;229(4):315-29

Piperidine in chronic schizophrenic patients: a controlled double-blind study. Luchins DJ, et al. **Biol Psychiatry** 1981 Jan;16(1):91-5

The reliability of 5-hydroxytryptamine induced platelet aggregation responses in schizophrenic patients treated with neuroleptic drugs. Knox JM, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):261-3

The effects of neuroleptic drugs on 5-hydroxytryptamine induced platelet aggregation in schizophrenic patients. Orr MW, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):255-9

Controlled trial of sulpiride in chronic schizophrenic patients. Edwards JG, et al. **Br J Psychiatry** 1980 Dec;137:522-9

Schizophrenia. Pyke J, et al. **Can Nurse** 1981 May;77(5):39-43

Plasma DBH activity: relation to genetic factors in schizophrenia. Baron M, et al. **Commun Psychopharmacol** 1980;4(3):197-202

Effect of propranolol treatment on serum prolactin level in schizophrenic patients. Elizur A, et al. **Commun Psychopharmacol** 1980;4(3):203-6

Prognosis in schizophrenia: individual differences in psychological response to a test dose of antipsychotic drug and their relationship to blood and saliva levels and treatment outcome. May PR, et al. **Compr Psychiatry** 1981 Mar-Apr;22(2):147-52

Clopenthixol decanoate in schizophrenia. Carney MW, et al. **Curr Med Res Opin** 1981;7(4):205-11

Plasma dopamine beta hydroxylase activity in chronic schizophrenic patients tested with single dose of 2-bromo-alpha ergocriptine (Parlodel). Vardi J, et al. **Encephale** 1981;7(1):95-103

With onions and tears: a multidimensional analysis of a counter-ritual. Levick SE, et al. **Fam Process** 1981 Mar;20(1):77-83

Benzodiazepines in schizophrenia: a need for reassessment. Nestoros JN. **Int Pharmacopsychiatry** 1980;15(3):171-9

A comparison of dopamine receptor blocking assay with plasma drug levels of haloperidol in schizophrenic patients. Kurland AA, et al. **J Clin Pharmacol** 1981 Jan;21(1):42-7

Viloxazine and the depressed schizophrenic—methodological issues. Kurland AA, et al. **J Clin Pharmacol** 1981 Jan;21(1):37-41

Pharmacomanometric studies of colonic motility as a guide to the chemotherapy of schizophrenia. Lechin F, et al. **J Clin Pharmacol** 1980 Nov-Dec;20(11-12):664-71

A comparative study of parenteral molindone and haloperidol in the acutely psychotic patient. Binder R, et al. **J Clin Psychiatry** 1981 May; 42(5):203-6

Thiothixene plasma levels and clinical response in acute schizophrenia. Reifler BV, et al. **J Clin Psychiatry** 1981 May;42(5):207-11

Levels of HIAA and VMA in C.S.F. of schizophrenics before and after treatment. Okasha A, et al. **J Egypt Med Assoc** 1978; 61(Suppl 1-2):38-50

Autonomous prolactin secretion in schizophrenic male on long-term neuroleptic therapy [letter] Semple CG, et al. **Lancet** 1981 Jul 11; 2(8237):103

An alternative mechanism of actions for neuroleptic and antidepressant drugs. Randall PL. **Med Hypotheses** 1981 Feb;7(2):251-60

Hemodialysis in schizophrenia: psychiatric aspects of treatment failure in a pilot study. Rorsman B, et al. **Neuropsychobiology** 1981; 7(3):127-36

Dextro-propranolol in schizophrenia. Hirsch SR, et al. **Prog Neuropsychopharmacol** 1980;4(6):633-7

Genetics and schizophrenic behavior. Kahn E. **Psychiatr Q** 1980 Winter; 52(4):251-69 (124 ref.)

A probable neuroleptic effect on platelet monoamine oxidase in chronic schizophrenic patients. DeLisi LE, et al. **Psychiatry Res** 1981 Feb; 4(1):95-107

Nongenetic factors affecting human platelet monoamine oxidase [proceedings] Friedhoff AJ, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):101-3

Natural and therapeutic environmental indicators of maintenance dosage requirements [proceedings] Hogarty GE. **Psychopharmacol Bull** 1981 Jan;17(1):36-7

Plasma levels of chlorpromazine and clinical response [proceedings] van Putten T, et al. **Psychopharmacol Bull** 1981 Jan;17(1):113-5

A double-blind comparison of trebenzomine and thioridazine in the treatment of schizophrenia. Georgotas A, et al. **Psychopharmacology (Berlin)** 1981;73(3):292-4

Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge. Kolakowska T, et al. **Psychopharmacology (Berlin)** 1981;72(3):283-5

A clinical and pharmacodynamic evaluation of sulpiride. Rao VA, et al. **Psychopharmacology (Berlin)** 1981;73(1):77-80

Serum and CSF levels of haloperidol by radioimmunoassay and radioreceptor assay during high-dose therapy of resistant schizophrenic patients. Rimón R, et al. **Psychopharmacology (Berlin)** 1981; 73(2):197-9

[Preliminary observations on immunoglobulins in schizophrenics (author's transl)] Huo KJ. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1979; 12(3):161-3 (Chi)

[A study of renovation rate of dopamine and 5-hydroxytryptamine in brain in chronic schizophrenics (author's transl)] Shen YC. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1979;12(3):158-60 (Chi)

[Modifications of cerebral amine metabolism in psychiatric illness] Linkowski P, et al. **Acta Psychiatr Belg** 1980 Sep-Oct;80(5):559-73 (38 ref.) (Fre)

[Relation of pharmacotherapy, regulation of life situations and analytically-oriented psychotherapy in schizophrenic psychoses under the conditions of an ambulatory psychiatric practice] Schmidt P. **Agressologie** 1980;21(A):27-9 (Eng. Abstr.) (Ger)

[Neurochemistry and clinical psychiatry (author's transl)] Gross G. **Fortschr Neurol Psychiatr** 1981 Jan;49(1):34-42 (Eng. Abstr.) (Ger)

[The course of schizophrenic psychoses treated with neuroleptics] Rüther E, et al. **MMW** 1981 May 8;123(19):803-4 (Ger)

[Modification of long-term schizophrenia by somato-therapeutic measures] Gross G, et al. **Psychiatr Clin (Basel)** 1980;13(3-4):179-92 (Eng. Abstr.) (Ger)

[Modification of schizophrenia by intensive neuroleptic therapy and the course of the disease after withdrawal of neuroleptic drugs] Steiner S. **Psychiatr Clin (Basel)** 1980;13(3-4):165-78 (Eng. Abstr.) (Ger)

[Peculiarities and difficulties in the systematic drug therapy of chronic schizophrenics (schizophrenic 'defect')] Lange E, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1981 Jan;33(1):34-8 (Eng. Abstr.) (Ger)

[Biochemical approach to schizophrenia] Lipcsey A. **Orv Hetil** 1980 Nov 23;121(47):2863-70 (Hun)

[Effectiveness of treating early-onset malignant schizophrenia with psychotropic drugs and their combinations] Sobolev ES, et al. **Zh Nevropatol Psikhiatr** 1981;81(1):114-21 (Eng. Abstr.) (Rus)

SCHIZOPHRENIA, DISORGANIZED

[Amineptine and amotival syndrome (author's transl)] Deniker P, et al. **Encephale** 1981;7(1):59-64 (Eng. Abstr.) (Fre)

SCHIZOPHRENIA, PARANOID

Paranoid schizophrenia. A serpent which licked my eyes... Hansford M. **Nurs Mirror** 1981 May 7;152(19):30-3

SELF STIMULATION

The central basis of motivation: intracranial self-stimulation studies. Olds ME, et al. **Annu Rev Psychol** 1981;32:523-74 (246 ref.)

Reward and detection thresholds for brain stimulation: dissociative effects of cocaine. Kornetsky C, et al. **Brain Res** 1981 Mar 30; 209(2):496-500

Intracranial self-stimulation: mapping against the lateral boundaries of the dopaminergic cells of the substantia nigra. Wise RA. **Brain Res** 1981 May 25;213(1):190-4

Self-stimulation and locomotor changes indicating 'latent' anticholinergic activity by an atypical neuroleptic (thioridazine). Herberg LJ, et al. **Neuropharmacology** 1981 Jan;20(1):55-60

Intravenous self-administration of nomifensine in rats: implications for abuse potential in humans. Spyraki C, et al. **Science** 1981 Jun 5; 212(4499):1167-8

SENSORY DEPRIVATION

Role of intracortical inhibition in deprivation amblyopia: reversal by microiontophoretic bicuculline. Burchfiel JL, et al. **Brain Res** 1981 Feb 16;206(2):479-84

Cortical effects of monocular deprivation: suppression or deafferentation? [news] Movshon JA. **Nature** 1981 May 28;291(5813):284-5

The role of GABAergic inhibition in the cortical effects of monocular deprivation. Sillito AM, et al. **Nature** 1981 May 28;291(5813):318-20

SEROTONIN

Reversed effect of chlorpromazine on hypothalamic serotonin levels of rats with complete deafferentation of the medial basal hypothalamus. Bánky Z, et al. **Acta Biol Acad Sci Hung** 1980;31(1-3):25-32

Enhancement of the sensitivity of Tetrahymena to a second hormonal influence by hormone pretreatment. Csaba G, et al. **Acta Biol Med Ger** 1980;39(10):1027-30

Effect of epinephrine and 5-hydroxytryptamine on in vitro thyroid iodine organification. Masini-Repiso AM, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):207-12

Stimulation by serum of aldosterone production from rat adrenal glomerulosa cells in vitro: relationships to K+, serotonin and angiotensin II. Mendelsohn FA, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):231-42

Immunohistochemical characterization of monoamine-containing neurons in the central nervous system by antibodies to serotonin and noradrenalin. A study in the rat and the lamprey (Lampetra fluviatilis). Steinbusch HW, et al. **Acta Histochem [Suppl] (Jena)** 1981;24:107-22

Effect of prolonged acetylcholinesterase inhibition on postnatal brain development in rabbit. I. Level of serotonin in different brain regions. Maślińska D, et al. **Acta Neuropathol [Suppl] (Berl)** 1981;7:52-5

The action of antidepressant drugs on 5-hydroxy-tryptamine uptake by platelets—relationship to therapeutic effect. Coppen A, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):236-43

Pre- and postsynaptic effects of zimelidine and norzimelidine on the serotoninergic system: single cell studies in the rat. de Montigny C, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):79-90

The pharmacology of zimelidine: a 5-HT selective reuptake inhibitor. Ogren SO, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(Suppl 290):127-51

Specific norepinephrine and serotonin uptake inhibitors in man: a crossover study with pharmacokinetic, biochemical, neuroendocrine and behavioral parameters. Potter WZ, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):152-65

A simple, specific, radioenzymatic assay for picogram quantities of serotonin or acetylserotonin in biological fluids and tissues. Hussain MN, et al. **Anal Biochem** 1981 Feb;111(1):105-10

Morphology, histochemistry, and distribution of serotonin-containing cells in tracheal epithelium of adult rabbit. Dey RD, et al. **Anat Rec** 1981 Jan;199(1):23-31

Evidence for the involvement of serotoninergic system in the male-induced ovo-implantation failure (Bruce effect) in mice. Sahu SC, et al. **Ann Endocrinol (Paris)** 1980 Sep-Oct;41(5):425-9

Increased whole blood serotonin concentrations in chronic schizophrenic patients. DeLisi LE, et al. **Arch Gen Psychiatry** 1981 Jun; 38(6):647-50

Short-term and repetitive administration of oral tryptophan in normal men. Effects on blood tryptophan, serotonin, and kynurenine concentrations. Yuwiler A, et al. **Arch Gen Psychiatry** 1981 Jun; 38(6):619-26

Effects of Ro 11-2465, a new psychotropic agent on the uptake of serotonin by human platelets—in vitro determination of the IC50. Lenehan T, et al. **Arch Int Pharmacodyn Ther** 1981 Jan; 249(1):147-52

Distribution of the radioactivity in the central nervous system of the developing rat following intracisternal or subcutaneous administration of 14C-5,7-dihydroxytryptamine. Sievers J, et al. **Bibl Anat** 1981; (19):302-7

Induction of serotonin secretion by cross-linking of surface receptors of a derivative of wheat germ agglutinin on human platelets. Ganguly P, et al. **Biochem Biophys Res Commun** 1981 Mar 16;99(1):176-82

2-nitroimipramine: a selective irreversible inhibitor of [3H] serotonin uptake and [3H] imipramine binding in platelets. Rehavi M, et al. **Biochem Biophys Res Commun** 1981 Apr 15;99(3):954-9

The effect of ouabain on the release of 5-hydroxytryptamine from superfused synaptosomes. Collard KJ, et al. **Biochem Soc Trans** 1981 Feb;9(1):109-10

Plasma free and total tryptophan, blood serotonin, and the hyperactivity syndrome: no evidence for the serotonin deficiency hypothesis. Ferguson HB, et al. **Biol Psychiatry** 1981 Mar;16(3):231-8

Management of depression with serotonin precursors. van Praag HM. **Biol Psychiatry** 1981 Mar;16(3):291-310

The reliability of 5-hydroxytryptamine induced platelet aggregation responses in schizophrenic patients treated with neuroleptic drugs. Knox JM, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):261-3

The effects of neuroleptic drugs on 5-hydroxytryptamine induced platelet aggregation in schizophrenic patients. Orr MW, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):255-9

Differential effect of benserazide (Ro4-4602) on the concentration of indoleamines in rat pineal and hypothalamus. Arendt J, et al. **Br J Pharmacol** 1981 Feb;72(2):257-62

Effect of hyperoxia on uptake and metabolism of 5-hydroxytryptamine and beta-phenylethylamine in rat lung: a sex difference. Ben-Harari RR, et al. **Br J Pharmacol** 1981 Jun;73(2):461-6

5-Hydroxytryptamine induces relaxation of goat pulmonary veins: evidence for the noninvolvement of M and D-tryptamine receptors. Chand N. **Br J Pharmacol** 1981 Feb;72(2):233-7

In vivo pharmacological studies on the interactions between tryptamine and 5-hydroxytryptamine. Jones RS. **Br J Pharmacol** 1981 Jun;73(2):485-93

Further studies on 5-hydroxytryptamine transport in pancreatic islets and isolated beta-cells. Lindström P. **Br J Pharmacol** 1981 Jun;73(2):385-91

5-hydroxytryptamine controls ACh-receptor sensitivity of bullfrog sympathetic ganglion cells. Akasu T, et al. **Brain Res** 1981 Apr 27;211(1):217-20

Synaptic remodeling of serotonin axon terminals in rat agranular cerebellum. Beaudet A, et al. **Brain Res** 1981 Feb 16;206(2):305-29

Serotonergic and peptidergic projections to the spinal cord demonstrated by a combined retrograde HRP histochemical and immunocytochemical staining method. Bowker RM, et al. **Brain Res** 1981 May 4;211(2):412-7

Serotonergic projections from the ventral medulla to the intermediolateral cell column in the rat. Loewy AD, et al. **Brain Res** 1981 Apr 27;211(1):146-52

Apparent serotonergic modulation of the dose-dependent biphasic response of neostriatal neurons produced by D-amphetamine. Rebec GV, et al. **Brain Res** 1981 Apr 6;210(1-2):277-89

Serotonin-immunoreactive cells in the superior cervical ganglion of the rat. Evidence for the existence of separate serotonin- and catecholamine-containing small ganglionic cells. Verhofstad AA, et al. **Brain Res** 1981 May 11;212(1):39-49

Evidence of the modulatory role of serotonin in acetylcholine release from striatal interneurons. Vizi ES, et al. **Brain Res** 1981 May 11;212(1):89-99

Morphine analgesia and newly synthesized 5-hydroxytryptamine in the dorsal and the ventral halves of the spinal cord of the rat. Weil-Fugazza J, et al. **Brain Res** 1981 Jun 15;214(2):440-4

The identification of serotonergic neurons in the nucleus raphe magnus by conduction velocity. Wessendorf MW, et al. **Brain Res** 1981 Jun 9;214(1):168-73

Contractile effects of 5-hydroxytryptamine in isolated intrapulmonary arteries and veins. Gruetter CA, et al. **Can J Physiol Pharmacol** 1981 Feb;59(2):157-62

Different influences of two types of diets commonly used for rats on a series of parameters related to the metabolism of central serotonin and noradrenaline. Héroux O, et al. **Can J Physiol Pharmacol** 1981 Feb;59(2):108-12

Location and release of TRH and 5-HT from amphibian skin. Bennett GW, et al. **Cell Biol Int Rep** 1981 Feb;5(2):151-8

The selective inhibition of serotonin-induced contractions of rabbit cerebral vascular smooth muscle by calcium-antagonistic dihydropyridines. An investigation of the mechanism of action of nimodipine. Towart R. **Circ Res** 1981 May;48(5):650-7

Liquid-chromatographic determination of serotonin and tryptophan in whole blood and plasma [letter] Anderson GM, et al. **Clin Chem** 1981 May;27(5):775-6

A modified assay method for determining serotonin uptake in human platelets. Arora RC, et al. **Clin Chim Acta** 1981 May 5;112(2):225-33

Effects of hormones on the RNA-synthesis of Tetrahymena pyriformis. Csaba G, et al. **Comp Biochem Physiol [C]** 1981;68C(2):251-3

Blood-brain barrier for serotonin in the eel (Anguilla anguilla L.). Genot G, et al. **Comp Biochem Physiol [C]** 1981;68C(2):247-50

Serotonin stimulates thyrotropin-releasing hormone release from superfused rats hypothalami. Chen YF, et al. **Endocrinology** 1981 Jun;108(6):2359-66

A serotonergic mechanism of the prolactin-stimulating action of metoclopramide. Fang VS, et al. **Endocrinology** 1981 May;108(5):1622-7

Dopamine in hypophysial portal plasma and prolactin in systemic plasma of rats treated with 5-hydroxytryptamine. Pilotte NS, et al. **Endocrinology** 1981 Jun;108(6):2137-41

Brain serotonin turnover correlates inversely with plasma adrenocorticotropin during the triphasic response to adrenalectomy in rats. Van Loon GR, et al. **Endocrinology** 1981 Jun;108(6):2269-76

Simultaneous determination of femtomole quantities of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in brain using HPLC with electrochemical detection. Lacković Z, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):347-52

Differential effects of clomipramine and clorgyline on the sensitivity of cortical neurons to serotonin: effect of chronic treatment. Olpe HR. **Eur J Pharmacol** 1981 Jan 29;69(3):375-7

Relative activities of substances related to 5-hydroxytryptamine as depolarizing agents of superior cervical ganglion cells. Wallis D, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):381-92

Blood pressure responses to local application of serotonergic agents in the nucleus tractus solitarii. Wolf WA, et al. **Eur J Pharmacol** 1981 Jan 29;69(3):291-9

Long-term effects of a tryptophan-free diet on serotonin metabolism and sleep-waking balance in rats. Lanoir J, et al. **Exp Brain Res** 1981;41(3-4):346-57

Competition between platelets and lung for 5-hydroxytryptamine uptake. Steinberg H, et al. **Exp Lung Res** 1980 Jun;1(2):121-30

Effect of monoamines on firing rate and thermal sensitivity of neurons in the preoptic area of awake rabbits. Gordon CJ, et al. **Exp Neurol** 1981 May;72(2):352-65

A biphasic effect of estradiol on serotonin metabolism in rat pineal organ cultures. Cardinali DP, et al. **Experientia** 1981 Feb 15;37(2):203-4

Serum serotonin, free tryptophan and plasma cyclic AMP levels in autistic children -with special reference to their relation to hyperkinesia. Hoshino Y, et al. **Fukushima J Med Sci** 1979;26(3-4):79-91

Rates of indoleamine synthesis in maturing mouse brain. Baker PC, et al. **Gen Pharmacol** 1981;12(3):151-4

Proton: substrate stoichiometries during active transport of biogenic amines in chromaffin ghosts. Johnson RG, et al. **J Biol Chem** 1981 Jun 10;256(11):5773-80

Amine transport in chromaffin granule ghosts. pH dependence implies cationic form is translocated. Knoth J, et al. **J Biol Chem** 1981 Jul 10;256(13):6541-3

Separation of dissociated thyroid follicular and parafollicular cells: association of serotonin binding protein with parafollicular cells. Bernd P, et al. **J Cell Biol** 1981 Mar;88(3):499-508

The organization of indoleamine neurons in the brain of the rhesus monkey (Macaca mulatta). Schofield SP, et al. **J Comp Neurol** 1981 Apr 10;197(3):369-83

Altered sensitivity to footshock after selective serotonin depletion: comparison of electrolytic lesions and neurotoxin injections in the medial forebrain bundle of the rat. Simansky KJ, et al. **J Comp Physiol Psychol** 1981 Apr;95(2):341-50

Further investigations on Bernard-Soulier platelet abnormalities. Rendu F, et al. **J Lab Clin Med** 1981 May;97(5):689-99

Effect of L-tryptophan on mouse brain 5-hydroxytryptamine: comparison of values obtained using a fluorimetric assay and a liquid Chromatographic assay with electrochemical detection. Marsden CA. **J Neurochem** 1981 May;36(5):1621-6

Application of high performance liquid chromatography with electrochemical detection to neurochemical analysis: measurement of catecholamines, serotonin and metabolites in rat brain. Mefford IN. **J Neurosci Methods** 1981 Feb;3(3):207-24 (47 ref.)

Evidence for a presynaptic inhibitory action of 5-hydroxytryptamine in a mammalian sympathetic ganglion. Dun NJ, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):714-8

The effects of p-chloroamphetamine administration on locomotor activity and serotonin in neonatal and adult rats. Lucot JB, et al. **J Pharmacol Exp Ther** 1981 Jun;217(3):738-44

Effect of progesterone therapy on the responses of the isolated rat stomach fundus strip preparations to 5-hydroxytryptamine and acetylcholine. Qayum A, et al. **JPMA** 1981 Apr;31(4):84-8

The effect of 5-hydroxytryptamine on the slow inward current of bullfrog atrium. Tokimasa T. **Jpn Heart J** 1981 Mar;22(2):227-37

Effect of imipramine on central 5-hydroxytryptamine turnover and metabolism in rats. Segawa T, et al. **Jpn J Pharmacol** 1980 Dec;30(6):789-93

Effect of serotonin on uterine blood flow in pregnant and nonpregnant sheep. Clark KE, et al. **Life Sci** 1980 Dec 22-29;27(25-26):2655-61

Disruption of 5-hydroxytryptaminergic neuronal function blocks the action of morphine on tuberoinfundibular dopaminergic neurons. Demarest KT, et al. **Life Sci** 1981 Mar 23;28(12):1345-51

Mechanism of stimulation of cardiac myocyte beating rate by 5-hydroxytryptamine. Higgins TJ, et al. **Life Sci** 1981 Mar 2;28(9):999-1005

The effect of morphine on the content of serotonin, 5-hydroxyindole acetic acid and substance-P in the nuclei raphe magnus and reticularis gigantocellularis. Lakoski JM, et al. **Life Sci** 1980 Dec 22-29;27(25-26):2639-44

Role of cyclic AMP in a serotonin-evoked slow inward current in snail neurones. Deterre P, et al. **Nature** 1981 Apr 30;290(5809):783-5

Brain serotonin and 5-hydroxyindoleacetic acid concentrations and serotonin synthesis following tetrahydro-beta-carboline administration in mice. Buckholtz NS. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):215-21

Serotonin-receptor-mediated modulation of Ca2+-dependent 5-hydroxytryptamine release from neurones of the rat brain cortex.

Göthert M. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov; 314(3):223-30

Persistence of circadian rhythms of melatonin and N-acetylserotonin in the serum of rats after pinealectomy. Yu HS, et al. **Neuroendocrinology** 1981 May;32(5):262-5

Monoamine uptake into synaptosomes from various regions of rat brain following lithium administration and withdrawal. Ahluwalia P, et al. **Neuropharmacology** 1981 May;20(5):483-7

Similar motor effects of 5-HT and TRH in rats following chronic spinal transection and 5.7-dihydroxytryptamine injection. Barbeau H, et al. **Neuropharmacology** 1981 May;20(5):477-81

Effects of phenytoin on mouse cerebellar 5-hydroxytryptamine and norepinephrine. Fry BW, et al. **Neuropharmacology** 1981 Jun; 20(6):623-5

Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat. Jones DL, et al. **Neuropharmacology** 1981 Jan;20(1):29-37

The functional importance of increased brain tryptophan in the serotonergic response to restraint stress. Kennett GA, et al. **Neuropharmacology** 1981 Jan;20(1):39-43

A diurnal rhythm of N-acetylserotonin in the retina of rats. Pang SF, et al. **Neurosci Lett** 1981 Jan 20;21(2):197-200

Organization of ascending serotonin systems in the adult rat brain. A radioautographic study after intraventricular administration of [3H]5-hydroxytryptamine. Parent A, et al. **Neuroscience** 1981; 6(2):115-38

Distribution of serotonin-immunoreactivity in the central nervous system of the rat-cell bodies and terminals. Steinbusch HW. **Neuroscience** 1981; 6(4):557-618

Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Vachon L, et al. **Neuroscience** 1981; 6(2):189-94

The effect of tryptolines (1, 2, 3, 4-tetrahydro-beta-carbolines) on monoamine metabolism and the platelet aggregation response in human platelets. Youdim MB, et al. **Neuroscience** 1981;6(4):801-10

Central 5-hydroxytryptamine and the effects of hallucinogens and phenobarbital on operant responding in rats. Commissaris RL, et al. **Pharmacol Biochem Behav** 1981 May;14(5):595-601

Tryptophan deprivation: effects on mouse-killing and reactivity in the rat. Vergnes M, et al. **Pharmacol Biochem Behav** 1981; 14 Suppl 1:19-23

Effect of immobilization and of elevation of the 5-hydroxytryptamine concentrations in the brain stem on liver tryptophan pyrrolase activity in a hibernator [the golden hamster]. Novotná R. **Physiol Bohemoslov** 1981;30(1):27-33

Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. Heron DS, et al. **Proc Natl Acad Sci USA** 1980 Dec; 77(12):7463-7

NMR studies of 5-hydroxytryptamine transport through large unilamellar vesicle membranes. Viscio DB, et al. **Proc Natl Acad Sci USA** 1981 Mar;78(3):1638-42

Serotonin involvement in the regulation of gonadotropin secretion during lactation in the rat. Coppings RJ, et al. **Proc Soc Exp Biol Med** 1981 Apr;166(4):536-41

Evidence that it is possible to cause anorexia by increasing release and/or directly stimulating postsynaptic serotonin receptors in the brain. Samanin R, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):363-9

Monoamine theories of sleep: the role of serotonin—a review [proceedings] Morgane PJ. **Psychopharmacol Bull** 1981 Jan; 17(1):13-7 (27 ref.)

Studies on the role of serotonin in avoidance learning [proceedings] Ogren SO. **Psychopharmacol Bull** 1981 Jan;17(1):17-9

Increased brain serotonergic and noradrenergic activity after repeated systemic administration of the beta-2 adrenoceptor agonist salbutamol, a putative antidepressant drug. Hallberg H, et al. **Psychopharmacology (Berlin)** 1981;73(3):201-4

Lesion of serotonergic neurons antagonizes clonidine induced suppression of avoidance behavior and locomotor activity in rats. Kostowski W, et al. **Psychopharmacology (Berlin)** 1981;73(3):261-4

Catecholamine-serotonin interaction effects on activity in rats neonatally treated with 6-hydroxydopamine. Olds ME, et al. **Psychopharmacology (Berlin)** 1981;73(1):31-3

Peripheral correlates of serotonergically-influenced behaviors in vervet monkeys (Cercopithecus aethiops sabaeus). Raleigh MJ, et al. **Psychopharmacology (Berlin)** 1981;72(3):241-6

The effects of d-amphetamine and potassium on serotonin release and metabolism in rat cerebral cortex tissue. Homan HD, et al. **Res Commun Chem Pathol Pharmacol** 1981 Feb;31(2):223-40

Prolonged stimulation of respiration by endogenous central serotonin. Millhorn DE, et al. **Respir Physiol** 1980 Dec;42(3):171-88

Two pools of amines in synaptic vesicles of rat pineal nerves. Pellegrino de Iraldi A, et al. **Rev Can Biol** 1981 Mar;40(1):101-9

Binding of 5-hydroxytryptamine to brain hydrophobic proteins. Inhibition by structural analogues and ions. Cabello FM. **Rev Esp Fisiol** 1980 Dec; 36(4):409-12

Some characteristics of mouse platelet aggregation and a comparison of the activity of a range of compounds in mouse and human platelet-rich plasma in vitro. Nunn B. **Thromb Haemost** 1981 Feb 23;45(1):1-5

Platelet-foreign surface interactions: the release reaction from singly adherent platelets and adherent platelet aggregates. Whicher SJ, et al. **Trans Am Soc Artif Intern Organs** 1980;26:268-73

[A study of renovation rate of dopamine and 5-hydroxytryptamine in brain in chronic schizophrenics (author's transl)] Shen YC. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1979;12(3):158-60 **(Chi)**

[The serotonergic fibers in the striatum. Ultrastructural characteristics (author's transl)] Arluison M. **J Physiol (Paris)** 1981 Apr;77(1):45-51 (71 ref.) (Eng. Abstr.) **(Fre)**

[Effect of reserpine on monoamine uptake by rat brain synaptosomes] Blaschke M, et al. **Acta Biol Med Ger** 1980;39(11-12):1205-12 (Eng. Abstr.) **(Ger)**

[Development of biological psychiatric depression research (author's transl)] Matussek N. **MMW** 1981 May 8;123(19):793-4 (Eng. Abstr.) **(Ger)**

[Modulation of the effect of morphine on the isolated guinea pig intestine by noradrenaline and serotonin] Sarto G. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):394-400 (Eng. Abstr.) **(Ita)**

[Interaction of indoleamines with serotonergic receptors of brain synaptosomes] Uzbekov MG, et al. **Biokhimiia** 1980 Jan;45(1):109-12 (Eng. Abstr.) **(Rus)**

[pH gradient in the membranes of serotonin-containing granules of thrombocytes: principles for studying them using fluorescent amino-derivatives of acridine] Kozlov VK, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):155-7 (Eng. Abstr.) **(Rus)**

[Nonspecific suppressor cells in the inhibiting action of serotonin on immunogenesis] Devoino LV, et al. **Dokl Akad Nauk SSSR** 1981; 256(2):506-9 **(Rus)**

[Changes in neuronal responses to multiple administrations of serotonin] Solntseva EI, et al. **Dokl Akad Nauk SSSR** 1981;256(6):1499-503 **(Rus)**

[Histamine and serotonin study in 1 blood sample] Proshina LIa. **Lab Delo** 1981;(2):90-3 (Eng. Abstr.) **(Rus)**

[Histamine and serotonin content in immunocompetent tissues and blood in vagotomized rats] Aksenova VM. **Patol Fiziol Eksp Ter** 1981 Jan-Feb;(1):23-6 (Eng. Abstr.) **(Rus)**

SEX BEHAVIOR, ANIMAL

Effects of cannabinoids and female exposure on the pituitary-testicular axis in mice: possible involvement of prostaglandins. Dalterio S, et al. **Biol Reprod** 1981 Mar;24(2):315-22

Bisexual behavior in male rats treated neonatally with antibodies to luteinizing hormone-releasing hormone. Kalcheim C, et al. **J Comp Physiol Psychol** 1981 Feb;95(1):36-44

Delta-9-Tetrahydrocannabinol stimulates receptive and proceptive sexual behaviors in female hamsters. Turley WA Jr, et al. **Pharmacol Biochem Behav** 1981 May;14(5):745-7

[The influence of oxazepam and diazepam on the sexual behaviour and level of GABA biogenic amines in a male rat's brain (author's transl)] Borzęcki Z, et al. **Ann Univ Mariae Curie Sklodowska [Med]** 1979; 34:371-6 (Eng. Abstr.) **(Pol)**

SLEEP

Effect of cannabidiol on cytochrome P-450 and hexobarbital sleep time. Bornheim LM, et al. **Biochem Pharmacol** 1981 Mar 1;30(5):503-7

The effect of p-bromomethamphetamine (V-111) on sleep on the rat. Juvancz P. **Eur J Pharmacol** 1981 Apr 9;70(4):461-6

Phasic hippocampal activity during paradoxical sleep in the rat: selective suppression after diazepam administration. Monmaur P. **Experientia** 1981 Mar 15;37(3):261-2

Bromocriptine, dihydroergotoxine and sleep in rats: effects of repeated administration. Radulovacki M, et al. **Gerontology** 1981;27(3):152-7

Enhancement of hexobarbital-induced sleep by lysine and its metabolites. Chang YF, et al. **Life Sci** 1981 Jan 26;28(4):407-13

Monoamine theories of sleep: the role of serotonin—a review [proceedings] Morgane PJ. **Psychopharmacol Bull** 1981 Jan; 17(1):13-7 (27 ref.)

SLEEP DEPRIVATION

Circadian variations in cardiovascular parameters during sleep deprivation. A noninvasive study of young healthy men. Ahnve S, et al. **Eur J Applied Physiol** 1981;46(1):9-19

Changes of response to dopaminergic drugs in rats submitted to REM-sleep deprivation. Tufik S. **Psychopharmacology (Berlin)** 1981; 72(3):257-60

SLEEP, REM

Phenoxybenzamine and bromocriptine attenuate need for REM sleep in rats. Radulovacki M, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):371-5

Changes of response to dopaminergic drugs in rats submitted to REM-sleep deprivation. Tufik S. **Psychopharmacology (Berlin)** 1981; 72(3):257-60

[Beta-adrenergic receptors and paradoxical sleep in the rat] Lanfumey L, et al. **C R Acad Sci [D] (Paris)** 1981 Mar 2;292(9):645-7 (Eng. Abstr.) **(Fre)**

SLEEP STAGES

Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat. Borbély AA, et al. **Behav Brain Res** 1981 Jan; 2(1):1-22

Long-term effects of a tryptophan-free diet on serotonin metabolism and sleep-waking balance in rats. Lanoir J, et al. **Exp Brain Res** 1981; 41(3-4):346-57

Diurnal rhythm of plasma immunoreactive beta-endorphin and its relationship to sleep stages and plasma rhythms of cortisol and prolactin. Dent RR, et al. **J Clin Endocrinol Metab** 1981 May;52(5):942-7

SODIUM

Role of calcium and sodium in strophanthidin inotropy in cardiac Purkinje fibers. Bhattacharyya ML, et al. **Am J Physiol** 1981 Apr; 240(4):H561-70

Sodium-calcium interactions in the renal proximal convoluted tubule of the rabbit. Friedman PA, et al. **Am J Physiol** 1981 Jun; 240(6):F558-68

Role of cyclic GMP in cholinergic activation of Na-K pump in duck salt gland. Stewart DJ, et al. **Am J Physiol** 1981 May; 240(5):C207-14

Is ouabain-sensitive rubidium or potassium uptake a measure of sodium pump activity in isolated cardiac muscle? Akera T, et al. **Biochim Biophys Acta** 1981 Feb 6;640(3):779-90

Permeability of reconstituted sarcoplasmic reticulum vesicles. Reconstitution of the K+, Na+ channel. Young RC, et al. **Biomembranes** 1981 Jan 22;640(2):409-18

Further evidence for the involvement of Na+ channels in the release of adrenal catecholamine: the effect of scorpion venom and grayanotoxin I. Ito S, et al. **Br J Pharmacol** 1981 Jan;72(1):61-7

Exocytotic secretion of catecholamines from the cat adrenal medulla by sodium deprivation: involvement of calcium influx mechanism. Nishimura S, et al. **Br J Pharmacol** 1981 Feb;72(2):305-17

Possible occurrence of Na+-dependent Ca2+ influx mechanism in isolated bovine chromaffin cells. Sorimachi M, et al. **Brain Res** 1981 Mar 16;208(2):442-6

Release of noradrenaline from the rat tail artery induced by inhibition of the sodium pump in calcium-free solution. Palatý V. **Can J Physiol Pharmacol** 1981 Apr;59(4):347-50

Melittin stimulates Na entry, Na-K pump activity and DNA synthesis in quiescent cultures of mouse cells. Rozengurt E, et al. **Cell** 1981 Mar; 23(3):781-8

Effects of cations on brown adipose tissue in relation to possible metabolic consequences of membrane depolarisation. Nedergaard J. **Eur J Biochem** 1981;114(1):159-67

Jejunal water and electrolyte secretion induced by L-arginine in man. Hegarty JE, et al. **Gut** 1981 Feb;22(2):108-13

Human fetal membranes: investigations on membrane potentials and membrane 24Na permeability in vitro and the possible involvement of acetylcholine. Welsch F. **Gynecol Obstet Invest** 1981;12(3):113-22

Sodium and rubidium uptake in cells transformed by Rous sarcoma virus. Bader JP, et al. **J Cell Physiol** 1981 Feb;106(2):235-43

Mechanisms for the effects of acetylcholine on sodium transport in frog skin. Cuthbert AW, et al. **J Membr Biol** 1981 Mar 15;59(1):65-75

Avid Na+-dependent, high-affinity uptake of alpha-ketoglutarate by nerve terminal enriched material from mouse cerebellum. Shank RP, et al. **Life Sci** 1981 Feb 23;28(8):843-50

Effect of monovalent cations on the aggregation of tobacco mosaic virus by chondroitin sulfate. Sano Y, et al. **Microbiol Immunol** 1981; 25(2):155-61

Sodium current depression by lidocaine and quinidine in isolated ventricular cells. Lee KS, et al. **Nature** 1981 May 28; 291(5813):325-7

[Relation between renal hemodynamic parameters and urinary concentrations of sodium and solutes suggestive of various methods of controlling renal function] Agnoli GC, et al. **Boll Soc Ital Biol Sper** 1981 Feb 28;57(4):442-8 (Eng. Abstr.) **(Ita)**

[Mechanisms of the renal action of dopamine and their dependence on changes in the sodium balance. II. Studies on water-salt depletion] Agnoli GC, et al. **Boll Soc Ital Cardiol** 1979;24(12):1331-49 **(Ita)**

[Mechanisms of the renal action of dopamine and thier dependence on changes in sodium balance. Studies on water-salt retention] Agnoli GC, et al. **Boll Soc Ital Cardiol** 1979;24(12):1315-29 **(Ita)**

SOMATOTROPIN RELEASE INHIBITING HORMONE

Rate of thymidine incorporation and incidence of parenchymal cell division in adult rat hypophyseal cell cultures. Effect of thyroliberin and somatostatin. Rappay G, et al. **Acta Biol Acad Sci Hung** 1980; 31(1-3):249-55

Effect of somatostatin on regional splanchnic blood flows in man. Angiographic studies. Samnegård H, et al. **Acta Chir Scand [Suppl]** 1980; Suppl 500:71-3

Effect of intraluminal pH on the release of somatostatin and gastrin into antral, bulbar and ileal pouches of conscious dogs. Uvnäs-Wallensten K, et al. **Acta Physiol Scand** 1980 Dec;110(4):391-400

Effect of D-Val1, D-Trp8-somatostatin on the motility of the stomach, duodenum and jejunum. Chernish SM, et al. **Am J Gastroenterol** 1981 Jan;75(1):36-40

Release of somatostatin from rodent antral mucosae maintained in organ culture. Lichtenberger LM, et al. **Am J Physiol** 1981 Jul; 241(1):G59-66

Four hormones in the pancreas of the lizard, Anolis carolinensis. Rhoten WB, et al. **Anat Rec** 1981 Jan;199(1):89-97

Lack of effect of somatostatin on the glucagon-induced alterations of hepatic metabolism of [1-14C]oleate. Weinstein I, et al. **Biochim Biophys Acta** 1981 Apr 23;664(1):124-32

Glucagon action upon plasma post-heparin lipolytic and monoglyceride hydrolase activities. Studies involving administration of exogenous hormone during suppression of endogenous hormone secretion with somatostatin. de Basilico MZ, et al. **Biomedicine** 1980 Nov; 33(7):213-6

Somatostatin-28, somatostatin-14 and somatostatin analogs: effects on thermoregulation. Brown M, et al. **Brain Res** 1981 Jun 9; 214(1):127-35

Somatostatin in the auditory system of the rat. Takatsuki K, et al. **Brain Res** 1981 May 25;213(1):211-6

Gastric inhibitory polypeptide stimulated secretion of somatostatinlike immunoreactivity from the stomach: inhibition by acetylcholine or vagal stimulation. McIntosh CH, et al. **Can J Physiol Pharmacol** 1981 May; 59(5):468-72

Synthesis of a glycotripeptide and a glycosomatostatin containing the 3-O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)-L-serine residue. Lavielle S, et al. **Carbohydr Res** 1981 Mar 2;89(2):229-36

Solid-phase synthesis of two glycopeptides containing the amino acid sequence 5 to 9 of somatostatin. Lavielle S, et al. **Carbohydr Res** 1981 Mar 2;89(2):221-8

The origin of somatostatin fibers in the median eminence and neural lobe of Rana temporaria. Dierickx K, et al. **Cell Tissue Res** 1981; 215(1):41-5

Nerves containing substance P, vasoactive intestinal polypeptide, enkephalin or somatostatin in the guinea-pig taenia coli. Distribution, ultrastructure and possible functions. Leander S, et al. **Cell Tissue Res** 1981;215(1):21-39

Evidence for somatostatin, gastrin and pancreatic polypeptide-like substances in the mucosa cells of the gut in fishes with and without stomach. Noaillac-Depeyre J, et al. **Cell Tissue Res** 1981; 216(1):193-203

Simple extraction method and radioimmunoassay for somatostatin in human plasma. Peeters TL, et al. **Clin Chem** 1981 Jun;27(6):888-91

Altered ability of the liver to produce glucose following a period of glucagon deficiency. Deri JJ, et al. **Diabetes** 1981 Jun;30(6):490-5

Effect of somatostatin on the flow rate and triglyceride levels of thoracic duct lymph in normal and vagotomized dogs. Nakabayashi H, et al. **Diabetes** 1981 May;30(5):440-5

Previous exposure to glucose enhances somatostatin secretion from the isolated perfused rat pancreas. Grill V, et al. **Diabetologia** 1981 Apr; 20(4):495-500

Effect of a new hypoglycaemic agent (HB 699) on the in vivo secretion of pancreatic hormones in the dog. Ribes G, et al. **Diabetologia** 1981 Apr;20(4):501-5

Possible involvement of the cholinergic system in hormonal secretion by the perfused pancreas from ventromedial-hypothalamic lesioned rats. Rohner-Jeanrenaud F, et al. **Diabetologia** 1981 Mar;20(3):217-22

Autonomic function and control of pancreatic somatostatin. Samols E, et al. **Diabetologia** 1981 Mar;20 Suppl:388-92

The effect of somatostatin on bombesin-stimulated serum gastrin and gastric acid secretion in man. Jansen JB, et al. **Digestion** 1981; 21(4):193-7

Use of the mouse vas deferens assay to evaluate the action of somatostatin peptides on gastric acid secretion. Meyers CA, et al. **Digestion** 1981; 21(1):21-4

Effect of somatostatin and calcium deprivation on cholecystokinin or caerulein-induced insulin and glucagon release from the isolated perfused rat pancreas. Otsuki M, et al. **Endocrinol Jpn** 1980 Dec; 27 Suppl 1:95-102

Effect of somatostatin on blood levels of motilin and the interdigestive myoelectric complex in dogs. Poitras P, et al. **Endocrinol Jpn** 1980 Dec; 27 Suppl 1:163-6

Role of glucagon and somatostatin in insulin release. Taniguchi H, et al. **Endocrinol Jpn** 1980 Dec;27 Suppl 1:103-7

Effect of intraventricular injection of neurotensin and other various bioactive peptides on plasma immunoreactive somatostatin levels in rat hypophysial portal blood. Abe H, et al. **Endocrinology** 1981 May; 108(5):1939–43

Isolation and characterization of rat hypothalamic somatostatin–14. Bohlen P, et al. **Endocrinology** 1981 May;108(5):2008–10

Somatostatin–28: selective action on the pancreatic beta–cell and brain. Brown M, et al. **Endocrinology** 1981 Jun;108(6):2391–6

Effect of insulin on glucose– and arginine–stimulated somatostatin secretion from the isolated perfused rat pancreas. Gerber PP, et al. **Endocrinology** 1981 Jul;109(1):279–83

Effect of calcium on the secretion of somatostatin and insulin from pancreatic islets. Kanatsuka A, et al. **Endocrinology** 1981 Jun; 108(6):2254–7

Heterogeneity of somatostatin–like peptides in rat brain, pancreas, and gastrointestinal tract. Trent DF, et al. **Endocrinology** 1981 Jun; 108(6):2033–8

Effects of somatostatin–14 and somatostatin–28 on bombesin–stimulated release of gastrin, insulin, and glucagon in the dog. Vaysse N, et al. **Endocrinology** 1981 May;108(5):1843–7

Factors modulating the secretion of thyrotropin and other hormones of the thyroid axis. Hedge GA, et al. **Environ Health Perspect** 1981 Apr; 38:57–63

The effect of somatostatin on haemostasis in dogs. Gabryelewicz A, et al. **Folia Haematol (Leipz)** 1981;108(1):125–31

Effect of antisomatostatin gamma–globulin on gastrin release in rats. Chiba T, et al. **Gastroenterology** 1981 Aug;81(2):321–6

TRH, GH–RIH, and LH–RH in metamorphosing Xenopus laevis. King JA, et al. **Gen Comp Endocrinol** 1981 May;44(1):20–7

Demonstration of peptides immunologically related to vertebrate neurohormones in Dugesia lugubris (Turbellaria, Tricladida). Schilt J, et al. **Gen Comp Endocrinol** 1981 Mar;43(3):331–5

Correlative immunocytochemical and electron microscopic studies: identification of (entero)glucagon– somatostatin– and pancreatic polypeptide–like–containing cells in the human colon. Lehy T, et al. **Histochemistry** 1981;71(1):67–80

Failure of somatostatin and beta–endorphin to affect bovine adrenal cortex cells in vitro. Diel F, et al. **Horm Metab Res** 1981 Feb;13(2):95–8

Effects of antisomatostatin and antiglucagon sera on insulin release from isolated Langerhans' islets of rats. Tanigawa K, et al. **Horm Metab Res** 1981 Feb;13(2):78–80

Inhibition of islet prohormone to hormone conversion by incorporation of arginine and lysine analogs. Noe BD. **J Biol Chem** 1981 May 25; 256(10):4940–6

Release of somatostatin–like immunoreactivity from the perfused canine thyroid. Selective stimulatory effect of calcium ions. Laurberg P, et al. **J Clin Invest** 1981 May;67(5):1451–6

Immunohistochemical localization of substance–P, somatostatin, and methionine–enkephalin in the spinal cord and dorsal root ganglia of the North American opossum, Didelphis virginiana. Ditirro FJ, et al. **J Comp Neurol** 1981 May 10;198(2):351–63

Somatostatin decreases food intake of rats and baboons. Lotter EC, et al. **J Comp Physiol Psychol** 1981 Apr;95(2):278–87

The effect of somatostatin on pancreatic endocrine responses mediated via the parasympathetic innervation in the conscious calf. Bloom SR, et al. **J Physiol (Lond)** 1980 Nov;308:29–38

Non–vasoactive intestinal polypeptide, nonsomatostatin fundic inhibitoy mechanism. Soon–Shiong P, et al. **J Surg Res** 1981 May; 30(5):473–77

Action of prosomatostatin [letter] Bommelaer G, et al. **Lancet** 1981 Apr 25;1(8226):949

Systemic and pulmonary haemodynamic effects of somatostatin [letter] Hallemans R, et al. **Lancet** 1981 Jun 6;1(8232):1270

Stimulatory effect of somatostatin on norepinephrine release from rat brain cortex slices. Tsujimoto A, et al. **Life Sci** 1981 Feb 23;28(8):903–10

Role of cyclic nucleotides in the inhibition of growth–hormone secretion by somatostatin. Bicknell RJ, et al. **Mol Cell Endocrinol** 1981 Apr; 22(1):85–94

Absence of luteinizing hormone–releasing and anti–fertility properties in a glucagon–selective somatostatin analogue. Bex FJ, et al. **Nature** 1981 Jun 25;291(5817):672–3

Selective effects of somatostatin–14, –25 and –28 on in vitro insulin and glucagon secretion. Mandarino L, et al. **Nature** 1981 May 7; 291(5810):76–7

Ionic channels involved in the LHRH and SRIF release from rat mediobasal hypothalamus. Drouva SV, et al. **Neuroendocrinology** 1981 Mar;32(3):155–62

Opiate receptors modulate LHRH and SRIF release from mediobasal hypothalamic neurons. Drouva SV, et al. **Neuroendocrinology** 1981 Mar; 32(3):163–7

Somatostatin–like immunoreactivity in amacrine cells of the chicken retina. Buckerfield M, et al. **Neuroscience** 1981;6(4):689–95

Gastrointestinal secretory, motor, circulatory, and metabolic effects of prosomatostatin. Konturek SJ, et al. **Proc Natl Acad Sci USA** 1981 Mar; 78(3):1967–71

The biological activity of catfish pancreatic somatostatin. Oyama H, et al. **Regul Pept** 1981 Mar;1(6):387–96

The kinetics of somatostatin inhibition of gastric acid secretion. Thomas WE. **Regul Pept** 1980 Dec;1(3):245–51

Beneficial effect of somatostatin in phalloidin–intoxicated rats. Influence on survival rate, biochemical and morphological data, and 3H–demethylphalloin absorption rate by the liver. Wdowinski JM, et al. **Res Exp Med (Berl)** 1981.178(2):155–63

The effect of somatostatin on fasting and postprandial plasma GIP, serum insulin, and blood glucose in man. Jorde R, et al. **Scand J Gastroenterol** 1981;16(1):113–9

Gastrectomy with and without duodenal transit: release of glucagon, insulin and somatostatin. Heil T, et al. **Scand J Gastroenterol [Suppl]** 1981;67:83–7

[Somatostain: a pancreatic hormone which may be important] Strosser MT, et al. **Journ Annu Diabetol Hotel Dieu** 1981;:197–210 (51 ref.) (Fre)

[Inhibition of glucose and leucin absorption by somatostatin in the dog (author's transl)] Mörz R, et al. **Res Exp Med (Berl)** 1981; 178(3):241–6 (Eng. Abstr.) (Ger)

[Somatostatin. I: Structure, biosynthesis and effect] Zühlke H, et al. **Z Gesamte Inn Med** 1981 Jan 15;36(2):51–5 (Eng. Abstr.) (Ger)

STEREOTYPED BEHAVIOR

Ipsiversive turning behaviour after discrete unilateral lesions of the dorsal mesencephalic reticular formation by kainic acid. Mulas A, et al. **Brain Res** 1981 Mar 16;208(2):468–72

Cats develop tolerance to d–amphetamine's effects upon locomotion and stereotyped behaviors. Jacobs BL, et al. **Eur J Pharmacol** 1981 Jan 29; 69(3):353–6

Estrogen potentiates the stereotypy induced by dopamine agonists in the rat. Chiodo LA, et al. **Life Sci** 1981 Feb 16;28(7):827–35

Drug–environment interaction: context dependency of cocaine–induced behavioral sensitization. Post RM, et al. **Life Sci** 1981 Feb 16; 28(7):755–60

The stereotyped behavior syndrome: a new model and proposed therapy. Kryzhanovsky GN, et al. **Pharmacol Biochem Behav** 1981 Mar; 14(3):273–81

Effect of morphine on circling behaviour in rats with 6–hydroxydopamine striatal lesions and electrolesions of the raphe nucleus. Slater P. **Pharmacol Biochem Behav** 1981 May;14(5):625–30

Pharmacokinetic study of apomorphine–induced stereotypy in food deprived rats. Watanabe H, et al. **Pharmacol Biochem Behav** 1981 Apr; 14(4):493–6

Use of the intracerebral injection technique to elucidate mechanisms of apomorphine climbing and its antagonism in the mouse. Costall B, et al. **Psychopharmacology (Berlin)** 1981;73(1):91–4

[Neurophysiologic and pharmacologic evidence of autoregulationin the nigrostriatal system] Arushanian EB, et al. **Biull Eksp Biol Med** 1981 Feb;91(2):133–6 (Eng. Abstr.) (Rus)

STRESS, PSYCHOLOGICAL

Biochemical and circulatory parameters during purely mental stress. Danner SA, et al. **Acta Med Scand** 1981;209(4):305–8

The effect of acute neurogenic stress on corticosterone and Cu an Zn levels in rats. Armario A, et al. **Agressologie** 1980;21(5):259–62

Regional responses of rat brain noradrenergic neurones to acute intense stress. Nakagawa R, et al. **Pharmacol Biochem Behav** 1981 May; 14(5):729–32

Mechanism of stress–induced subsensitivity to norepinephrine. Stone EA. **Pharmacol Biochem Behav** 1981 May;14(5):719–23

Plasma catecholamines in rats: daily variations in basal levels and increments in response to stress. McCarty R, et al. **Physiol Behav** 1981 Jan;26(1):27–31

Adrenal hormones and brain catecholamines responses to morning and afternoon immobilization stress in rats. Torrellas A, et al. **Physiol Behav** 1981 Jan;26(1):129–33

[Studies on stress in psychiatric patients (author's transl)] Ackenheil M, et al. **MMW** 1981 May 8;123(19):805–8 (Eng. Abstr.) (Ger)

[Determination of psychological stress in sea pilot based on urinary catecholamine excretion] Geister R, et al. **Zentralbl Arbeitsmed Arbeitsschutz Prophyl Ergonomie** 1980 Dec; 30(12):458–63 (Ger)

[Activation of the cerebral GABA–ergic inhibiting system in stress] Pavlova VI, et al. **Patol Fiziol Eksp Ter** 1981 Jan–Feb;(1):26–30 (Eng. Abstr.) (Rus)

SUBSTANCE P

Effect of intracerebroventricular administration of substance P and its hexapeptide fragment on the estrus cycle in female rats. Jakubowska–Naziemblo B, et al. **Acta Physiol Pol** 1980;31(6):637–45

Effect of substance P and its C–terminal hexapeptide on gastric and pancreatic secretion in the dog. Konturek SJ, et al. **Am J Physiol** 1981 Jul;241(1):G74–81

Activity of substance P analogs substituted at the Gly9 and Gln6 positions. Blumberg S, et al. **Biochem Biophys Res Commun** 1981 Mar 31; 99(2):752–8

Effect of substance P and its natural analogues on gastric emptying of the conscious rat. Bertaccini G, et al. **Br J Pharmacol** 1981 Feb; 72(2):221-3

The effects of substance P and related peptides on alpha-amylase release from rat parotid gland slices. Brown CL, et al. **Br J Pharmacol** 1981 Jun;73(2):517-23

Circadian variations in substance P, luliberin (LH-RH) and thyroliberin (TRH) contents in hypothalamic and extrahypothalamic brain nuclei of adult male rats. Kerdelhue B, et al. **Brain Res** 1981 Feb 16; 206(2):405-13

Substance P decreases a potassium conductance of spinal cord neurons in cell culture. Nowak LM, et al. **Brain Res** 1981 Jun 15; 214(2):416-23

Behavioral evidence that substance P may be a spinal cord sensory neurotransmitter. Piercey MF, et al. **Brain Res** 1981 Apr 6; 210(1-2):407-12

Immunoreactive substance P in the chicken gut: distribution, development and possible functional significance. Brodin E, et al. **Cell Tissue Res** 1981;216(3):455-69

Nerves containing substance P, vasoactive intestinal polypeptide, enkephalin or somatostatin in the guinea-pig taenia coli. Distribution, ultrastructure and possible functions. Leander S, et al. **Cell Tissue Res** 1981;215(1):21-39

Effect of intraventricular injection of neurotensin and other various bioactive peptides on plasma immunoreactive somatostatin levels in rat hypophysial portal blood. Abe H, et al. **Endocrinology** 1981 May; 108(5):1939-43

Synthesis and biological properties of enzyme-resistant analogues of substance P. Sandberg BE, et al. **Eur J Biochem** 1981 Feb; 114(2):329-37

Substance P in human cord blood and its degradation by placenta in vitro. Skrabanek P, et al. **Eur J Obstet Gynaecol Reprod Biol** 1980 Dec; 11(3):157-61

In vitro release of substance P from spinal cord slices by capsaicin congeners. Bucsics A, et al. **Eur J Pharmacol** 1981 Apr 24; 71(1):71-7

Central blood pressure effects of substance P and angiotensin II: role of the sympathetic nervous system and vasopressin. Unger T, et al. **Eur J Pharmacol** 1981 Apr 24;71(1):33-42

Persistent action of N-methylated analogs of substance P on rat parotid slices. Laufer R, et al. **FEBS Lett** 1981 Jan 26;123(2):291-4

Antagonistic action of baclofen on substance P-induced depolarization in the isolated spinal cord of the frog. Kudo Y, et al. **Gen Pharmacol** 1981,12(3):145-9

Immunocytochemical study of substance P containing nerve terminals in rat spinal cord. Technical considerations. Kakudo K, et al. **Histochemistry** 1981;71(1):17-32

In vitro contraction of the pupillary sphincter by substance P and its stable analogs. Cohen S, et al. **Invest Ophthalmol Vis Sci** 1981 Jun; 20(6):717-21

Characterization of neuropeptides by reversed-phase, ion-pair liquid chromatography with post-column detection by radioimmunoassay. Application to thyrotropin-releasing hormone, substance P, and vasopressin. Spindel E, et al. **J Chromatogr** 1981 Mar 13; 222(3):381-7

Immunohistochemical localization of substance-P, somatostatin, and methionine-enkephalin in the spinal cord and dorsal root ganglia of the North American opossum, Didelphis virginiana. Ditirro FJ, et al. **J Comp Neurol** 1981 May 10;198(2):351-63

Stimulatory and inhibitory effects of substance P on rat submandibular secretion. Martinez JR, et al. **J Dent Res** 1981 Jun;60(6):1031-8

Participation of prostaglandins in the vasodepressor effect of substance P. Pals DT, et al. **J Pharm Pharmacol** 1981 Feb;33(2):110-1

The effect of morphine on the content of serotonin, 5-hydroxyindole acetic acid and substance-P in the nuclei raphe magnus and reticularis gigantocellularis. Lakoski JM, et al. **Life Sci** 1980 Dec 22-29; 27(25-26):2639-44

Does substance P participate in water transport and excretion? Güllner HG. **Med Hypotheses** 1981 Mar;7(3):311-4

Substance P immunoreactive neurons following neonatal administration of capsaicin. Cuello AC, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jan;315(3):185-94

Indirect evidence for the importance of axonal transport in maintenance of stores of the mediator of neurogenic oedema. Morton CR, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):277-80

Further characterization of the binding of substance P to a fraction from rabbit brain enriched in synaptic membranes. Nakata Y, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1980 Nov;314(3):211-4

Response of striatonigral substance P systems to a dopamine receptor agonist and antagonist. Hanson G, et al. **Neuropharmacology** 1981 Jun; 20(6):541-8

The cornea is not innervated by substance P-containing primary afferent neurons. Neuhuber W, et al. **Neurosci Lett** 1981 Feb 23;22(1):5-9

Projections of substance P-containing neurons within the guinea-pig small intestine. Costa M, et al. **Neuroscience** 1981;6(3):411-24

Immunoreactive substance P in sympathetic ganglia: distribution and sensitivity towards capsaicin. Gamse R, et al. **Neuroscience** 1981; 6(3):437-41

An immunohistochemical study of enkephalins and other neuropeptides in the striatum of the cat with evidence that the opiate peptides are arranged to form mosaic patterns in register with the striosomal compartments visible by acetylcholinesterase staining. Graybiel AM, et al. **Neuroscience** 1981;6(3):377-97

Human spinal neurons: innervation by both substance P and enkephalin. LaMotte CC, et al. **Neuroscience** 1981;6(4):713-23

Peptide containing nerves in the ureter of the guinea-pig and cat. Wharton J, et al. **Neuroscience** 1981;6(5):969-82

Substance P as a baro- and chemoreceptor afferent neurotransmitter: immunocytochemical and neurochemical evidence in the rat. Helke CJ, et al. **Peptides (Fayetteville)** 1980 Spring;1(1):1-9

Influence of substance P on the behavioral changes induced by haloperidol in rats. Jolicoeur FB, et al. **Peptides (Fayetteville)** 1980 Spring; 1(1):103-7

Substance P activity in the bullfrog retina: localization and identification in several vertebrate species. Eskay RL, et al. **Science** 1981 May 29; 212(4498):1049-50

[Distribution of substance P and methionine enkephalin in dorsolateral pontine tegmentum of the cat. Immunofluorescence study] Charnay Y, et al. **C R Acad Sci [D] (Paris)** 1981 Feb 2;292(5):435-40 (Eng. Abstr.) **(Fre)**

[The activity of dipeptidyl peptidase IV in various organs and tissues of the rat and its possible relation with substance P metabolism] Labsch B, et al. **Pharmazie** 1981;36(2):161-3 **(Ger)**

SUBSTANCE USE DISORDERS

Use of a drug-screening service in an inner-city teaching hospital. Bury RW, et al. **Med J Aust** 1981 Feb 7;1(3):132-3

SUCKING BEHAVIOR

Decreased dopamine turnover in the median eminence in response to suckling in the lactating rat. Selmanoff M, et al. **Brain Res** 1981 May 11;212(1):101-15

SYMPATHOMIMETICS

Differential beta-adrenergic sensitivity of atrial tissue assessed by chronotropic and inotropic responses to several sympathomimetic amines. Marquez MT, et al. **Acta Physiol Lat Am** 1978; 28(4-5):193-9

Pindolol in orthostatic hypotension [letter] Nyberg G. **Br Med J** 1981 May 23;282(6277):1704

Intracerebroventricular injection of sympathomimetic drugs inhibits both heat production and heat loss mechanisms in the rat. Lin MT, et al. **Can J Physiol Pharmacol** 1980 Aug;58(8):896-902

Effect of increased adrenergic activity on the relationship between electrical and mechanical systole. Boudoulas H, et al. **Circulation** 1981 Jul;64(1):28-33

Cholinergic effect of 4-aminopyridine and adrenergic effect of 4-methyl-2-aminopyridine in cardiac muscle. Glover WE. **Eur J Pharmacol** 1981 Apr 24;71(1):21-31

Responses of the rat anococcygeus muscle to sympathomimetics. Fanimo O, et al. **Gen Pharmacol** 1981;12(3):205-8

[Effects of parasympathomimetic and sympathomimetic drugs on the sublingual glands of rats] Abe K, et al. **Gifu Shika Gakkai Zasshi** 1980 Jun;8(1):36-52 (Eng. Abstr.) **(Jpn)**

[Procedure for using adrenomimetic preparations in heart surgery] Solov'ev GM, et al. **Kardiologiia** 1981 Feb;21(2):26-31 (Eng. Abstr.) **(Rus)**

SYNAPTIC RECEPTORS

The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures. Shibla DB, et al. **Brain Res** 1981 Apr 6;210(1-2):471-4

gamma-Aminobutyric acid regulation of the benzodiazepine receptor: biochemical evidence for pharmacologically different effects of benzodiazepines and propyl beta-carboline-3-carboxylate. Ehlert FJ, et al. **Eur J Pharmacol** 1981 Apr 9;70(4):593-5

Molecular sizes of benzodiazepine receptors and the interacting GABA receptors in the membrane are identical. Chang LR, et al. **FEBS Lett** 1981 Apr 20;126(2):309-12

Benzodiazepine receptor: heterogeneity in rabbit brain. Yokoi I, et al. **Life Sci** 1981 Apr 6;28(14):1591-5

Discrimination of functionally heterogeneous receptor subpopulations: antipsychotic and antidopaminergic properties of metoclopramide [proceedings] Rotrosen J, et al. **Psychopharmacol Bull** 1981 Jan; 17(1):110-3

TASK PERFORMANCE AND ANALYSIS

Psychophysiological effects of repetitive tasks. Weber A, et al. **Ergonomics** 1980 Nov;23(11):1033-46

TESTOSTERONE

Effect of zinc supplementation on serum testosterone level in adult male sickle cell anemia subjects. Prasad AS, et al. **Am J Hematol** 1981; 10(2):119–27

Gonadotropin-releasing hormone analog and testosterone synergistically inhibit spermatogenesis. Heber D, et al. **Endocrinology** 1981 May; 108(5):2019–21

The role of hypothalamic adrenergic receptors in preventing testosterone-induced androgenization in the female rat brain. Raum WJ, et al. **Endocrinology** 1981 Jul;109(1):273–8

Bromocriptine stimulates testosterone production by mouse testes in vitro. Bartke A, et al. **Fertil Steril** 1981 Apr;35(4):472–6

Plasma thyroxine and testosterone levels in the red fox (Vulpes vulpes L.) during the annual cycle. Maurel D, et al. **Gen Comp Endocrinol** 1981 Mar;43(3):402–4

Inhibition of the action of sex steroids by gonadotropin-releasing hormone (GnRH) agonists: a new biological effect. Sundaram K, et al. **Life Sci** 1981 Jan 5;28(1):83–8

Impact of social conflict between mice on testosterone binding in the central nervous system. Raab A, et al. **Neuroendocrinology** 1981 May; 32(5):272–7

Influence of castration and testosterone propionate on [3H]noradrenaline metabolism in various structures of male rat brain. Bekhtereva EP. **Neurosci Behav Physiol** 1980 Nov–Dec;10(6):471–3

Effect of androgens on the rate of muscle protein breakdown in rats treated with glucocorticoids. Santidrian S, et al. **Reproduccion** 1980 Oct–Dec;4(4):331–3

Delta9-tetrahydrocannabinol increase plasma testosterone concentrations in mice. Dalterio S, et al. **Science** 1981 Jul 31;213(4507):581–3

[Endocrinology and diseases of the testis in children] Zweymüller E. **Wien Med Wochenschr** 1981 Feb 15;131(3):68–72 (Ger)

THIOPROPERAZINE

[Effect of aminazine and majeptil on proliferation of peripheral blood lymphocytes cultivated with phytohemagglutinin] Mitkevich SP, et al. **Zh Nevropatol Psikhiatr** 1981;81(2):115–7 (Eng. Abstr.) (Rus)

THIORIDAZINE

Self-stimulation and locomotor changes indicating 'latent' anticholinergic activity by an atypical neuroleptic (thioridazine). Herberg LJ, et al. **Neuropharmacology** 1981 Jan;20(1):55–60

Change in human electroretinography associated with thioridazine administration. Miyata M, et al. **Ophthalmologica** 1980; 181(3–4):175–80

A double-blind comparison of trebenzomine and thioridazine in the treatment of schizophrenia. Georgotas A, et al. **Psychopharmacology (Berlin)** 1981;73(3):292–4

[Effect of thioridazine on sexual responsiveness in the male (phalloplethysmographic study)] Topiar A. **Agressologie** 1980; 21(A):49–51 (Eng. Abstr.) (Ger)

[Case of melleril poisoning] Davidovich DA. **Sud Med Ekspert** 1981 Apr–Jun;24(2):58 (Rus)

THIOTHIXENE

Exaggerated hyperprolactinemia in response to thiothixene [letter] Ash PR, et al. **Arch Neurol** 1981 Aug;38(8):534–5

Thiothixene plasma levels and clinical response in acute schizophrenia. Reifler BV, et al. **J Clin Psychiatry** 1981 May;42(5):207–11

THYROID HORMONES

Effect of thyroidectomy on choline acetyltransferase in rat hypothalamic nuclei. Kojima M, et al. **Brain Res** 1981 Mar 23;209(1):227–30

The thyroid lysosomal system: dynamic state of the organelles in relation to iodine release. Miquelis R, et al. **Eur J Cell Biol** 1981 Apr; 24(1):70–3

Erythrocytic and granulocytic differentiation of transplanted bone marrow cells in mice treated with thyroid hormones. Mikeska J, et al. **Folia Biol (Praha)** 1981;27(2):126–34

Morphological picture of hormone synthesis in the thyroid and its dependence on neurohumoral regulatory mechanisms. Volkova OV, et al. **Folia Morphol (Praha)** 1981;29(1):46–8

Thyroid hormone effects on beta-adrenergic receptors in isolated fat cells in rats. Pfeifle B, et al. **Horm Metab Res** 1981 Apr;13(4):218–21

Relationship between thyrotropin, thyroid hormones, thyroxine-binding globulin and estradiol-17 beta levels in normal pregnancy. Sawhney RC, et al. **Indian J Med Res** 1981 Jan;73:41–52

Thyroid hormones are required for daily rhythms of plasma corticosterone and prolactin concentration. Ottenweller JE, et al. **Life Sci** 1981 Mar 2;28(9):1033–40

MOde of entry of steroid and thyroid hormones into cells. Rao GS. **Mol Cell Endocrinol** 1981 Feb;21(2):97–108 (68 ref.)

Effects of open-heart surgery on thyroid hormone levels. Barta E, et al. **Resuscitation** 1980 Dec;8(4):233–41

[Structure of thyroglobulin and its function in thyroid gland (author's transl)] Pawelczak K, et al. **Postepy Biochem** 1980;26(4):559–83 (132 ref.) (Pol)

[Hormonal and lipid metabolic changes in chronic occupational methylmethacralate poisoning] Makarov IA, et al. **Gig Tr Prof Zabol** 1981 Apr;(4):20–2 (Eng. Abstr.) (Rus)

THYROTROPIN

The TSH response to TRH is exaggerated in primary testicular failure and normal in the male castrate. LeRoith D, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):103–8

Further evidence of the dual role of noradrenaline in regulation of thyrotrophin secretion in male rats. Männistö PT, et al. **Acta Endocrinol (Copenh)** 1981 Jun;97(2):213–20

Serum prolactin and thyrotrophin responses to thyrotrophin-releasing hormone at different times of the day in normal women. Pérez-López FR, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):7–11

Influence of TRH and TSH on the ultrastructure of rat pineal gland. Karasek M. **Acta Med Pol** 1980;21(4):347–8

Effect of trifluoperazine, D600, and phenytoin on depolarization- and thyrotropin-releasing hormone-induced thyrotropin release from rat pituitary tissue. Fleckman A, et al. **Endocrinology** 1981 Jun; 108(6):2072–7

Studies on the mechanism of 3,5,3'-triiodothyronine-induced suppression of secretagogue-induced thyrotropin release in vitro. Gard TG, et al. **Endocrinology** 1981 Jun;108(6):2046–53

Evidence for a possible role for Ca++ in the 3,5,3'-triiodothyronine inhibition of thyrotropin-releasing hormone-induced secretion of thyrotropin by rat anterior pituitary in vitro. Schrey MP, et al. **Endocrinology** 1981 May;108(5):1690–6

Factors modulating the secretion of thyrotropin and other hormones of the thyroid axis. Hedge GA, et al. **Environ Health Perspect** 1981 Apr; 38:57–63

Pharmacological studies of the involvement of hypothalamic prostaglandins in the regulation of thyrotropin secretion. Wright KC, et al. **Environ Health Perspect** 1981 Apr;38:83–8

Morphological picture of hormone synthesis in the thyroid and its dependence on neurohumoral regulatory mechanisms. Volkova OV, et al. **Folia Morphol (Praha)** 1981;29(1):46–8

Relationship between thyrotropin, thyroid hormones, thyroxine-binding globulin and estradiol-17 beta levels in normal pregnancy. Sawhney RC, et al. **Indian J Med Res** 1981 Jan;73:41–52

Effects of thyroidectomy, propylthiouracil, and thyroxine on pituitary content and immunocytochemical staining of thyrotropin (TSH) and thyrotropin releasing hormone (TRH). Childs GV, et al. **J Histochem Cytochem** 1981 Mar;29(3):357–63

Serum thyroxine, triiodothyronine, and TSH levels in iodine-deficient and iodine-sufficient rats before and after exposure to cold. Nakashima T, et al. **Proc Soc Exp Biol Med** 1981 May;167(1):45–50

Exhaustibility of pituitary thyrotropin pool in old age by repeated administration of thyrotropin releasing hormone. Szabolcs I, et al. **ZFA (Dresden)** 1981;36(1):23–8

[Human thyrotropin radioimmunoassay (heterogenous system) and its clinical application (author's transl)] Lin XT. **Chung Hua Nei Ko Tsa Chih** 1979;18(3):192–6 (Chi)

THYROXINE

Blood sugar, serum insulin and serum free fatty acid responses to slow graded glucose in thyroxine-treated dogs. Renauld A, et al. **Acta Diabetol Lat** 1980 Jul–Dec;17(3–4):189–97

Thyroid hormone-catecholamine interrelationships during exposure to cold. Storm H, et al. **Acta Endocrinol (Copenh)** 1981 May;97(1):91–7

Hormonal control of postnatal development of corticosteroid-binding globulin. D'Agostino J, et al. **Am J Physiol** 1981 Apr;240(4):E402–6

Free thyroxine and free thyroxine index in women taking oral contraceptives. Swanson MA, et al. **Clin Nucl Med** 1981 Apr; 6(4):168–71

Plasma corticosterone and thyroxine concentrations during chronic ingestion of crude oil in mallard ducks (Anas platyrhynchos). Rattner BA, et al. **Comp Biochem Physiol** [C] 1981;68C(2):103–7

Altered ontogenesis of muscarinic cholinergic receptor in mouse brain: effect of L-thyroxine and betamethasone. Ben-Baruch G, et al. **Endocrinology** 1981 Jul;109(1):235–9

Hormonal control of growth in the infant rat. Glasscock GF, et al. **Endocrinology** 1981 Jul;109(1):176–84

Calcium depletion stimulates thyroxine release from the thyroid. Maayan ML, et al. **Endocrinology** 1981 May;108(5):1987–8

In vivo and in vitro effects of adrenaline on conversion of thyroxine to triiodothyronine and to reverse-triiodothyronine in dog liver and heart. Nauman A, et al. **Eur J Clin Invest** 1980 Jun;10(3):189–92

Composition and efficacy of iodothyronine immunogens and host responsiveness in radioimmunoassay (RIA) for serum thyroxine (T4). Margherita S, et al. **Experientia** 1981 Mar 15;37(3):314–5

The effects of thyroxine treatment, in vivo and in vitro, on Ca2+ efflux from rat liver mitochondria. Shears SB, et al. **FEBS Lett** 1981 Apr 6;126(1):9-12

Cellular quantitation of hemoglobin transition during natural and thyroid-hormone-induced metamorphosis of the bullfrog, Rana catesbeiana. Forman LJ, et al. **Gen Comp Endocrinol** 1981 May; 44(1):1-12

Thyroid in reproduction of reptiles. Haldar-Misra C, et al. **Gen Comp Endocrinol** 1981 Apr;43(4):537-42

Plasma thyroxine and testosterone levels in the red fox (Vulpes vulpes L.) during the annual cycle. Maurel D, et al. **Gen Comp Endocrinol** 1981 Mar;43(3):402-4

Prolactin inhibits the induction of its own renal receptors in Rana catesbeiana tadpoles. White BA, et al. **Gen Comp Endocrinol** 1981 Jan; 43(1):30-8

Cell population kinetics in tadpole limb epidermis during thyroxine-induced, spontaneous, and prolactin-inhibited metamorphosis. Wright ML, et al. **Gen Comp Endocrinol** 1981 Apr; 43(4):451-61

Correlation between plasma thyroxine levels and corticosterone-binding activity in intact, ovariectomized, and ovariectomized estrogen-treated rats. Calvano SE, et al. **Horm Metab Res** 1981 Mar;13(3):171-4

Combined effects of neonatal thyroxine treatment and neonatal castration on sebum production in adult male rats. Toh YC. **J Endocrinol** 1981 May;89(2):225-8

Effects of thyroidectomy, propylthiouracil, and thyroxine on pituitary content and immunocytochemical staining of thyrotropin (TSH) and thyrotropin releasing hormone (TRH). Childs GV, et al. **J Histochem Cytochem** 1981 Mar;29(3):357-63

Effect of thyroxine on nerve growth factor concentration in neonatal mouse brain. Walker P, et al. **Life Sci** 1981 Apr 13-20; 28(15-16):1777-87

Serum thyroxine, triiodothyronine, and TSH levels in iodine-deficient and iodine-sufficient rats before and after exposure to cold. Nakashima T, et al. **Proc Soc Exp Biol Med** 1981 May;167(1):45-50

Systemic thyroxin levels in sheep with a bioartificial thyroid using xenogeneic canine tissue. White DC, et al. **Trans Am Soc Artif Intern Organs** 1980;26:423-7

[Determination of half-life time for the key enzymes of the pentose phosphate pathway--glucose-6-phosphate dehydrogenase and transketolase] Kudriavtseva GV, et al. **Biokhimiia** 1980 Jan; 45(1):118-23 (Eng. Abstr.) **(Rus)**

[Regulation of genetic activity by thyroid hormones. II. Specificity of interaction of cytoplasmic thyroxine receptor isolated from human embryonal fibroblasts and HeLa cells with DNA] Abdukarimov A, et al. **Probl Endokrinol (Mosk)** 1981 Mar-Apr;27(2):66-70 (Eng. Abstr.) **(Rus)**

[Regulation of genetic activity by thyroid hormones. Effect of purified cytoplasmic hormone-receptor complex on the chromatin template activity] Abdukarimov A, et al. **Probl Endokrinol (Mosk)** 1981 Jan-Feb; 27(1):50-3 (Eng. Abstr.) **(Rus)**

[Conditions for using thyroxine as an antimutagen after whole-body x-ray irradiation] Timchenko OI, et al. **Radiobiologiia** 1981 Mar-Apr; 21(2):204-10 (Eng. Abstr.) **(Rus)**

TRANQUILIZING AGENTS

Effects of halopemide on GABA receptor binding, uptake and release. Loonen AJ, et al. **Brain Res** 1981 Apr 6;210(1-2):485-92

Health beliefs, social networks, and tranquilizer use. Radelet ML. **J Health Soc Behav** 1981 Jun;22(2):165-73

[Neuropharmacological actions of some N-phenyl piperazine derivatives (author's transl)] Zou G, et al. **Yao Hsueh Hsueh Pao** 1981 May; 16(5):321-7 (Eng. Abstr.) **(Chi)**

TRANQUILIZING AGENTS, MAJOR

Long-term neuroleptic treatment. Benefits and risks. Proceedings from a workshop, Copenhagen, 6th-7th September, 1979. **Acta Psychiatr Scand [Suppl]** 1981;63(291):1-159

The need for long-term neuroleptic treatment in schizophrenia. Dencker SJ. **Acta Psychiatr Scand [Suppl]** 1981;63(291):29-43

The role of neuroleptics in an integrated treatment program for chronic schizophrenics. Gottfries I, et al. **Acta Psychiatr Scand [Suppl]** 1981; 63(291):44-55

Antipsychotic medications. Harris E. **Am J Nurs** 1981 Jul; 81(7):1316-23

Neuroleptic drugs are nonstereospecific inhibitors of calmodulin-stimulated phosphodiesterase activity. Norman JA. **Ann NY Acad Sci** 1980;356:415-6

Phospholipid-sensitive calcium-dependent protein kinase: inhibition by antipsychotic drugs. Schatzman RC, et al. **Biochem Biophys Res Commun** 1981 Feb 12;98(3):669-76

The reliability of 5-hydroxytryptamine induced platelet aggregation responses in schizophrenic patients treated with neuroleptic drugs. Knox JM, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):261-3

The effects of neuroleptic drugs on 5-hydroxytryptamine induced platelet aggregation in schizophrenic patients. Orr MW, et al. **Br J Clin Pharmacol** 1981 Mar;11(3):255-9

Chronopharmacological studies of neuroleptics. Nagayama H, et al. **Curr Dev Psychopharmacol** 1981;6:191-214 (53 ref.)

Clopenthixol decanoate in schizophrenia. Carney MW, et al. **Curr Med Res Opin** 1981;7(4):205-11

Lytic action of neurotropic drugs on retroviruses in vitro. Wunderlich V, et al. **Eur J Cancer** 1980 Sep;16(9):1127-32

Solubilization of neuroleptic/dopamine receptors of human brain striatum. Davis A, et al. **Eur J Pharmacol** 1981 Mar 26;70(3):321-9

A radioreceptor assay for neuroleptic drugs in plasma. Lader SR. **J Immunoassay** 1980;1(1):57-75

The effects of neuroleptic drugs on the social interactions of hospitalized psychotic patients. Rosen AJ, et al. **J Nerv Ment Dis** 1981 Apr; 169(4):240-3

Drug levels after withdrawal of long-term depot neuroleptics [letter] Amdisen A, et al. **Lancet** 1981 Jun 27;1(8235):1425

Autonomous prolactin secretion in schizophrenic male on long-term neuroleptic therapy [letter] Semple CG, et al. **Lancet** 1981 Jul 11; 2(8237):103

Des-tyrosine-gamma-endorphin: H-reflex response similar to neuroleptics. Metz J, et al. **Life Sci** 1981 May 4;28(18):2003-8

An alternative mechanism of actions for neuroleptic and antidepressant drugs. Randall PL. **Med Hypotheses** 1981 Feb;7(2):251-60

Stimulation of prolactin secretion by neuroleptics in rats with medial basal hypothalamic lesions. Cheung CY, et al. **Neuroendocrinology** 1981 Jun; 32(6):370-4

A probable neuroleptic effect on platelet monoamine oxidase in chronic schizophrenic patients. DeLisi LE, et al. **Psychiatry Res** 1981 Feb; 4(1):95-107

A double-blind comparison of trebenzomine and thioridazine in the treatment of schizophrenia. Georgotas A, et al. **Psychopharmacology (Berlin)** 1981;73(3):292-4

Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge. Kolakowska T, et al. **Psychopharmacology (Berlin)** 1981;72(3):283-5

Electrophysiologic interactions of antipsychotic drugs with central noradrenergic pathways. Marwaha J, et al. **Psychopharmacology (Berlin)** 1981;73(2):126-33

Behavioral and biochemical studies of the scopolamine-induced reversal of neuroleptic activity. Ondrusek MG, et al. **Psychopharmacology (Berlin)** 1981;73(1):17-22

Cholinergic rebound in neuroleptic withdrawal syndromes. Lieberman J. **Psychosomatics** 1981 Mar;22(3):253-4

[Neuroleptic-tricyclic antidepressant combination. Pharmacological aspects and therapeutic interest (author's transl)] Boulenger JP, et al. **Encephale** 1981;7(1):5-28 (114 ref.) (Eng. Abstr.) **(Fre)**

[Experience with reactivant in psychiatric patients] Guensberger E, et al. **Agressologie** 1980;21(A):63-5 (Eng. Abstr.) **(Ger)**

[The course of schizophrenic psychoses treated with neuroleptics] Rüther E, et al. **MMW** 1981 May 8;123(19):803-4 **(Ger)**

[Long-term treatment of outpatients with depot neuroleptics (author's transl)] Saameli W. **Praxis** 1981 Feb 3;70(6):206-10 (Eng. Abstr.) **(Ger)**

[Modification of long-term schizophrenia by somato-therapeutic measures] Gross G, et al. **Psychiatr Clin (Basel)** 1980;13(3-4):179-92 (Eng. Abstr.) **(Ger)**

[Psychopathologic changes during 20 days of antidepressive or neuroleptic therapy] Woggon B. **Psychiatr Clin (Basel)** 1980;13(3-4):150-64 (Eng. Abstr.) **(Ger)**

[Psychotropic agents and the neuroendocrine system] Matussek N. **Verh Dtsch Ges Inn Med** 1980;86:100-6 **(Ger)**

[Effectiveness of treating early-onset malignant schizophrenia with psychotropic drugs and their combinations] Sobolev ES, et al. **Zh Nevropatol Psikhiatr** 1981;81(1):114-21 (Eng. Abstr.) **(Rus)**

TRANQUILIZING AGENTS, MINOR

Sedative/anxiolytic effects of antidepressants in animals. Ogren SO, et al. **Acta Psychiatr Scand [Suppl]** 1981;63(Suppl 290):277-88

The benzodiazepine--GABA--chloride ionophore receptor complex: common site of minor tranquilizer action. Paul SM, et al. **Biol Psychiatry** 1981 Mar;16(3):213-29

Therapeutic monograph on anxiolytic-sedative drugs. **Can Med Assoc J** 1981 Jun 1;124(11):1439-46

Tranquilizers not overprescribed for anxiety [news] Korcok M. **JAMA** 1981 Jul 3;246(1):14

Methods and methodological considerations in measuring anti-anxiety effects of tranquilizing drugs. Debus G, et al. **Prog Neuropsychopharmacol** 1980;4(4-5):391-404

[Role of the GABA-ergic link in the development of the tranquilizing effect in cats] Kozlovskaia MM, et al. **Biull Eksp Biol Med** 1981; 91(1):45-8 (Eng. Abstr.) **(Rus)**

TRANYLCYPROMINE

A method for measurement of tranylcypromine in rat brain regions using gas chromatography with electron capture detection. Calverley DG, et al. **Biochem Pharmacol** 1981 Apr;30(8):861–7

The interaction of tyramine with a single dose of tranylcypromine in healthy volunteers. Peet M, et al. **Br J Clin Pharmacol** 1981 Feb; 11(2):212–4

Vesicular noradrenaline stores in peripheral nerves of the rat and their modification by tranylcypromine. Fillenz M, et al. **Br J Pharmacol** 1981 Jun;73(2):401–4

Antidepressant efficacy of tranylcypromine isomers: a controlled study. Moises HW, et al. **J Neural Transm** 1981;50(2–4):185–92

Role of monoamines in behavior of reserpinized rats given tranylcypromine stereoisomers. Smith DF. **J Neural Transm** 1981; 50(2–4):193–200

AUTHOR SECTION

A

Abdel-Aziz MT, Khair El-Din AA, Khayyal MT, et al: Effect of prolonged administration of oral contraceptives and psychotropic drugs on some ovarian adrenocortical functions. J Egypt Med Assoc 1978; 61(11-12):703-9

Abdukarimov A, Guliamova TG, Aripdzhanov AA, et al: Reguliatsiia geneticheskoĭ aktivnosti tireoidnymi gormonami. II. Spetsifichnost' vzaĭmodeĭstviia tsitoplazmaticheskogo retseptora tiroksina iz fibroblastov embryona cheloveka i kletok HeLa s DNK. Probl Endokrinol (Mosk) 1981 Mar-Apr;27(2):66-70 (Eng. Abstr.) **(Rus)**

Abdukarimov A, Adylova AT, Kkhan MZ: Reguliatsiia geneticheskoĭ aktivnosti tireoidnymi gormonami. 1. Vliianie ochishchennogo tsitoplazmaticheskogo gormon-retseptornogo kompleksa na matrichnuiu aktivnost' khromatina. Probl Endokrinol (Mosk) 1981 Jan-Feb;27(1):50-3 (Eng. Abstr.) **(Rus)**

Abe H, Chihara K, Chiba T, et al: Effect of intraventricular injection of neurotensin and other various bioactive peptides on plasma immunoreactive somatostatin levels in rat hypophysial portal blood. Endocrinology 1981 May;108(5):1939-43

Abe K, Ohno M, Funabiki R, et al: [Effects of parasympathomimetic and sympathomimetic drugs on the sublingual glands of rats] Gifu Shika Gakkai Zasshi 1980 Jun;8(1):36-52 (Eng. Abstr.) **(Jpn)**

Abel PW, Urquilla PR, Goto K, et al: Chronic reserpine treatment alters sensitivity and membrane potential of the rabbit saphenous artery. J Pharmacol Exp Ther 1981 May;217(2):430-9

Aberg A: Controlled cross-over study of a 5-HT uptake inhibiting and an NA uptake inhibiting antidepressant. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):244-55

Abernethy DR, Greenblatt DJ, Shader RI: Treatment of diazepam withdrawal syndrome with propranolol. Ann Intern Med 1981 Mar; 94(3):354-5

Abernethy DR, Greenblatt DJ: Effects of desmethyldiazepam on diazepam kinetics: a study of effects of a metabolite on parent drug disposition. Clin Pharmacol Ther 1981 Jun;29(6):757-61

Acheson AL, Kapatos G, Zigmond MJ: The effects of phosphorylating conditions on tyrosine hydroxylase activity are influenced by assay conditions and brain region. Life Sci 1981 Mar 23;28(12):1407-20

Ackenheil M, Engel RR: Stress-Untersuchungen bei psychiatrischen Patienten. MMW 1981 May 8;123(19):805-8 (Eng. Abstr.) **(Ger)**

Adám-Vizi V, Váradi G, Simon P: Reduction of Vanadate by ascorbic acid and noradrenaline in synaptosomes. J Neurochem 1981 May; 36(5):1616-20

Adams PR: Acetylcholine receptor kinetics. J Membr Biol 1981 Feb 28; 58(3):161-74 (132 ref.)

Adams TE, Spies HG: Binding characteristics of gonadotropin-releasing hormone receptors throughout the estrous cycle of the hamster. Endocrinology 1981 Jun;108(6):2245-53

Adashi EY, Hsueh AJ: Stimulation of beta 2-adrenergic responsiveness by follicle-stimulating hormone in rat granulosa cells in vitro and in vivo. Endocrinology 1981 Jun;108(6):2170-8

Advis JP, Wiener SL, Ojeda SR: Changes in ovarian 3 alpha-androstanediol response to human chorionic gonadotropin during puberty in the rat: modulatory role of prolactin. Endocrinology 1981 Jul;109(1):223-8

Agnati LF, Benfenati F, Capelli M, et al: Effects of the interaction between methysergide and clonidine on growth hormone and prolactin secretion in normal man. Neurosci Lett 1981 Feb 6;21(3):333-8

Agnoli GC, Cacciari M, Cariani A, et al: Modi di azione renale della dopamina e loro dipendenza dalle alterazioni del bilancio sodico. Nota i. Studi eseguiti in ritenzione idro-salina. Boll Soc Ital Cardiol 1979; 24(12):1315-29 **(Ita)**

Agnoli GC, Cacciari M, Garutti C, et al: Relazioni tra parametri emodinamici renali e concentrazioni urinarie del sodio e dei soluti suggestive di alcune modalita' di controllo della funzione renale. Boll Soc Ital Biol Sper 1981 Feb 28;57(4):442-8 (Eng. Abstr.) **(Ita)**

Agnoli GC, Cacciari M, Cariani A, et al: Modi di azione renale della dopamina e loro dipendenza dalle alterazioni del bilancio sodico.Nota II. Studi eseguiti in deplezione idro-salina. Boll Soc Ital Cardiol 1979; 24(12):1331-49 **(Ita)**

Agranoff BW: Neurochemistry of man: noninvasive approaches. Biol Psychiatry 1981 Mar;16(3):211-2

Agrawal AK, Squibb RE: Effects of acrylamide given during gestation on dopamine receptor binding in rat pups. Toxicol Lett 1981 Jan; 7(3):233-8

Agrawal AK, Tilson HA, Bondy SC: 3,4,3',4'-Tetrachlorobiphenyl given to mice prenatally produces long-term decreases in striatal dopamine and receptor binding sites in the caudate nucleus. Toxicol Lett 1981 Mar;7(6):417-24

Agrawal AK, Squibb RE, Bondy SC: The effects of acrylamide treatment upon the dopamine receptor. Toxicol Appl Pharmacol 1981 Mar 30; 58(1):89-99

Agrawal AK, Seth PK, Squibb RE, et al: Neurotransmitter receptors in brain regions of acrylamide- treated rats. I: Effects of a single exposure to acrylamide. Pharmacol Biochem Behav 1981 Apr;14(4):527-31

Agurell S: Biogenic amines and depression (introduction to symposium). Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):17-9

Ahluwalia P, Singhal RL: Monoamine uptake into synaptosomes from various regions of rat brain following lithium administration and withdrawal. Neuropharmacology 1981 May;20(5):483-7

Ahmed M, Burton JS, Hadgraft J, et al: Thermodynamics of partitioning and efflux of phenothiazines from liposomes. J Membr Biol 1981 Feb 28;58(3):181-9

Ahmed SA, Gowda HS: Phenothiazines as reagents for the detection of faecal occult blood. Clin Chim Acta 1981 Apr 9;111(2-3):275-8

Ahnve S, Theorell T, Akerstedt T, et al: Circadian variations in cardiovascular parameters during sleep deprivation. A noninvasive study of young healthy men. Eur J Applied Physiol 1981;46(1):9-19

Ahrén B, Lundquist I: Adrenalectomy and chemical sympathectomy by 6-hydroxydopamine. Effects on basal and stimulated insulin secretion. Pfluegers Arch 1981 Apr;390(1):17-21

Aidara D, Tahiri-Zagret C, Robyn C: Serum prolactin concentrations in mangabey (Cercocebus atys lunulatus) and patas (Erythrocebus patas) monkeys in response to stress, ketamine, TRH, sulpiride and levodopa. J Reprod Fertil 1981 May;62(1):165-72

Airaksinen MM, Mikkoaen E: Affinity of beta-carbolines on rat brain benzodiazepine and opiate binding sites. Med Biol 1980 Dec;58(6):341-4

Akaike N, Nishi K, Oyama Y: Inhibitory effects of propranolol on the calcium current of Helix neurones. Br J Pharmacol 1981 Jun;73(2):431-4

Akasu T, Hirai K, Koketsu K: 5-hydroxytryptamine controls ACh-receptor sensitivity of bullfrog sympathetic ganglion cells. Brain Res 1981 Apr 27;211(1):217-20

Akera T, Yamamoto S, Temma K, et al: Is ouabain-sensitive rubidium or potassium uptake a measure of sodium pump activity in isolated cardiac muscle? Biochim Biophys Acta 1981 Feb 6;640(3):779-90

Akers RM, Bauman DE, Capuco AV, et al: Prolactin regulation of milk secretion and biochemical differentiation of mammary epithelial cells in periparturient cows. Endocrinology 1981 Jul;109(1):23-30

Akers RM, Bauman DE, Goodman GT, et al: Prolactin regulation of cytological differentiation of mammary epithelial cells in periparturient cows. Endocrinology 1981 Jul;109(1):31-40

Akhtar RA, Abdel-Latif AA: Requirement for calcium ions in acetylcholine-stimulated phosphodiesteratic cleavage of phosphatidyl-myo-inositol 4,5-bisphosphate in rabbit iris smooth muscle. Biochem J 1980 Dec 15;192(3):783-91

Akoev GN: Catecholamines, acetylcholine and excitability of mechanoreceptors. Prog Neurobiol 1980;15(4):269-94

Aksenova VM: Soderzhanie gistamina i serotonina v immunokompetentnykh tkaniakh i krovi pri vagotomii u krys. Patol Fiziol Eksp Ter 1981 Jan-Feb;(1):23-6 (Eng. Abstr.) **(Rus)**

Alamanni MC, Pirisino G, Savelli F, et al: 3-Metilchinossalin-2(1H)-oni 1,6-disostituiti. Effetto sull'acquisizione e sulla modificazione di una risposta condizionata di 'avoidance' nel ratto. Farmaco [Sci] 1981 May; 36(5):359-71 (Eng. Abstr.) **(Ita)**

Albert DJ, Chew GL: The septal forebrain and the inhibitory modulation of attack and defense in the rat. A review. Behav Neural Biol 1980 Dec;30(4):357-88 (192 ref.)

Alderdice MT, Volle RL: Multiple actions of beta-bungarotoxin on acetylcholine release at amphibian motor nerve terminals. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):126-30

Aldwin L, Kabakoff DS: Metabolite interference in homogeneous enzyme immunoassay of phenytoin [letter] Clin Chem 1981 May;27(5):770-1

Alevy YG, Witherspoon C, Bellone CJ: Anti-TMA immunity in mice. III. Induction of L-tyrosine-p-azophenyltrimethylammonium (tyr(TMA)) specific helper T cells by the monovalent antigen or idiotypic antisera. J Immunol 1981 Jun;126(6):2390-6

Allen MD, Greenblatt DJ: Comparative protein binding of diazepam and desmethyldiazepam. J Clin Pharmacol 1980 Nov-Dec;20(11-12):639-43

Almasi W, Gerke DC, Frewin DB: A comparative study on the retention of 3H lignocaine and 3H prilocaine in the presence of various vasoconstrictors. Aust Dent J 1980 Dec;25(6):316-8

Alvarez N, Hartford E, Cavalleri E: Low blood levels of phenobarbital due to poor gastrointestinal solubility of phenobarbital tablets [letter] Ann Neurol 1981 Mar;9(3):309-10

Alvarez Gómez JA, Alvarez Ossorio R, Aguilar Alenda R, et al: Evolución de las tasas de pseudocolinesterasa plasmática en sangre conservada A.C.D. Rev Esp Anestesiol Reanim 1981 Jan;28(1):30-5 (Eng. Abstr.) **(Spa)**

Aman MC, Wakeman P: A simple system for control of the continuous performance test in psychopharmacological research. Prog Neuropsychopharmacol 1980;4(6):621-6

Amar A, Sanyal AK: Immobilization stress in rats: effect on rectal temperature and possible role of brain monoamines in hypothermia. Psychopharmacology (Berlin) 1981;73(2):157-60

Amdisen A, Thomsen NJ: Drug levels after withdrawal of long-term depot neuroleptics [letter] Lancet 1981 Jun 27;1(8235):1425

Amir A, Teomy S, Kalir A: The effect of phencyclidine on noradrenaline uptake by bovine chromaffin granules. Monogr Neural Sci 1980; 7:129-37

Amitai G, Ashani Y, Shahar A, et al: Fluorescent organophosphates: novel probes for studying aging-induced conformational changes in inhibited

AUTHOR SECTION

acetylcholinesterase and for localization of cholinesterase in nervous tissue. Monogr Neural Sci 1980;7:70–84

Amlie JP: Digitalis og kinidin. Tidsskr Nor Laegeforen 1981 Apr; 101(11):655–7 (Nor)

Anand-Srivastava MB, Johnson RA: Role of phospholipids in coupling of adenosine and dopamine receptors to striatal adenylate cyclase. J Neurochem 1981 May;36(5):1819–28

Anderson GM, Young JG, Cohen DJ, et al: Amperometric determination of 3–methoxy–4–hydroxyphenylethyleneglycol in human cerebrospinal fluid. J Chromatogr 1981 Jan 2;222(1):112–5

Anderson GM, Young JG, Cohen DJ, et al: Liquid–chromatographic determination of serotonin and tryptophan in whole blood and plasma [letter] Clin Chem 1981 May;27(5):775–6

Anderson JM, Gimbrone MA Jr, Alexander RW: Angiotensin II stimulates phosphorylation of the myosin light chain in cultured vascular smooth muscle cells. J Biol Chem 1981 May 25;256(10):4693–6

Anderton BH, Axford JS, Cohn P, et al: Inhibition of lymphocyte capping and transformation by propranolol and related compounds. Br J Pharmacol 1981 Jan;72(1):69–74

Andreu R, Barrett EF: Calcium dependence of evoked transmitter release at very low quantal contents at the frog neuromuscular junction. J Physiol (Lond) 1980 Nov;308:79–97

Andrews WW, Allison WS: 1–fluoro–2, 4–dinitrobenzene modifies a tyrosine residue when it inactivates the bovine mitochondrial F(1)–ATPase. Biochem Biophys Res Commun 1981 Apr 15;99(3):813–9

Angel A, Clarke KA: The effects of trimethadione on pentetrazol–induced discharges of primary muscle spindle afferents from the hind limb of the rat. Br J Pharmacol 1981 Jan;72(1):75–9

Angeli P, Brasili L, Giardinà D, et al: Molecular requirements of the active site of cholinergic receptors XV: Synthesis and biological activity of 2,3–dehydrodeoxamuscarone and 2,3–dehydrodeoxamuscarines. J Pharm Sci 1981 May;70(5):489–92

Anholt R, Lindstrom J, Montal M: Stabilization of acetylcholine receptor channels by lipids in cholate solution and during reconstitution in vesicles. J Biol Chem 1981 May 10;256(9):4377–87

Ankermann H: Der Einfluss adrenerger beta–Rezeptorenblocker auf den Sauerstoffverbrauch narkotisierter Ratten und die kalorigene Wirkung des Adrenalins. Acta Biol Med Ger 1980;39(11–12):1227–34 (Eng. Abstr.) (Ger)

Annunziato L, Di Renzo G, Quattrone A, et al: Brain neurotransmitters regulating TRH producing neurons. Pharmacol Res Commun 1981 Jan; 13(1):1–10 (47 ref.)

Antelman SM, Chiodo LA: Repeated antidepressant treatments induce a long–lasting dopamine autoreceptor subsensitivity: is daily treatment necessary for clinical efficacy? [proceedings] Psychopharmacol Bull 1981 Jan;17(1):92–4

Aoki K, Terasawa N, Kuroiwa Y: Enzyme immunoassay for phenobarbital. Chem Pharm Bull (Tokyo) 1980 Nov;28(11):3291–5

Apfelbach R: Instinctive predatory behavior of mustelids (Mustela putorius f. furo, Mustela vison f. dom.) modified by benzodiazepine derivatives. Pharmacol Biochem Behav 1981;14 Suppl 1:43–6

Araie M, Takase M: [Effects of pilocarpine and carteolol, a new beta–adrenergic blocking agent on human aqueous humor dynamics (author's transl)] Nippon Ganka Gakkai Zasshi 1980 Dec 10; 84(12):2085–91 (Eng. Abstr.) (Jpn)

Arendt J, Ho AK, Land C, et al: Differential effect of benserazide (Ro4–4602) on the concentration of indoleamines in rat pineal and hypothalamus. Br J Pharmacol 1981 Feb;72(2):257–62

Arieli A, Lepkifker E: The antidepressant effect of lithium. Curr Dev Psychopharmcol 1981;6:165–90 (58 ref.)

Arito H, Sudo A, Suzuki Y: Aggressive behavior of the rat induced by repeated administration of cadmium. Toxicol Lett 1981 Mar;7(6):457–61

Arluison M: Les fibres nerveuses sérotonergiques du striatum chez le rat et leurs caractéristiques ultrastructurales. J Physiol (Paris) 1981 Apr; 77(1):45–51 (71 ref.) (Eng. Abstr.) (Fre)

Armario A, Balasch J, Martinez E: The effect of acute neurogenic stress on corticosterone and Cu an Zn levels in rats. Agressologie 1980; 21(5):259–62

Armstrong DM, Pickel VM, Joh TH, et al: Immunocytochemical localization of catecholamine synthesizing enzymes and neuropeptides in area postrema and medial nucleus tractus solitarius of rat brain. J Comp Neurol 1981 Mar 1;196(3):505–17

Arnauld E, Dufy B, Pestre M, et al: Effects of estrogens on the responses of caudate neurons to microiontophoretically applied dopamine. Neurosci Lett 1981 Feb 6;21(3):325–31

Aronstam RS: Interactions of tricyclic antidepressants with a synaptic ion channel. Life Sci 1981 Jan 5;28(1):59–64

Arora RC, Meltzer HY: A modified assay method for determining serotonin uptake in human platelets. Clin Chim Acta 1981 May 5; 112(2):225–33

Arqueros L, Daniels AJ: Manganese as agonist and antagonist of calcium ions: dual effect upon catecholamine release from adrenal medulla. Life Sci 1981 Mar 30;28(13):1535–40

Arushanian EB, Toipyshev BA: Neirofiziologicheskie i farmakologicheskie dokazatel'stva samoreguliatsii v nigro–striatnol sisteme. Biull Eksp Biol Med 1981 Feb;91(2):133–6 (Eng. Abstr.) (Rus)

Asch RH, Van Sickle M, Rettori V, et al: Absence of LH–RH binding sites in corpora lutea from rhesus monkeys (Macacca mulatta). J Clin Endocrinol Metab 1981 Jul;53(1):215–17

Ash PR, Bouma D: Exaggerated hyperprolactinemia in response to thiothixene [letter] Arch Neurol 1981 Aug;38(8):534–5

Ashman RF, Karlan BR: Inhibition of antigen–induced and anti–immunoglobulin–induced capping by hydrocortisone and propranolol. Immunopharmacology 1981 Feb;3(1):41–7

Attia MA, Aboutaleb AE, Habib FS: A study on the release of prednisone from new ointment bases containing various additives. Pharmazie 1981; 36(1):21–3

Aunis D, García AG: Correlation between catecholamine secretion from bovine isolated chromaffin cells and [3H]–ouabain binding to plasma membranes. Br J Pharmacol 1981 Jan;72(1):31–40

Axelson M, Setchell KD: Conjugation of lignans in human urine. FEBS Lett 1980 Dec 15;122(1):49–53

Azanza MJ: Benzodiazepines, barbiturates and baclofen interaction within the GABA–receptors. Gen Pharmacol 1981;12(3):123–8 (20 ref.)

B

Bacopoulos NG, Ware PL: Dopamine receptors in rat frontal cortex: pharmacological properties in vivo and in vitro. Life Sci 1980 Dec 22–29;27(25–26):2489–94

Bacopoulos NG: Biochemical mechanism of tolerance to neuroleptic drugs; regional differences in rat brain. Eur J Pharmacol 1981 Apr 9; 70(4):585–6

Bader JP, Okazaki T, Brown NR: Sodium and rubidium uptake in cells transformed by Rous sarcoma virus. J Cell Physiol 1981 Feb; 106(2):235–43

Bagadia VN: Research center reports. Current research activities in India. Psychopharmacol Bull 1981 Apr;17(2):14–6

Baggio G, Ferrari F: DPI, a supposed selective agonist of inhibitory dopamine receptors, strongly increases rat diuresis through alpha–adrenergic receptor activation. Life Sci 1981 Mar 30; 28(13):1449–56

Bahr JM, Ben–Jonathan N: Preovulatory depletion of ovarian catecholamines in the rat. Endocrinology 1981 May;108(5):1815–20

Baichwal AR, Tipnis HP, Kulkarni RD, et al: Bioavailability in humans of solid dosage forms of phenytoin marketed in India. Indian J Med Res 1980 Dec;72:916–9

Bailey HR, Davies E, Morrison IJ: Oxazepam in the treatment of anxiety associated with depression: results of treatment in 1600 cases (Studies in depression, VI). Curr Med Res Opin 1981;7(3):156–63

Bailey R, Crisp E, Jackson DM, et al: Chronic L–DOPA treatment of mice: a behavioural and biochemical study. J Neural Transm 1981; 50(2–4):209–24

Baker PC, Hoff KM, Goodrich CA: Rates of indoleamine synthesis in maturing mouse brain. Gen Pharmacol 1981;12(3):151–4

Bakhit C, Morgan ME, Gibb JW: Propranolol differentially blocks the methamphetamine–induced depression of tryptophan hydroxylase in various rat brain regions. Neurosci Lett 1981 Apr 9;23(1):99–103

Balding F Jr, Geller HM: Sodium valproate enhancement of gamma–aminobutyric acid (GABA) inhibition: electrophysiological evidence for anticonvulsant activity. J Pharmacol Exp Ther 1981 May; 217(2):445–50

Baldwin DM, Downs TR: Release of LH and FSH by anterior pituitary cell suspensions from female rats during the estrous cycle and from estrogen–treated ovariectomized rats. Biol Reprod 1981 Apr; 24(3):581–90

Ban TA, Wilson WH, McEvoy JP: Amoxapine: a review of literature. Int Pharmacopsychiatry 1980;15(3):166–70 (21 ref.)

Bandman AL, Vasilenko ET, Pshenkina NN: Nekotorye biokhimicheskie i povedencheskie éffekty morfina na fone amizila u krys. Biull Eksp Biol Med 1981 Feb;91(2):185–8 (Eng. Abstr.) (Rus)

Banki CM, Molnar G, Fekete I: Correlation of individual symptoms and other clinical variables with cerebrospinal fluid amine metabolites and tryptophan in depression. Arch Psychiatr Nervenkr 1981;229(4):345–53

Bánky Z, Halász B: Reversed effect of chlorpromazine on hypothalamic serotonin levels of rats with complete deafferentation of the medial basal hypothalamus. Acta Biol Acad Sci Hung 1980;31(1–3):25–32

Bannister SJ, van der Wal S, Dolan JW, et al: Liquid–chromatographic analysis for common tricyclic antidepressant drugs and their metabolites in serum or plasma with the technicon 'FAST–LC' system. Clin Chem 1981 Jun;27(6):849–55

Bannon MJ, Michaud RL, Roth RH: Mesocortical dopamine neurons. Lack of autoreceptors modulating dopamine synthesis. Mol Pharmacol 1981 Mar;19(2):270–5

Banschbach MW, Geison RL, Hokin–Neaverson M: Effects of cholinergic stimulation on levels and fatty acid composition of diacylglycerols in mouse pancreas. Biochim Biophys Acta 1981 Jan 26;663(1):34–45

Barbeau H, Bédard P: Similar motor effects of 5–HT and TRH in rats following chronic spinal transection and 5.7–dihydroxytryptamine injection. Neuropharmacology 1981 May;20(5):477–81

Barbeau H, Bédard P: Denervation supersensitivity to

AUTHOR SECTION

5-hydroxytryptophan in rats following spinal transection and 5,7-dihydroxytryptamine injection. Neuropharmacology 1981 Jun; 20(6):611-6

Barkey RJ, Shani J, Lahav M, et al: Effect of prolactin and prostaglandins on the stimulation of prolactin binding sites in the male rat liver. Mol Cell Endocrinol 1981 Feb;21(2):129-38

Barlow RB, Dawbarn D, Pycock CJ: A comparison of stereospecificity at central and peripheral 'muscarine-sensitive' acetylcholine receptors: observations with the enantiomeric forms of procyclidine and tricyclamol. Br J Pharmacol 1981 Feb;72(2):277-80

Barnes RJ, Guarino RA: Single- versus multiple-dose comparative trial of desipramine hydrochloride: a double-placebo method. J Clin Pharmacol 1980 Nov-Dec;20(11-12):681-8

Barnett G, Hawks R, Resnick R: Cocaine pharmacokinetics in humans. J Ethnopharmacol 1981 Mar-May;3(2-3):353-66

Barney CC, Spiers DE, Fregly MJ: Dipsogenesis in cold-acclimated rats. Aviat Space Environ Med 1981 Mar;52(3):171-6

Baron J, Redick JA, Guengerich FP: An immunohistochemical study on the localization and distributions of phenobarbital- and 3-methylcholanthrene-inducible cytochromes P-450 within the livers of untreated rats. J Biol Chem 1981 Jun 10;256(11):5931-7

Baron M, Levitt M, Perlman R: Plasma DBH activity: relation to genetic factors in schizophrenia. Commun Psychopharmacol 1980;4(3):197-202

Barron KW, Bishop VS: The influence of vagal afferents on the left ventricular contractile response to intracoronary administration of catecholamines in the conscious dog. Circ Res 1981 Jul;49(1):159-69

Barry J: Convergences et articulation réciproque des neurones aminergiques et peptidergiques dans l'hypothalamus. Ann Endocrinol (Paris) 1980 Nov-Dec;41(6):457-65 (Eng. Abstr.) **(Fre)**

Barta E, Kužela L, Langer P, et al: Effects of open-heart surgery on thyroid hormone levels. Resuscitation 1980 Dec;8(4):233-41

Barth A, Klinger W: Influence of phenobarbital, chlorpromazine, progesterone and phenylbutazone on the biliary cholesterol excretion in rats. Acta Biol Med Ger 1980;39(11-12):1217-26

Bartke A, Lackritz RM: Bromocriptine stimulates testosterone production by mouse testes in vitro. Fertil Steril 1981 Apr;35(4):472-6

Barton CH, Sterling ML, Vaziri ND: Phencyclidine intoxication: clinical experience in 27 cases confirmed by urine assay. Ann Emerg Med 1981 May;10(5):243-6

Bastecký J, Kalvach Z, Hálková E, et al: High doses of clorotepin in chronic schizophrenia (preliminary report). Agressologie 1980; 21(A):31-5

Batra KK, Omand J, Baselt RC: Serum quinidine concentrations as measured by direct fluorometry, double-extraction fluorometry, and enzyme immunoassay [letter] Clin Chem 1981 May;27(5):780-1

Batrinos ML, Anapliotou M, Panitsa-Faflia C, et al: Results of three-times-per-week long-term administration of a luteinizing hormone-releasing hormone (LHRH) analog, D-Ser-(TBU)6-LHRH-(EA)10 in primary amenorrhea. Fertil Steril 1981 May;35(5):515-20

Baumann P: Thérapie médicamenteuse de la dépression: apports et limites des dosages plasmatiques de tricycliques. Schweiz Med Wochenschr 1981 Feb 14;111(7):228-39 (112 ref.) (Eng. Abstr.) **(Fre)**

Baur S, Grant B, Wooton J: Cyclic nucleotides of canine antral smooth muscle. Effects of acetylcholine, catecholamines and gastrin. Biochim Biophys Acta 1981 Jan 7;672(1):1-6

Baxter CF, Tachiki KH, Blaser SM, et al: Changes in blood plasma osmolelity and states of mania. Neurochem Res 1981 Jan;6(1):47-53

Beaudet A, Sotelo C: Synaptic remodeling of serotonin axon terminals in rat agranular cerebellum. Brain Res 1981 Feb 16;206(2):305-29

Beaumont A, Fuentes JA, Hughes H, et al: Opioid peptide precursors in striatum. FEBS Lett 1980 Dec 15;122(1):135-7

Beauwens R, Rentmeesters M: Role of calmodulin antidiuretic hormone mediated water transport. Biochem Biophys Res Commun 1981 Mar 31;99(2):491-5

Bech P, Allerup P, Gram LF, et al: The Hamilton depression scale. Evaluation of objectivity using logistic models. Acta Psychiatr Scand 1981 Mar;63(3):290-9

Beck O, Jonsson G: In vivo formation of 5-methoxytryptamine from melatonin in rat. J Neurochem 1981 Jun;36(6):2013-8

Becker JB, Ramirez VD: Experimental studies on the development of sex differences in the release of dopamine from striatal tissue fragments in vitro. Neuroendocrinology 1981 Mar;32(3):168-73

Beckmann H: Die medikamentöse therapie der depressionen. Nervenarzt 1981 Mar;52(3):135-46 **(Ger)**

Bedford JA, Wilson MC, Elsohly HN, et al: The effects cocaine free extracts of the coca leaf on food consumption and locomotor activity. Pharmacol Biochem Behav 1981 May;14(5):725-8

Bedrak E, Harvey S, Chadwick A: Concentrations of pituitary, gonadal and adrenal hormones in serum of laying and broody white rock hens (Gallus domesticus). J Endocrinol 1981 May;89(2):197-204

Beisland HO, Fossberg E, Sander S: Combined treatment with estriol and alpha-adrenergic stimulation in elderly female patients with urinary incontinence. A pilot study. J Oslo City Hosp 1981 Mar;31(3):39-42

Bekhtereva EP: Influence of castration and testosterone propionate on [3H]noradrenaline metabolism in various structures of male rat brain. Neurosci Behav Physiol 1980 Nov-Dec;10(6):471-3

Bekku T: [Studies on voiding mechanism. 2. The effects of urethral distension on the vesical contraction reflex: neuropharmacological and neurophysiological aspects (author's transl)] Nippon Hinyokika Gakkai Zasshi 1980 Dec;71(12):1456-71 (Eng. Abstr.) **(Jpn)**

Beleslin DB, Samardžic R, Stefanovic-Denic K: 6-hydroxydopamine and aggression in cats. Pharmacol Biochem Behav 1981;14 Suppl 1:29-32

Beliakova NV, Kravetskaia TP, Krutiakov VM: Deistvie radioprotektorov 2-merkaptoétilamina i 5-metoksitriptamina na aktivnost' nekotorykh reparativnykh fermentov. Radiobiologiia 1981 Mar-Apr;21(2):198-203 (Eng. Abstr.) **(Rus)**

Bell GA, Morgan IG: The effects of colchicine and vinblastine on memory in chicks. Behav Brain Res 1981 May;2(3):301-22

Bellemann P, Potter VR: Amino acid transport, Na+/K+-ATPASE, and TAT induction in monolayer cultures of hepatocytes from developing rats. Ann NY Acad Sci 1980;349:385-6

Belmaker RH: Receptors, adenylate cyclase, depression, and lithium. Biol Psychiatry 1981 Apr;16(4):333-50

Belova TI, Kvetnanskii R, Dobrakovova M, et al: Katekholaminy v strukturakh mozga krys, razlichaiushchikhsia po testu 'otkrytogo polia'. Biull Eksp Biol Med 1981 Feb;91(2):136-8 (Eng. Abstr.) **(Rus)**

Belsham GJ, Denton RM, Tanner MJ: Use of a novel rapid preparation of fat-cell plasma membranes employing Percoll to investigate the effects of insulin and adrenaline on membrane protein phosphorylation within intact fat-cells. Biochem J 1980 Nov 15;192(2):457-67

Ben-Baruch G, Egozi Y, Kloog Y, et al: Altered ontogenesis of muscarinic cholinergic receptor in mouse brain: effect of L-thyroxine and betamethasone. Endocrinology 1981 Jul;109(1):235-9

Ben-Harari RR, Lanir A, Youdim MB: Effect of hyperoxia on uptake and metabolism of 5-hydroxytryptamine and beta-phenylethylamine in rat lung: a sex difference. Br J Pharmacol 1981 Jun;7[illegible](2):461-6

Benardo LS, Prince DA: Acetylcholine induced modulation of hippocampal pyramidal neurons. Brain Res 1981 Apr 27;211(1):22[illegible]

Béndek G, Hahn Z: Effect of amphetamine on the metabolism and incorporation of [3H]-thymidine into DNA of developing rat brain. Dev Neurosci 1981;4(1):55-65

Benderly A, Coutts RT, Mak AL, et al: Effects of the optical isomers of 2-amino-3-fluoro-1-phenylpropane (monofluoroamphetamine) hydrochloride on uptake and release of dopamine in rat striatum in vitro. Experientia 1981 Mar 15;37(3):294-5

Benedikter L, Mey T: Onset and magnitude of cardiovascular response to dobutamine and AR-L 115 BS, a new positive inotropic agent with additional vasodilating activity, in normal subjects. Arzneimittelforsch 1981;31(1a):239-42

Benfey BG, Brasili L, Melchiorre C, et al: Potentiation and inhibition of nicotinic effects on striated muscle by the tetramine disulfide benextramine. Can J Physiol Pharmacol 1980 Aug;58(8):984-8

Benkert O, Maier W: Biologisch-psychiatrische Forschung und psychiatrische Pharmakotherapie. Methodenkritische Anmerkungen. MMW 1981 May 8;123(19):795-9 (Eng. Abstr.) **(Ger)**

Bennett GW, Balls M, Clothier RH, et al: Location and release of TRH and 5-HT from amphibian skin. Cell Biol Int Rep 1981 Feb;5(2):151-8

Benuck M, Berg MJ, Marks N: Met-enkephalin-Arg6-Phe7 metabolism: conversion to Met-enkephalin by brain and kidney dipeptidyl carboxypeptidases. Biochem Biophys Res Commun 1981 Mar 31; 99(2):630-6

Bergfeld J, Fliess FR: Orientierende Untersuchungen zur Auslösung der Ovulation bei Mäusen als Test für gonadotrope Präparate. 2. Mitteilung: Zur Aktivität von FSH, PMSG und Gn-RH. Arch Exp Veterinaermed 1981;35(1):143-8 (Eng. Abstr.) **(Ger)**

Bergman H, Glusman S, Harris-Warrick RM, et al: Noradrenaline augments tetanic potentiation of transmitter release by a calcium dependent process. Brain Res 1981 Jun 9;214(1):200-4

Bergman J, Johanson CE: The effects of electric shock on responding maintained by cocaine in rhesus monkeys. Pharmacol Biochem Behav 1981 Mar;14(3):423-6

Bergman RA, Lukaszewicz T, Wang SY: The detection of tetrahydrocannabinol in blood: a comparative study. J Anal Toxicol 1981 Mar-Apr;5(2):85-9

Berkowitz SA, Goldhammer AR, Hewlett EL, et al: Activation of prokaryotic adenylate cyclase by calmodulin. Ann NY Acad Sci 1980; 356:360

Bernardi MM, De Souza H, Palermo Neto J: Effects of single and long-term haloperidol administration on open field behavior of rats. Psychopharmacology (Berlin) 1981;73(2):171-5

Bernd P, Gershon MD, Nunez EA, et al: Separation of dissociated thyroid follicular and parafollicular cells: association of serotonin binding protein with parafollicular cells. J Cell Biol 1981 Mar;88(3):499-508

Bernstein JE, Swift RM, Soltani K, et al: Inhibition of axon reflex vasodilatation by topically applied capsaicin. J Invest Dermatol 1981 May;76(5):394-5

Berry H, Liyanage SP, Durance RA, et al: A double-blind study of benorylate and chlormezanone in musculoskeletal disease. Rheumatol Rehabil 1981 Feb 1;20(1):46-9

AUTHOR SECTION

Bertaccini G, de Castiglione R, Scarpignato C: Effect of substance P and its natural analogues on gastric emptying of the conscious rat. Br J Pharmacol 1981 Feb;72(2):221-3

Bertani-Dziedzic LM, Krstulovic AM, Dziedzic SW, et al: Analysis of urinary metanephrines by reversed-phase high-performance liquid chromatography and electrochemical detection. Clin Chim Acta 1981 Feb 19;110(1):1-8

Bertilsson L, Mellström B, Sjökvist F, et al: Slow hydroxylation of nortriptyline and concomitant poor debrisoquine hydroxylation: clinical implications [letter] Lancet 1981 Mar 7;1(8219):560-1

Bertram U, Kragh-Sørensen P, Rafaelsen OJ, et al: Saliva secretion following long-term antidepressant treatment with nortriptyline controlled by plasma levels. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):357-63

Bevan P, Bradshaw CM, Pun RY, et al: Electro-osmotic and iontophoretic release of noradrenaline from micropipettes. Experientia 1981 Mar 15; 37(3):296-7

Bex FJ, Corbin A, Sarantakis D, et al: Absence of luteinizing hormone-releasing and anti-fertility properties in a glucagon-selective somatostatin analogue. Nature 1981 Jun 25;291(5817):672-3

Beynen AC, Geelen MJ: Control of glycogen synthesis in isolated rat hepatocytes by insulin, glucagon & acetylcholine. Indian J Exp Biol 1981 Jan;19(1):46-8

Bhandari B, Nicholas DJ: Preparation of membrane vesicles in lithium chloride from cells of Nitrosomonas europaea. Anal Biochem 1980 Dec; 109(2):330-7

Bhatnagar YM, Carraway R: Bacterial peptides with C-terminal similarities to bovine neurotensin. Peptides (Fayetteville) 1981 Spring; 2(1):51-9

Bhattacharyya A, Madyastha KM, Bhattacharyya PK, et al: Studies on bicuculline binding sites on neuronal membrane using fluorescent antibody technique: comparative binding of GABA and bicuculline. Biochem Biophys Res Commun 1981 Jan 30;98(2):520-6

Bhattacharyya ML, Vassalle M: Role of calcium and sodium in strophanthidin inotropy in cardiac Purkinje fibers. Am J Physiol 1981 Apr;240(4):H561-70

Bhown AS, Mole JE, Bennett JC: An improved procedure for high-sensitivity microsequencing: use of aminoethyl aminopropyl glass beads in the Beckman sequencer and the ultrasphere ODS column for PTH amino acid identification. Anal Biochem 1981 Jan 15;110(2):355-9

Bicknell RJ, Schofield JG: Role of cyclic nucleotides in the inhibition of growth-hormone secretion by somatostatin. Mol Cell Endocrinol 1981 Apr;22(1):85-94

Bigalke H, Ahnert-Hilger G, Habermann E: Tetanus toxin and botulinum A toxin inhibit acetylcholine release from but not calcium uptake into brain tissue. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr; 316(2):143-8

Binder R, Glick I, Rice M: A comparative study of parenteral molindone and haloperidol in the acutely psychotic patient. J Clin Psychiatry 1981 May;42(5):203-6

Birdsall NJ, Burgen AS, Hammer R, et al: Pirenzepine—a ligand with original binding properties to muscarinic receptors.
Scand J Gastroenterol [Suppl] 1980;15(66):1-4

Bischoff F, Bryson G: Long-term estrogenization in mammals. IV. Body, adrenal, and testes weights; polydipsia; food intake; vasopressin administration; and serum corticosterone levels in estrogenized male Evans rats. Res Commun Chem Pathol Pharmacol 1981 May; 32(2):335-54

Bissell WG, Bank RL: Tricyclic overdose [letter] JAMA 1981 May 1; 245(17):1731-2

Biswas B, Jonsson G: Reversal of noradrenaline denervation-induced increase of beta-adrenoreceptor binding in rat neocortex by noradrenaline infusion. Eur J Pharmacol 1981 Jan 29;69(3):341-6

Bittner GD, Schatz RA: An examination of the residual calcium theory for facilitation of transmitter release. Brain Res 1981 Apr 6; 210(1-2):431-6

Bittner SE, Wagner GC, Aigner TG, et al: Effects of a high-dose treatment of methamphetamine on caudate dopamine and anorexia in rats.
Pharmacol Biochem Behav 1981 Apr;14(4):481-6

Björkman S: Neurotropic and pituitary effects of melanostatin (MIF), thyroliberin (TRH) and structurally related peptides.
Acta Pharm Suec 1980;17(6):352

Björkman S, Castensson S, Isacson D, et al: Synthesis and biological activities of thyroliberin (TRH) analogues with cysteine or cysteine derivatives in position one or two. Acta Pharm Suec 1980;17(6):297-306

Blackmore PF, El-Refai MF, Dehaye JP, et al: Blockade of hepatic alpha-adrenergic receptors and responses by chlorpromazine and trifluoperazine. FEBS Lett 1981 Jan 26;123(2):245-8

Blackwell B: Adverse effects of antidepressant drugs. Part 2: 'Second generation' antidepressants and rational decision making in antidepressant therapy. Drugs 1981 Apr;21(4):273-82 (120 ref.)

Blair ML: Inhibition of renin secretion by intrarenal alpha-adrenoceptor blockade. Am J Physiol 1981 Jun;240(6):E682-8

Blake J, Ferrara P, Li CH: Beta-endorphin: synthesis and radioligand binding activity of analogs containing cystine bridges.
Int J Pept Protein Res 1981 Feb;17(2):239-42

Blaschke M, Fischer HD, Rudolph E: Beeinflussung der Monaminaufnahme in Synaptosomen des Rattenhirns durch Reserpin. Acta Biol Med Ger 1980;39(11-12):1205-12 (Eng. Abstr.) (Ger)

Bloodworth RC: Clinical use of tricyclic antidepressant blood levels.
J Med Assoc Ga 1981 Jan;70(1):41-2

Bloom FE, Battenberg EL, Shibasaki T, et al: Localization of gamma-melanocyte stimulating hormone (gamma MSH)
immunoreactivity in rat brain and pituitary. Regul Pept 1980 Dec; 1(3):205-22

Bloom SR, Edwards AV, Järhult J: The effect of somatostatin on pancreatic endocrine responses mediated via the parasympathetic innervation in the conscious calf. J Physiol (Lond) 1980 Nov;308:29-38

Blumberg S, Vogel Z, Altstein M: Inhibition of enkephalin-degrading enzymes from rat brain and of thermolysin by amino acid hydroxamates. Life Sci 1981 Jan 19;28(3):301-6

Blumberg S, Teichberg VI: Activity of substance P analogs substituted at the Gly9 and Gln6 positions. Biochem Biophys Res Commun 1981 Mar 31;99(2):752-8

Blume HW, Pittman QJ, Renaud LP: Sensitivity of identified medial hypothalamic neurons to GABA, glycine and related amino acids; influence of bicuculline, picrotoxin and strychnine on synaptic inhibition. Brain Res 1981 Mar 23;209(1):145-58

Blundell JE, Tombros E, Rogers PJ, et al: Behavioural analysis of feeding: implications for the pharmacological manipulation of food intake in animals and man. Prog Neuropsychopharmacol 1980;4(4-5):319-26

Bo P, Maurelli M, Nappi G, et al: Lisuride and cerebral electrical activity in the rabbit. Farmaco [Sci] 1981 May;36(5):351-8

Bobbin RP, Morgan DN: Glutamate mimics the afferent transmitter in the Xenopus laevis lateral line. Birth Defects 1980;16(4):107-9

Bochain A, Estey L, Haronian G, et al: Determination of catecholamine permeability coefficients for passive diffusion across phospholipid vesicle membranes. J Membr Biol 1981;60(1):73-6

Bogatova RI, Cherniakova VN, Soboleva TN: Vliianie nekotorykh farmakologicheskikh preparatov i razlichnykh rezhimov
osveshchennosti na rabotosposobnost' cheloveka.
Kosm Biol Aviakosm Med 1981 Jan-Feb;15(1):92-3 (Rus)

Bogerts B: A brainstem atlas of catecholaminergic neurons in man, using melanin as a natural marker. J Comp Neurol 1981 Mar 20;197(1):63-80

Boguta G, Dancewicz AM: Radiation-induced dimerization of tyrosine and glycyltyrosine in aqueous solutions. Int J Radiat Biol 1981 Feb; 39(2):163-74

Bohlen P, Benoit R, Ling N, et al: Isolation and characterization of rat hypothalamic somatostatin-14. Endocrinology 1981 May;108(5):2008-10

Bohn MC, Goldstein M, Black IB: Role of glucocorticoids in expression of the adrenergic phenotype in rat embryonic adrenal gland.
Dev Biol 1981 Feb;82(1):1-10

Bohus B, de Kloet ER: Adrenal steroids and extinction behavior: antagonism by progesterone, deoxycorticosterone and dexamethasone of a specific effect of corticosterone. Life Sci 1981 Jan 26;28(4):433-40

Boismare F, Le Poncin-Lafitte M, Saligaut C, et al: Effets de l'hypoxie hypobare sur le conditionnement et les taux cérébraux d'ADP, d'AMP, de dopamine et de noradrenaline chez le rat traité ou non par le naftidrofuryl. J Pharmacol 1981 Jan-Mar;12(1):51-7 (Eng. Abstr.)
(Fre)

Boismare F, Saligaut C, Moore N, et al: Avoidance learning and mechanism of the protective effect of apomorphine against hypoxia. Aviat Space Environ Med 1981 May;52(5):299-303

Bolton TB, Clark JP: Actions of various muscarinic agonists on membrane potential, potassium efflux, and contraction of longitudinal muscle of guinea-pig intestine. Br J Pharmacol 1981 Feb;72(2):319-34

Bommelaer G, Pradayrol L, Ribet A: Action of prosomatostatin [letter] Lancet 1981 Apr 25;1(8226):949

Bondy B, Remien J: Differential binding of chlorpromazine to human blood cells: application of the hygroscopic desorption method.
Life Sci 1981 Jan 26;28(4):441-9

Bondy SC, Tilson HA, Agrawal AK: Neurotransmitter receptors in brain regions of acrylamide- treated rats. II: Effects of extended exposure to acrylamide. Pharmacol Biochem Behav 1981 Apr;14(4):533-7

Bone AH, Taufek HR: The inhibitory action of L-dihydroxyphenylalanine (L-dopa) in the presence of a monoamine oxidase inhibitor on protein synthesis in vivo and the partial amelioration of this by methionine supplementation. Biochem J 1980 Nov 15;192(2):703-7

Bönisch H: The rate constants for the efflux of deaminated metabolites of 3H-dopamine from the perfused rat heart.
Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):231-5

Bonnin JJ, Borel JC, Loppinet V: A propos de l'utilisation d'une therapeutique myorelaxante en vue de l'enregistrement de la relation centrée. Cah Prothese 1980 Apr;8(30):113-8 (Eng. Abstr.) (Fre)

Borbély AA, Neuhaus HU, Tobler I: Effect of p-chlorophenylalanine and tryptophan on sleep, EEG and motor activity in the rat.
Behav Brain Res 1981 Jan;2(1):1-22

Borgström B, Wollesen C: Effect of fenfluramine and related compounds on the pancreatic colipase/lipase system. FEBS Lett 1981 Apr 6; 126(1):25-8

Bornheim LM, Borys HK, Karler R: Effect of cannabidiol on cytochrome P-450 and hexobarbital sleep time. Biochem Pharmacol 1981 Mar 1;

30(5):503–7

Borri Voltattorni C, Minelli A, Borri P: The interaction of 2,3,4–trihydroxybenzylhydrazine with DOPA decarboxylase from pig kidney. Life Sci 1981 Jan 5;28(1):103–8

Borys HK, Karler R: Post–column derivatization procedure for the colorimetric analysis of tissue cannabinoids separated by high–performance liquid chromatography. J Chromatogr 1981 Jan 30; 205(2):303–23

Borzęcki Z, Rejowska J, Jarzębowski E, et al: Wpływ oksazepamu i diazepamu na zachowanie płciowe oraz poziom GABA i amin biogennych w mózgu samców szczurzych. Ann Univ Mariae Curie Sklodowska [Med] 1979;34:371–6 (Eng. Abstr.) (Pol)

Boschi G, Rips R: Effects of thyrotropin releasing hormone injections into different loci of rat brain on core temperature. Neurosci Lett 1981 Apr 9;23(1):93–8

Boss GR, Erbe RW: Decreased rates of methionine synthesis by methylene tetrahydrofolate reductase–deficient fibroblasts and lymphoblasts. J Clin Invest 1981 Jun;67(6):1659–64

Boudoulas H, Geleris P, Lewis RP, et al: Effect of increased adrenergic activity on the relationship between electrical and mechanical systole. Circulation 1981 Jul;64(1):28–33

Boulenger JP, Zarifian E: L'association neuroleptique–antidépresseur tricyclique. Aspects pharmacologiques et intérêt thérapeutique. Encephale 1981;7(1):5–28 (114 ref.) (Eng. Abstr.) (Fre)

Boutellier U, Koller EA: Propranolol and the respiratory, circulatory, and ECG responses to high altitude. Eur J Applied Physiol 1981; 46(2):105–19

Bowden CL, Redmond DE, Swann A, et al: Pretreatment amine neurotransmitter system interrelationships in depression [proceedings] Psychopharmacol Bull 1981 Jan;17(1):70–2

Bowers M Jr, Stitelman M, Stitelman JH: Neuropsychopharmacology research in psychiatry at Yale University. Psychopharmacol Bull 1981 Apr;17(2):17–39

Bowers MB Jr, Heninger GR, Sternberg D, et al: Clinical processes and central dopaminergic activity in psychotic disorders. Commun Psychopharmacol 1980;4(3):177–83

Bowker RM, Steinbusch HW, Coulter JD: Serotonergic and peptidergic projections to the spinal cord demonstrated by a combined retrograde HRP histochemical and immunocytochemical staining method. Brain Res 1981 May 4;211(2):412–7

Božeková L, Kovalčik V: Vplyv rezerpínu na aktivitu O–demetylázy a N–demetylázy v pečeni potkanov. Bratisl Lek Listy 1981 Feb; 75(2):161–6 (Eng. Abstr.) (Slo)

Bozler G, Hammer R: An international pharmacokinetic study on pirenzepine following a single oral dose. Scand J Gastroenterol [Suppl] 1980;15(66):27–33

Brabec W, Dapunt O: Vergleich der tokolytischen Wirksamkeit von Hexoprenalin und Ritodrine bei prostaglandininduzierten Wehen. Gynaekol Rundsch 1980 Jun;20 Suppl 2:230–4 (Ger)

Braff DL, Silverton L, Saccuzzo DP, et al: Impaired speed of visual information processing in marijuana intoxication. Am J Psychiatry 1981 May;138(5):613–7

Branconnier RJ, Cole JO, Ghazvinian S: The therapeutic profile of mianserin in mild elderly depressives [proceedings] Psychopharmacol Bull 1981 Jan;17(1):129–31

Brasili L, Melchiorre C, Belleau B, et al: Reactivation by cysteamine of vascular alpha adrenoceptors blocked by the tetramine disulfide benextramine and interaction of benextramine with phenoxybenzamine. Can J Physiol Pharmacol 1980 Dec;58(12):1490–3

Bray J, Turner AR, Dusel F: Lithium and the mitogenic response of human lymphocytes. Clin Immunol Immunopathol 1981 May;19(2):284–8

Bredesen JE, Ellingsen OF, Karlsen J: Rapid isothermal gas––liquid chromatographic determination of tricyclic antidepressants in serum with use of a nitrogen–selective detector. J Chromatogr 1981 Jan 16; 204:361–7

Brett LP, Levine S: The pituitary–adrenal response to 'minimized' schedule–induced drinking. Physiol Behav 1981 Feb;26(2):153–8

Brocas H, van Coevorden A, Seo H, et al: Dopaminergic control of prolactin mRNA accumulation in the pituitary of the male rat. Mol Cell Endocrinol 1981 Apr;22(1):25–30

Brodie RR, Chasseaud LF, Taylor T: Concentrations of N–descyclopropylmethylprazepam in whole–blood, plasma, and milk after administration of prazepam to humans. Biopharm Drug Dispos 1981 Jan–Mar;2(1):59–68

Brodin E, Alumets J, Håkanson R, et al: Immunoreactive substance P in the chicken gut: distribution, development and possible functional significance. Cell Tissue Res 1981;216(3):455–69

Brooks JC, Burke DH, Treml S: Effect of various stimulus parameters on electrically–induced catecholamine secretion by thin slices of bovine adrenal medulla. J Neural Transm 1981;50(2–4):201–7

Brosnihan KB, Szilagyi JE, Ferrario CM: Effect of chronic sodium depletion on cerebrospinal fluid and plasma catecholamines. Hypertension 1981 Mar–Apr;3(2):233–9

Brown CL, Hanley MR: The effects of substance P and related peptides on alpha–amylase release from rat parotid gland slices. Br J Pharmacol 1981 Jun;73(2):517–23

Brown EM: Lithium induces abnormal calcium–regulated PTH release in dispersed bovine parathyroid cells. J Clin Endocrinol Metab 1981 May;52(5):1046–8

Brown GL, Goodwin FK, Ballenger JC, et al: Cerebrospinal fluid amine metabolites and cyclic nucleotides in human aggression [proceedings] Psychopharmacol Bull 1981 Jan;17(1):63–5

Brown JA, Jahreis GP, Swank RT: The synthesis and processing of beta–glucuronidase in normal and egasyn deficient mouse kidney. Biochem Biophys Res Commun 1981 Mar 31;99(2):691–9

Brown M, Rivier J, Vale W: Somatostatin–28: selective action on the pancreatic beta–cell and brain. Endocrinology 1981 Jun;108(6):2391–6

Brown M, Ling N, Rivier J: Somatostatin–28, somatostatin–14 and somatostatin analogs: effects on thermoregulation. Brain Res 1981 Jun 9;214(1):127–35

Brown M: Neuropeptides: central nervous system effects on nutrient metabolism. Diabetologia 1981 Mar;20 Suppl:299–304 (28 ref.)

Brown MR: Thyrotropin releasing factor: a putative CNS regulator of the autonomic nervous system. Life Sci 1981 Apr 13–20; 28(15–16):1789–95

Brown OM: Cat heart acetylcholine: unilateral vagotomy studies with pyrolysis–mass fragmentography. Life Sci 1981 Feb 16;28(7):819–25

Broxterman HJ, Noach EL, van Valkenburg CF, et al: Cross–tolerance of dopamine metabolism to baclofen, gamma–butyrolactone and HA–966 in the striatum and olfactory tubercle of the rat. Life Sci 1981 Mar 2;28(9):973–81

Bruguerolle B, Jadot G, Valli M, et al: A propos des effets de quatre benzamides (métoclopramide, sulpiride, sultopride, tiapride) sur le cycle oestral de la rate. J Pharmacol 1981 Jan–Mar;12(1):27–36 (Eng. Abstr.) (Fre)

Bruguerolle B, Valli M, Jadot G, et al: Recherche des effets éventuels du propranolol sur le cycle oestral de la rattle. C R Soc Biol (Paris) 1981;175(1):87–90 (Eng. Abstr.) (Fre)

Bruinvels J, Moleman P: Stereospecific transport carrier systems for L–tyrosine and L–tryptophan in relation to monoamine synthesis. Essays Neurochem Neuropharmacol 1981;5:1–24 (33 ref.)

Brus R, Herman ZS, Sokola A, et al: Effect of prostaglandin synthesis inhibition on the central activity of noradrenaline in rats. Acta Physiol Pol 1981 Jan–Feb;32(1):47–51

Brüssow KP, Bergfeld J: Versuche zur Ovulationsauslösung bei präpuberalen weiblichen Jungschweinen mit Gn–RH vet. 'Berlin–Chemie'. Arch Exp Veterinaermed 1981;35(2):285–90 (Eng. Abstr.) (Ger)

Bryan LJ, O'Donnell SR: Kinetic analyses of the mechanisms of action of inhibitors of the extraneuronal uptake of adrenaline in smooth muscle cells of guinea–pig trachea. Naunyn Schmiedebergs Arch Pharmacol 1981 Jan;315(3):249–54

Buckerfield M, Oliver J, Chubb IW, et al: Somatostatin–like immunoreactivity in amacrine cells of the chicken retina. Neuroscience 1981;6(4):689–95

Buckholtz NS: Brain serotonin and 5–hydroxyindoleacetic acid concentrations and serotonin synthesis following tetrahydro–beta–carboline administration in mice. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):215–21

Buckley NM, Charney AN, Brazeau P, et al: Changes in cardiovascular and renal function during catecholamine infusions in developing swine. Am J Physiol 1981 Apr;240(4):F276–81

Bucsics A, Lembeck F: In vitro release of substance P from spinal cord slices by capsaicin congeners. Eur J Pharmacol 1981 Apr 24;71(1):71–7

Budd RD: Amphetamine radioimmunoassay––structure versus reactivity. Clin Toxicol 1981;18(3):299–316

Bulger RE, Cronin RE, Dobyan DC: Glomerular architectural changes after a two–hour infusion of norepinephrine. Am J Anat 1980 Dec; 159(4):379–84

Bunte T, Owada MK, Donner P, et al: Association of the transformation–specific protein pp60src with the membrane of an avian sarcoma virus. J Virol 1981 Jun;38(3):1034–47

Burchfiel JL, Duffy FH: Role of intracortical inhibition in deprivation amblyopia: reversal by microiontophoretic bicuculline. Brain Res 1981 Feb 16;206(2):479–84

Burger A, Ramberger R, Schmidt W: Einfluss der Polymorphie des Wirkstoffes auf die Eigenschaften von Tabletten. 3. Mitteilung: Kompressionsverhalten von Meprobamat. Pharmazie 1981;36(1):41–6 (Eng. Abstr.) (Ger)

Burgess CD: Effects of antidepressants on cardiac function. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):370–9

Burnham WM, Spero L, Okazaki MM, et al: Saturable binding of [3H]phenytoin to rat brain membrane fraction. Can J Physiol Pharmacol 1981 Apr;59(4):402–7

Burrows GH, Myers MM, Whittemore SR, et al: Calcium–sensitive accumulation of norepinephrine in rat cerebral cortex. Eur J Pharmacol 1981 Jan 29;69(3):301–12

Burstein S, Shoupe TS: Metabolic pathways for the transformation of delta 1–tetrahydrocannabinol in mouse hepatic microsomes. Drug Metab Dispos 1981 Mar–Apr;9(2):94–6

Bury RW, Mashford ML: Use of a drug–screening service in an inner–city teaching hospital. Med J Aust 1981 Feb 7;1(3):132-3

Busuioc A, Cotruţ M, Balan G, et al: Influenţa ionilor de litiu asupra unor enzime glicolitice şi oxidative din fraciunile subcelulare şi fracţiunile sinaptozomiale de cortex de şobolan.
Rev Med Chir Soc Med Nat Iasi 1980 Jul-Sep;84(3):515-20 (Eng. Abstr.) (Rum)

Butollo W: Behandlung chronischer Angst mit Verhaltenstherapie und Beta-Rezeptoren-Blocker - eine empirische Untersuchung.
Psychother Psychosom Med Psychol 1981 Mar;31(2):53-7 (Eng. Abstr.) (Ger)

Butz RF, Schroeder DH, Welch RM, et al: Radioimmunoassay and pharmacokinetic profile of bupropion in the dog.
J Pharmacol Exp Ther 1981 Jun;217(3):602-10

Buvinger WE, Stone LC, Heath HE: Biochemical genetics of tryptophan synthesis in Pseudomonas acidovorans. J Bacteriol 1981 Jul;147(1):62-8

Buznikov GA, Shmukler YB: Possible role of 'prenervous' neurotransmitters in cellular interactions of early embryogenesis: a hypothesis. Neurochem Res 1981 Jan;6(1):55-68

Bylund DB, Forte LR, Morgan DW, et al: Effects of chronic reserpine administration on beta adrenergic receptors, adenylate cyclase and phosphodiesterase of the rat submandibular gland.
J Pharmacol Exp Ther 1981 Jul;218(1):134-41

C

Cabello FM: Binding of 5-hydroxytryptamine to brain hydrophobic proteins. Inhibition by structural analogues and ions. Rev Esp Fisiol 1980 Dec;36(4):409-12

Cabezas JA, Reglero A, De Pedro A, et al: Hydrolysis of natural and synthetic substrates by alpha-L-fucosidase, beta-D-glucuronidase and beta-N-acetylhexosaminidase purified from molluscs. Int J Biochem 1981;13(3):389-93

Cahill AL, Ferguson SM, Ehret CF: Chronotypic induction of tyrosine aminotransferase by alpha-methyl-p-tyrosine. Life Sci 1981 Apr 6;28(14):1665-71

Caillard B, Klepping J, Guilland JC, et al: Catécholamines plasmatiques peropératoires au cours de la chirurgie cardio-vasculaire.
Ann Anesthesiol Fr 1981;22(1):27-31 (Eng. Abstr.) (Fre)

Cailleux A, Turcant A, Premel-Cabic A, et al: Identification and quantitation of neutral and basic drugs in blood by gas chromatography and mass spectrometry. J Chromatogr Sci 1981 Apr;19(4):163-76

Caine M, Perlberg S, Shapiro A: Phenoxybenzamine for benign prostatic obstruction. Review of 200 cases. Urology 1981 Jun;17(6):542-6

Caldwell HC, Westlake WJ, Schriver RC, et al: Steady-state lithium blood level fluctuations in man following administration of a lithium carbonate conventional and controlled-release dosage form. J Clin Pharmacol 1981 Feb-Mar;21(2):106-9

Calvano SE, Reynolds RW, Ladenslager ML, et al: Correlation between plasma thyroxine levels and corticosterone-binding activity in intact, ovariectomized, and ovariectomized estrogen-treated rats.
Horm Metab Res 1981 Mar;13(3):171-4

Calverley DG, McKim HR, Dewhurst WG: Inhibitory effect of some monoamine oxidase inhibitors on fluorescence assay for the o-methylated metabolites of the catecholamines.
J Pharmacol Methods 1981 Mar;5(2):179-81

Calverley DG, Baker GB, Coutts RT, et al: A method for measurement of tranylcypromine in rat brain regions using gas chromatography with electron capture detection. Biochem Pharmacol 1981 Apr;30(8):[illegible]61-7

Camier M, Lauber M, Nicolas P, et al: Mécanismes de biosynthèse de quelque neuropeptides hypothalamiques. Identification de formes précurseurs. Ann Endocrinol (Paris) 1980 Nov-Dec;41(6):466-77 (37 ref.) (Eng. Abstr.) (Fre)

Campagnoli C, Belforte L, Massara F, et al: Partial remission of hyperprolactinemic amenorrhea after bromocriptine-induced pregnancy. J Endocrinol Invest 1981 Jan-Mar;4(1):85-91

Campos F, Arruda F: Pharmacologic manipulations of brain catecholamines and the behavior of Callithrix jacchus (marmoset).
Psychopharmacology (Berlin) 1981;73(3):252-6

Cantwell DP: A clinician's guide to the use of stimulant medication for the psychiatric disorders of children. JDPB 1980 Sep;1(3):133-40 (58 ref.)

Caplová T, Zucha I, Heretik A: Die Kooperation der Pharmakotherapie und Psychotherapie: experimentelle Illustration. Agressologie 1980;21(A):37-9 (Eng. Abstr.) (Ger)

Cardinali DP, Vacas MI, Ritta MN: A biphasic effect of estradiol on serotonin metabolism in rat pineal organ cultures. Experientia 1981 Feb 15;37(2):203-4

Carey RM, Van Loon GR, Baines AD, et al: Decreased plasma and urinary dopamine during dietary sodium depletion in man.
J Clin Endocrinol Metab 1981 May;52(5):903-9

Carlen PL, Durand D: Modelling the postsynaptic location and magnitude of tonic conductance changes resulting from neurotransmitters or drugs.
Neuroscience 1981;6(5):839-46

Carlsson A: Some current problems related to the mode of action of antidepressant drugs. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):63-6

Carlsson C, Chapman AG: The effect of diazepam on the cerebral metabolic state in rats and its interaction with nitrous oxide.
Anesthesiology 1981 Jun;54(6):488-95

Carne S: Law and the general practitioner, assisting the police.
Br Med J [Clin Res] 1981 Jun 6;282(6279):1839-41

Carney MW, Rutherford P: Clopenthixol decanoate in schizophrenia.
Curr Med Res Opin 1981;7(4):205-11

Carraway R, Bhatnagar YM: Isolation, structure and biologic activity of chicken intestinal neurotensin. Peptides (Fayetteville) 1980 Summer;1(2):167-74

Carraway R, Bhatnagar YM: Immunochemical characterization of neurotensin-like peptides in chicken. Peptides (Fayetteville) 1980 Summer;1(2):159-65

Carroll J, Komanicky P, Melby JC: 5
alpha-Dihydro-11-deoxycorticosterone: effect on blood pressure in the rat. Steroids 1981 Jan;37(1):111-20

Carroll ME, France CP, Meisch RA: Intravenous self-administration of etonitazene, cocaine and phencyclidine in rats during food deprivation and satiation. J Pharmacol Exp Ther 1981 May;217(2):241-7

Cartoni GP, Ciardi M, Giarrusso A, et al: Reversed-phase high-performance liquid chromatographic detection of pemoline in doping control. J Chromatogr 1980 Dec 5;202(1):131-3

Cassens G, Kuruc A, Roffman M, et al: Alterations in brain norepinephrine metabolism and behavior induced by environmental stimuli previously paired with inescapable shock. Behav Brain Res 1981 May;2(3):387-407

Castellani A, Setlow RB: Harman inhibits the removal of pyrimidine dimers from the DNA of human cells. Biochem Biophys Res Commun 1981 Feb 12;98(3):823-8

Castellucci VF, Kandel ER, Schwartz JH, et al: Intracellular injection of t he catalytic subunit of cyclic AMP-dependent protein kinase simulates facilitation of transmitter release underlying behavioral sensitization in Aplysia. Proc Natl Acad Sci USA 1980 Dec;77(12):7492-6

Catravas JD, Waters IW: Acute cocaine intoxication in the conscious dog: studies on the mechanism of lethality. J Pharmacol Exp Ther 1981 May;217(2):350-6

Cautreels W, Jeanniot JP: Quantitative analysis of CM 6912 (ethyl loflazepate) and its metabolites in plasma and urine by chemical ionization gas chromatography mass spectrometry. Application to pharmacokinetic studies in man. Biomed Mass Spectrom 1980 Nov;7(11-12):565-71

Caviness VS Jr, Korde MG: Monoaminergic afferents to the neocortex: a developmental histofluorescence study in normal and Reeler mouse embryos. Brain Res 1981 Mar 23;209(1):1-9

Cenajek D, Chodera A, Godlewski J, et al: Investigations on the interaction between cyproheptadine and amphetamine. Acta Physiol Pol 1980;31(5):561-6

Cernáček P, Bečvárová H, Gerová Z, et al: Plasma tryptophan level in chronic renal failure. Clin Nephrol 1980 Nov;14(5):246-9

Cerrito F, Raiteri M: Supersensitivity of central noradrenergic presynaptic autoreceptors following chronic treatment with the antidepressant mianserin. Eur J Pharmacol 1981 Mar 26;70(3):425-6

Cesselin F, Soubrié P, Bourgoin S, et al: In vivo release of met-enkephalin in the cat brain. Neuroscience 1981;6(3):301-13

Chafetz MD, Thompson RG, Evans SH, et al: Biochemical specificity of septal hyperreactivity: a behavioral discrimination. Behav Brain Res 1981 May;2(3):409-20

Chamberlein HR: 'Hyperactivity' : still a maze of questions [editorial] JDPB 1980 Sep;1(3):99-101

Chambers CD, White OZ: Characteristics of high-frequency consumers of prescription psychoactive drugs. Chem Depend 1980;4(1-2):33-46

Chambers CD, White OZ: A study of phenmetrazine (Preludin) abuse. Chem Depend 1980;4(1-2):101-11

Champoux JJ: DNA is linked to the rat liver DNA nicking-closing enzyme by a phosphodiester bond to tyrosine. J Biol Chem 1981 May 25;256(10):4805-9

Chan HS, Freedman MH, Saunders EF: Lithium therapy of children with chronic neutropenia. Am J Med 1981 May;70(5):1073-7

Chan KM, Aguanno JJ, Jansen R, et al: Charcoal hemoperfusion for treatment of carbamazepine poisoning. Clin Chem 1981 Jul;27(7):1300-2

Chan YM, Soldin SJ, Swanson JM, et al: Gas chromatographic/mass spectrometric analysis of methylphenidate (ritalin) in serum.
Clin Biochem 1980 Dec;13(6):266-72

Chand N: 5-Hydroxytryptamine induces relaxation of goat pulmonary veins: evidence for the noninvolvement of M and D-tryptamine receptors. Br J Pharmacol 1981 Feb;72(2):233-7

Chang LR, Barnard EA, Lo MM, et al: Molecular sizes of benzodiazepine receptors and the interacting GABA receptors in the membrane are identical. FEBS Lett 1981 Apr 20;126(2):309-12

Chang RC, Huang WY, Arimura A, et al: Isolation, structure and synthesis of a heptapeptide with in vitro ACTH-releasing activity from porcine hypothalamus. Horm Metab Res 1981 Apr;13(4):228-32

Chang YF, Hernandez MF, Myslinski NR: Enhancement of hexobarbital-induced sleep by lysine and its metabolites. Life Sci 1981 Jan 26;28(4):407-13

AUTHOR SECTION

Channabasavanna SM, Sampath G, Rao BS, et al: Lithium response in the treatment of manic symptomatology. Indian J Med Res 1980 Dec; 72:908–9

Channing CP, Gagliano P, Hoover DJ, et al: Relationship between human follicular fluid inhibin F activity and steroid content. J Clin Endocrinol Metab 1981 Jun;52(6):1193–8

Charnay Y, Léger L, Dubois PM: Distribution de la substance P et de la méthionine-enkephaline dans la partie dorsolatérale du tegmentum pontique chez le chat. Etude par immunofluorescence. C R Acad Sci [D] (Paris) 1981 Feb 2;292(5):435–40 (Eng. Abstr.) (Fre)

Chaturvedi N, Goodman M, Bowers C: Topochemically related hormone structures. Synthesis of partial retro-inverso analogs of LH-RH. Int J Pept Protein Res 1981 Jan;17(1):72–88

Chelyshev YuA: Neurohistological and histochemical data on an additional fiber of some encapsulated receptors. Neurosci Behav Physiol 1980 Nov–Dec;10(6):525–9

Chen YF, Ramirez VD: Serotonin stimulates thyrotropin-releasing hormone release from superfused rats hypothalami. Endocrinology 1981 Jun;108(6):2359–66

Cheng CH, Wooten GF: Simultaneous radioenzymatic assay of dopamine and dihydroxyphenylacetic acid: an index of in vivo dopamine release. J Pharmacol Methods 1981 Mar;5(2):165–73

Cheng SC, Brunner EA: Inhibition of GABA metabolism in rat brain slices by halothane. Anesthesiology 1981 Jul;55(1):26–33

Cheng YS, Chen LB: Detection of phosphotyrosine-containing 34,000-dalton protein in the framework of cells transformed with Rous sarcoma virus. Proc Nat Acad Sci USA 1981 Apr;78(4):2388–92

Chernish SM, Miller RE, Rosenak BD, et al: Effect of D-Val1, D-Trp8-somatostatin on the motility of the stomach, duodenum and jejunum. Am J Gastroenterol 1981 Jan;75(1):36–40

Cheung CY, Neill AC, Weiner RI: Stimulation of prolactin secretion by neuroleptics in rats with medial basal hypothalamic lesions. Neuroendocrinology 1981 Jun;32(6):370–4

Chevrel B: Action d'un nouveau gastrocinétique sur la motilité gastro-intestinale: le dompéridone, antidopaminergique périphérique. Med Chir Dig 1981;10(2):175–8 (Fre)

Chi MS, El-Halawani ME, Waibel PE, et al: Effects of T-2 toxin on brain catecholamines and selected blood components in growing chickens. Poult Sci 1981 Jan;60(1):137–41

Chiba T, Kadowaki S, Taminato T, et al: Effect of antisomatostatin gamma-globulin on gastrin release in rats. Gastroenterology 1981 Aug; 81(2):321–6

Childs GV, Yang HY, Tobin RB, et al: Effects of thyroidectomy, propylthiouracil, and thyroxine on pituitary content and immunocytochemical staining of thyrotropin (TSH) and thyrotropin releasing hormone (TRH). J Histochem Cytochem 1981 Mar; 29(3):357–63

Chiodo LA, Caggiula AR, Saller CF: Estrogen potentiates the stereotypy induced by dopamine agonists in the rat. Life Sci 1981 Feb 16; 28(7):827–35

Chipkin RE, Morris DH, English MG, et al: Potent tetrapeptide enkephalins. Life Sci 1981 Mar 30;28(13):1517–22

Cho AK, Kammerer RC, Abe L: The identification of a new metabolite of phencyclidine. Life Sci 1981 Mar 2;28(9):1075–9

Choi DW, Farb DH, Fischbach GD: GABA-mediated synaptic potentials in chick spinal cord and sensory neurons. J Neurophysiol 1981 Apr; 45(4):632–43

Choi DW, Farb DH, Fischbach GD: Chlordiazepoxide selectively potentiates GABA conductance of spinal cord and sensory neurons in cell culture. J Neurophysiol 1981 Apr;45(4):621–31

Choi DW, Fischbach GD: GABA conductance of chick spinal cord and dorsal root ganglion neurons in cell culture. J Neurophysiol 1981 Apr; 45(4):605–20

Chojnacki M, Kralik P, Allen RH, et al: Neuroleptic-induced decrease in platelet MAO activity of schizophrenic patients. Am J Psychiatry 1981 Jun;138(6):838–40

Chow SA, Charkowski DM, Fischer LJ: Separation of phenytoin and its metabolites by high-performance liquid chromatography. Life Sci 1980 Dec 22–29;27(25–26):2477–82

Chrétien M, Seidah NG, Scherrer H: Endorphines: structure, rôles et biogénèse. Can J Physiol Pharmacol 1981 May;59(5):413–31 (218 ref.) (Eng. Abstr.) (Fre)

Chrétien M, Gossard F, Crine P, et al: New perspectives in neuropeptides. Biosynthesis from large precursors. The pro-opio-melanocortin model in the pars intermedia. Acta Psychiatr Belg 1980 Sep–Oct;80(5):699–713

Chrétien M, Seidah NG: Chemistry and biosynthesis of pro-opiomelanocortin. ACTH, MSH's, endorphins and their related peptides. Mol Cell Biochem 1981 Jan 28;34(2):101–27 (232 ref.)

Christie JE, Brown D: Comparison of the cardiovascular effects of amitriptyline and zimelidine using thoracic impedance cardiography. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):385–92

Christodoulou GN, Kokkevi A, Lykouras EP, et al: Effects of lithium on memory. Am J Psychiatry 1981 Jun;138(6):847–8

Cihák A, Kröger H: Tryptophan-mediated induction of hepatic enzymes stimulated by 5-azacytidine pretreatment. Biomedicine 1981 Feb; 34(1):18–22

Ciofalo FR: Effects of some membrane perturbers on alpha 1-adrenergic receptor binding. Neurosci Lett 1981 Feb 6;21(3):313–8

Claghorn JL, Mathew RJ: Clinical trials with new bicyclic and tetracyclic compounds: zimelidine and maprotiline [proceedings] Psychopharmacol Bull 1981 Jan;17(1):23–6

Clampit MK: Residual attentional deficits in adolescents. J Learn Disabil 1981 Apr;14(4):218–9

Clark KE, Mills EG, Otte TE, et al: Effect of serotonin on uterine blood flow in pregnant and nonpregnant sheep. Life Sci 1980 Dec 22–29; 27(25–26):2655–61

Clark MJ, Redford DS, Baddour HM, et al: Quinidine-induced thrombocytopenia. Oral Surg 1981 May;51(5):478–80

Cleaves GR, Ryan TE, Schlesinger RW: Identification and characterization of type 2 dengue virus replicative intermediate and replicative form RNAs. Virology 1981 May;111(1):73–83

Cocks DA, Dyer TF, Edgar K: Simple and rapid gas-liquid chromatographic method for estimating carbamazepine in serum. J Chromatogr 1981 Mar 13;222(3):496–500

Cohen NJ, Sullivan J, Minde K, et al: Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. J Abnorm Child Psychol 1981 Mar;9(1):43–54

Cohen NL, Alpert M, Friedhoff AJ: Clinical trial of halazepam and clorazepate: considerations of a single bedtime dose [proceedings] Psychopharmacol Bull 1981 Jan;17(1):134–5 (eng)

Cohen S, Dusman E, Blumberg S, et al: In vitro contraction of the pupillary sphincter by substance P and its stable analogs. Invest Ophthalmol Vis Sci 1981 Jun;20(6):717–21

Cohn JB, Gottschalk LA: Double-blind comparison of ketazolam and placebo using once-a-day dosing. J Clin Pharmacol 1980 Nov–Dec; 20(11–12):676–80

Cole AE, Shinnick-Gallagher P: Comparison of the receptors mediating the catecholamine hyperpolarization and slow inhibitory postsynaptic potential in sympathetic ganglia. J Pharmacol Exp Ther 1981 May; 217(2):440–4

Coletti-Previero MA, Mattras H, Descomps B, et al: Purification and substrate characterization of a human enkephalin-degrading aminopeptidase. Biochim Biophys Acta 1981 Jan 15;657(1):122–7

Collard KJ, Williams SR: The effect of ouabain on the release of 5-hydroxytryptamine from superfused synaptosomes. Biochem Soc Trans 1981 Feb;9(1):109–10

Collingridge GL, Davies J: The influence of striatal stimulation and putative neurotransmitters on identified neurones in the rat substantia nigra. Brain Res 1981 May 18;212(2):345–59

Colt EW, Wardlaw SL, Frantz AG: The effect of running on plasma beta-endorphin. Life Sci 1981 Apr 6;28(14):1637–40

Commissaris RL, Lyness WH, Moore KE, et al: Central 5-hydroxytryptamine and the effects of hallucinogens and phenobarbital on operant responding in rats. Pharmacol Biochem Behav 1981 May; 14(5):595–601

Commissiong JW, Karoum F, Reiffenstein RJ, et al: Cyclobenzaprine: a possible mechanism of action for its muscle relaxant effect. Can J Physiol Pharmacol 1981 Jan;59(1):37–44

Commissiong JW: Evidence that the noradrenergic coeruloospinal projection decussates at the spinal level. Brain Res 1981 May 11; 212(1):145–51

Connolly RG: Treatment of fibromyositis with fluphenazine and amitriptyline: a preliminary report. Del Med J 1981 Apr;53(4):189–91

Conrad MJ, Singer SJ: The solubility of amphipathic molecules in biological membranes and lipid bilayers and its implications for membrane structure. Biochemistry 1981 Feb 17;20(4):808–18

Constantinidis J, Dick P, Tissot R: Antidepressants and serotonin neurons of the raphe. Neuropsychobiology 1981;7(3):113–21

Cools AR: Role of the neostriatal dopaminergic activity in sequencing and selecting behavioural strategies: facilitation of processes involved in selecting the best strategy in a stressful situation. Behav Brain Res 1980 Oct;1(5):361–78

Coons HW, Peloquin LJ, Klorman R, et al: Effect of methylphenidate ~~on young adult's vigilance and event-related potentials.~~ Electroencephalogr Clin Neurophysiol 1981 Apr;51(4):373–87

Cooper DS, Gelenberg AJ, Wojcik JC, et al: The effect of amoxapine and imipramine on serum prolactin levels. Arch Intern Med 1981 Jul; 141(8):1023–5

Cooper SJ, Burnett G, Brown K: Food preference following acute or chronic chlordiazepoxide administration: tolerance to an antineophobic action. Psychopharmacology (Berlin) 1981;73(1):70–4

Cooper TB, Bost R, Sunshine I: Postmortem blood and tissue levels of loxapine and its metabolites. J Anal Toxicol 1981 Mar–Apr;5(2):99–100

Cooper SA: Antianxiety, sedative hypnotics. Clin Prevent Dent 1981 Jan–Feb;3(1):25–6

Coppen A, Swade C, Wood K: The action of antidepressant drugs on 5-hydroxy-tryptamine uptake by platelets—relationship to therapeutic effect. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):236–43

Coppen A, Abou-Saleh M, Milln P, et al: Current concepts of lithium therapy [letter] Br J Hosp Med 1981 Mar;25(3):309–10

Coppings RJ, McCann SM: Serotonin involvement in the regulation of gonadotropin secretion during lactation in the rat. Proc Soc Exp Biol Med 1981 Apr;166(4):536–41

Cordero JF, Oakley GP, Greenberg F, et al: Is Bendectin a teratogen? JAMA 1981 Jun 12;245(22):2307–10

Cornelissen PJ, Beijersbergen van Henegouwen GM, Mohn GR: Structure and photobiological activity of 7–chloro–1,4–benzodiazepines. Studies on the phototoxic effects of chlordiazepoxide, desmethylchlordiazepoxide and demoxepam using a bacterial indicator system. Photochem Photobiol 1980 Nov;32(5):653–9

Cossum PA, Roberts MS: Availability of isosorbide dinitrate, diazepam and chlormethiazole, from i.v. delivery systems. Eur J Clin Pharmacol 1981 Feb;19(3):181–5

Costa D, Glăţescu M, Marcu I, et al: Chlorpromazine–induced decrease of red cell aggregability. Med Interne 1981 Jan–Mar;19(1):83–7

Costa G, Trovato A, Abate F, et al: Ruolo del sistema prostaglandinico nel controllo monoaminergico della liberazione di prolattina nel ratto. Boll Soc Ital Biol Sper 1979 Aug 15;55(15):1492–7 (Eng. Abstr.) (Ita)

Costa M, Furness JB, Llewellyn–Smith IJ, et al: Projections of substance P–containing neurons within the guinea–pig small intestine. Neuroscience 1981;6(3):411–24

Costall B, Naylor RJ, Nohria V: Use of the intracerebral injection technique to elucidate mechanisms of apomorphine climbing and its antagonism in the mouse. Psychopharmacology (Berlin) 1981;73(1):91–4

Costello JB, Poklis A: Treatment of massive phenobarbital overdose with dopamine diuresis. Arch Intern Med 1981 Jun;141(7):938–40

Cotler S, Puglisi CV, Gustafson JH: Determination of diazepam and its major metabolites in man and in the cat by high–performance liquid chromatography. J Chromatogr 1981 Jan 2;222(1):95–106

Coull BM, Owens DK, Cutler RW: The release of endogenous amino acids into the vitreous of the intact eye of the albino rat: effect of light, potassium, and ouabain. Brain Res 1981 Apr 6;210(1–2):301–9

Coulter DB, Whelan SC, Wilson RC, et al: Determination of blood pressure by indirect methods in dogs given acetylpromazine maleate. Cornell Vet 1981 Jan;71(1):75–84

Cox B, Lee TF, Parkes J: Decreased ability to cope with heat and cold linked to a dysfunction in a central dopaminergic pathway in elderly rats. Life Sci 1981 May 4;28(18):2039–44

Coy DH, Kastin AJ: Tyrosine–modified analogs of methionine–enkephalin and their effects on the mouse vas deferens. Peptides (Fayetteville) 1980 Summer;1(2):175–7

Creese I, Sibley DR: Receptor adaptations to centrally acting drugs. Annu Rev Pharmacol Toxicol 1981;21:357–91 (235 ref.)

Crews FT, Paul SM, Goodwin FK: Acceleration of beta–receptor desensitization in combined administration of antidepressants and phenoxybenzamine. Nature 1981 Apr 30;290(5809):787–9

Crimaldi AA, Kuo IC, Coffee CJ: Effect of trifluoperazine on cyclic nucleotide phosphodiesterase activity in crude homogenates of bovine adrenal medulla. Ann NY Acad Sci 1980;356:367–8

Crocker MC: Intravascular guanethidine in the treatment of extravasated vasopressin [letter] N Engl J Med 1981 Jun 4;304(23):1430

Csaba G, Németh G: Changes of receptor cooperation in Tetrahymena by re–exposure to hormones. Acta Biol Acad Sci Hung 1980; 31(1–3):43–7

Csaba G, Németh G: Enhancement of the sensitivity of Tetrahymena to a second hormonal influence by hormone pretreatment. Acta Biol Med Ger 1980;39(10):1027–30

Csaba G, Ubornyák L: Effects of hormones on the RNA–synthesis of Tetrahymena pyriformis. Comp Biochem Physiol [C] 1981;68C(2):251–3

Cubells JF, Joseph JA: Neostriatal dopamine receptor loss and behavioral deficits in the senescent rat. Life Sci 1981 Mar 16;28(11):1215–8

Cuello AC, Gamse R, Holzer P, et al: Substance P immunoreactive neurons following neonatal administration of capsaicin. Naunyn Schmiedebergs Arch Pharmacol 1981 Jan;315(3):185–94

Cunningham J, Marshall J, Neal MJ: The radioautographical localization in the vertebrate retina of [3H]–(+ or –)–cis–aminocyclohexane carboxylic acid (ACHC); a selective inhibitor of neuronal GABA transport. Exp Eye Res 1981 Apr;32(4):445–50

Cuomo V, Cortese I, Racagni G: Effects of morphine and chlordiazepoxide on locomotor activity in two inbred strains of mice. Pharmacol Res Commun 1981 Jan;13(1):87–93

Currie AJ, Fraser HM, Sharpe RM: Human placental receptors for luteinizing hormone releasing hormone. Biochem Biophys Res Commun 1981 Mar 16;99(1):332–8

Curzon G, Kantamaneni BD, Tricklebank MD: A comparison of an improved o–phthalaldehyde fluorometric method and high pressure liquid chromatography in the determination of brain 5–hydroxyindoles of rats treated with L–tryptophan and p–chlorophenyl–alanine. Br J Pharmacol 1981 Jun;73(2):555–61

Cuthbert AW, Wilson SA: Mechanisms for the effects of acetylcholine on sodium transport in frog skin. J Membr Biol 1981 Mar 15;59(1):65–75

Cvejic V, Mrsulja BB: Catecholamine turnover in rat cerebral cortex and caudate following repeated treatment with dihydroergotoxine. Gerontology 1981;27(1–2):7–12

D

Dacheux F: Ultrastructural localization of corticotropin, beta–lipotropin, and alpha– and beta–endorphin in the porcine anterior pituitary. Cell Tissue Res 1981;215(1):87–101

Dacheux F: Ultrastructural localization of gonadotropin–releasing hormone in the porcine gonadotropic cells. Cell Tissue Res 1981; 216(1):143–50

D'Agata R, Vicari E, Aliffi A, et al: Direct evidence in men for a role of endogenous oestrogens on gonadotrophin release. Acta Endocrinol (Copenh) 1981 Jun;97(2):145–9

D'Agostino J, Henning SJ: Hormonal control of postnatal development of corticosteroid–binding globulin. Am J Physiol 1981 Apr; 240(4):E402–6

Dahl LE, Dencker SJ, Lundin L: A double–blind study of dothiepin hydrochloride (Prothiaden) and amitriptyline in out–patients with masked depression. J Int Med Res 1981;9(2):103–7

Dale SL, Holbrook MM, Melby JC: 19–Nor–deoxycorticosterone in the neutral fraction of human urine. Steroids 1981 Jan;37(1):103–9

Dalkin AC, Bourne GA, Pieper DR, et al: Pituitary and gonadal gonadotropin–releasing hormone receptors during sexual maturation in the rat. Endocrinology 1981 May;108(5):1658–64

Dalsass M, Kiser S, Mendershausen M, et al: Medial prefrontal cortical projections to the region of the dorsal periventricular catecholamine system. Neuroscience 1981;6(4):657–65

Dalterio S, Bartke A, Harper MJ, et al: Effects of cannabinoids and female exposure on the pituitary–testicular axis in mice: possible involvement of prostaglandins. Biol Reprod 1981 Mar;24(2):315–22

Dalterio S, Bartke A, Mayfield D: Delta9–tetrahydrocannabinol increase plasma testosterone concentrations in mice. Science 1981 Jul 31; 213(4507):581–3

Dalterio SL, Michael SD, Macmillan BT, et al: Differential effects of cannabinoid exposure and stress on plasma prolactin, growth hormone and corticosterone levels in male mice. Life Sci 1981 Feb 16;28(7):761–6

Dan T, Gemba M: Inhibitory action of calcium antagonists on ATP–dependent calcium uptake by the renal cortical microsomes. Jpn J Pharmacol 1980 Dec;30(6):913–7

Danesino C, Gimelli G, Cuoco C, et al: Triplex gene dosage effect of beta–glucuronidase and possible assignment to band q22 in a partial duplication 7q. Hum Genet 1981;56(3):371–3

Danner SA, Endert E, Koster RW, et al: Biochemical and circulatory parameters during purely mental stress. Acta Med Scand 1981; 209(4):305–8

Daoud A, Khila M, Cherif A, et al: La dopamine dans le traitement des états de choc septique. Tunis Med 1981 Jan–Feb;59(1):848–51 (Eng. Abstr.) (Fre)

Darragh A, Lambe R, Scully M, et al: Investigation in man of the efficacy of a benzodiazepine antagonist, Ro 15–1788. Lancet 1981 Jul 4; 2(8236):8–10

Davidovich DA: Sluchai otravleniia mellerilom. Sud Med Ekspert 1981 Apr–Jun;24(2):58 (Rus)

Davidson J, Linnoila M, Raft D, et al: MAO inhibition and control of anxiety following amitriptyline therapy. A pilot study. Acta Psychiatr Scand 1981 Feb;63(2):147–52

Davis A, Madras B, Seeman P: Solubilization of neuroleptic/dopamine receptors of human brain striatum. Eur J Pharmacol 1981 Mar 26; 70(3):321–9

Davis AJ: An obligation to treat vs. a right to refuse. Am J Nurs 1981 Jul;81(7):1370

Davis R, Koelle GB: Electron microscope localization of acetylcholinesterase and butyrylcholinesterase in the superior cervical ganglion of the cat. II. Preganglionically denervated ganglion. J Cell Biol 1981 Mar;88(3):581–90

Davison TF, Flack IH: Changes in the peripheral blood leucocyte populations following an injection of corticotrophin in the immature chicken. Res Vet Sci 1981 Jan;30(1):79–82

Dawson R Jr, Lorden JF: Behavioral and neurochemical effects of neonatal administration of monosodium L–glutamate in mice. J Comp Physiol Psychol 1981 Feb;95(1):71–84

Dearing ME, Branch MN: Effects of chlorpromazine on food–maintained and observing behavior. Psychopharmacology (Berlin) 1981;73(3):281–5

de Basilico MZ, Castro G, Nusimovich B, et al: Glucagon action upon plasma post–heparin lipolytic and monoglyceride hydrolase activities. Studies involving administration of exogenous hormone during suppression of endogenous hormone secretion with somatostatin. Biomedicine 1980 Nov;33(7):213–6

Debus G, Janke W: Methods and methodological considerations in measuring anti–anxiety effects of tranquilizing drugs. Prog Neuropsychopharmacol 1980;4(4–5):391–404

de Cuyper HJ, van Praag HM, Mulder–Hajonides WR, et al: Pharmacokinetics of clomipramine in depressive patients. Psychiatry Res 1981 Apr;4(2):147–56

Dees WL, Sorensen AM Jr, Kemp WM, et al: Immunohistochemical localization of gonadotropin–releasing hormone (GnRH) in the brain and infundibulum of the sheep. Cell Tissue Res 1981;215(1):181–91

De Gaetani CF, Sannicola Botticelli C, Di Gregorio C, et al: Changes

AUTHOR SECTION

in pituitary LHRH incorporation during the rat estrous cycle, and in rats made anovulatory by various experimental procedures. J Endocrinol Invest 1981 Jan–Mar;4(1):59–63

DeGennaro M, Hymen R, Crannell AM, et al: Antidepressant drug therapy. Am J Nurs 1981 Jul;81(7):1304–10

de Gomez Dumm IN, de Alaniz MJ, Brenner RR: Effect of epinephrine and dibutyryl cyclic AMP on delta 5-desaturation activity of rat liver microsomes. Lipids 1980 Dec;15(12):1064–6

de Greef WJ, Plotsky PM, Neill JD: Dopamine levels in hypophysial stalk plasma and prolactin levels in peripheral plasma of the lactating rat: effects of a simulated suckling stimulus. Neuroendocrinology 1981 Apr;32(4):229–33

Dehlin O, Björnsson G, Lundström J: Zimelidine to geriatric patients: a pharmacokinetic and clinical study. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):410–24

Deiser R, Schindler R: Das Verlaufsbild langjähriger Behandlungen mit Fluphenazindekanoat (Dapotum D). Psychiatr Clin (Basel) 1980; 13(3–4):193–205 (Eng. Abstr.) **(Ger)**

de Jongh GD, van den Wildenberg HM, Nieuwenhuyse H, et al: The metabolism of mianserin in women, rabbits, and rats: identification of the major urinary metabolites. Drug Metab Dispos 1981 Jan–Feb; 9(1):48–53

de Kloet ER, Palkovits M, Mezey E: Opiocortin peptides: localization, source and avenues of transport. Pharmacol Ther 1981;12(2):321–51 (193 ref.)

de Koning J, Tijssen AM, van Dieten JA, et al: Comparison between the effects of LH-RH and raised K+ concentration on release of LH from pituitary glands of female rats in vitro. FEBS Lett 1981 Apr 20; 126(2):199–202

De la Torre JC: An improved approach to histofluorescence using the SPG method for tissue monoamines. J Neurosci Methods 1980 Oct; 3(1):1–5

del Castillo E, Rapoport AL, Bonetto R, et al: Glomerulopressin in dogs' mesenteric blood flow and prostaglandins. Horm Metab Res 1981 Feb; 13(2):126–7

d'Elia G, Hällström T, Nyström C, et al: Zimelidine vs maprotiline in depressed outpatients. A preliminary report. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):225–35

Delini-Stula A, Vassout A: The effects of antidepressants on aggressiveness induced by social deprivation in mice. Pharmacol Biochem Behav 1981; 14 Suppl 1:33–41

DeLisi LE, Wise CD, Bridge TP, et al: A probable neuroleptic effect on platelet monoamine oxidase in chronic schizophrenic patients. Psychiatry Res 1981 Feb;4(1):95–107

DeLisi LE, Neckers LM, Weinberger DR, et al: Increased whole blood serotonin concentrations in chronic schizophrenic patients. Arch Gen Psychiatry 1981 Jun;38(6):647–50

de Longraye J: Pondéral Retard. Soins 1981 Jan 20;26(2):45–6 **(Fre)**

DeLorenzo RJ, Burdette S, Holderness J: Benzodiazepine inhibition of the calcium–calmodulin protein kinase system in brain membrane. Science 1981 Jul 31;213(4507):546–9

DeLorenzo RJ: Role of calmodulin in neurotransmitter release and synaptic function. Ann NY Acad Sci 1980;356:92–109

del Pozo E, von Graffenried B, Brownell J, et al: Endocrine effect of a methionine–enkephalin derivative (FK 33–824) in man. Horm Res 1980;13(2):90–7

De Maio D, Sesso M, Levi Minzi A, et al: Evaluation of the clinical efficacy of single daily doses of antidepressants. Prog Neuropsychopharmacol 1980;4(6):607–12

Demarest KT, Moore KE: Disruption of 5-hydroxytryptaminergic neuronal function blocks the action of morphine on tuberoinfundibular dopaminergic neurons. Life Sci 1981 Mar 23;28(12):1345–51

Dembiec D, Cohen G: Potassium-induced release of [3H]catecholamine from brain: effects of pre-exposure to catecholamine uptake inhibitors. J Pharmacol Exp Ther 1981 Jun;217(3):727–32

de Melo AC, Perec CJ, Rubio MC: Acetylcholine-like activity in the fruit of the black nightshade (Solanaceae). Acta Physiol Lat Am 1978; 28(4–5):19–26

de Montigny C, Blier P, Caillé G, et al: Pre- and postsynaptic effects of zimelidine and norzimelidine on the serotoninergic system: single cell studies in the rat. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):79–90

DeMyer MK, Shea PA, Hendrie HC, et al: Plasma tryptophan and five other amino acids in depressed and normal subjects. Arch Gen Psychiatry 1981 Jun;38(6):642–6

Dencker SJ: The need for long-term neuroleptic treatment in schizophrenia. Acta Psychiatr Scand [Suppl] 1981;63(291):29–43

Dencker SJ, Enoksson P, Johansson R, et al: Late (4–8 years) outcome of treatment with megadoses of fluphenazine enanthate in drug-refractory schizophrenics. Acta Psychiatr Scand 1981 Jan; 63(1):1–12

De Nicola AF, Weisenberg LS, Arakelian MC, et al: Effects of bromocriptine on [3H]estradiol binding in cytosol of anterior pituitary. Endocrinology 1981 Jul;109(1):83–6

Deniker P: Principles of French pharmaco-clinical classification. Prog Neuropsychopharmacol 1980;4(4–5):455–68 (12 ref.)

Deniker P, Lôo H, Zarifian E, et al: Etude préliminaire en ouvert de l'amineptine sur le syndrome déficitaire des hébéphrènes et des toxicomanes au décours du sevrage. Encephale 1981;7(1):59–64 (Eng. Abstr.) **(Fre)**

Dent RR, Guilleminault C, Albert LH, et al: Diurnal rhythm of plasma immunoreactive beta-endorphin and its relationship to sleep stages and plasma rhythms of cortisol and prolactin. J Clin Endocrinol Metab 1981 May;52(5):942–7

Deri JJ, Williams PE, Steiner KE, et al: Altered ability of the liver to produce glucose following a period of glucagon deficiency. Diabetes 1981 Jun;30(6):490–5

Desarmenien M, Feltz P, Headley PM, et al: SL 75 102 as a gama-aminobutyric acid agonist: experiments on dorsal root ganglion neurones in vitro. Br J Pharmacol 1981 Feb;72(2):355–64

Descarries L, Bosler O, Berthelet F, et al: Innervation dopaminergique du néostriatum: nouvelle possibilité d'investigation radioautographique. J Physiol (Paris) 1981 Apr;77(1):53–61 (Eng. Abstr.) **(Fre)**

Dessi S, Porcu M, Andria C, et al: Cholesterol HDL in phenobarbital-treated male and female Wistar rats. Res Commun Chem Pathol Pharmacol 1981 Feb;31(2):375–8

Detera SD, Friedberg F: Sequence of the CNBr peptide containing the putative essential tyrosine of Bacillus amyloliquefaciens alpha amylase. Int J Pept Protein Res 1981 Jan;17(1):93–106

Deterre P, Paupardin-Tritsch D, Bockaert J, et al: Role of cyclic AMP in a serotonin-evoked slow inward current in snail neurones. Nature 1981 Apr 30;290(5809):783–5

Deutsch SI, Peselow ED, Banay-Schwartz M, et al: Effect of lithium on glycine levels in patients with affective disorders. Am J Psychiatry 1981 May;138(5):683–4

Deverina IS: Omekhanizme tormozheniia khlorgilinom i deprenilom okislitel'nogo dezaminirovaniia tiramina mitokhondrial'noi monoaminoksidazoi pecheni krys. Biokhimiia 1980 Oct;45(10):1897–908 (Eng. Abstr.) **(Rus)**

Devoino LV, Morozova NB: Nespetsificheskie kletki-supressory v ugnetaiushchem deistvii serotonina na immunogenez. Dokl Akad Nauk SSSR 1981;256(2):506–9 **(Rus)**

Dewey EA, Maylin GA, Ebel JG, et al: The metabolism of promazine and acetylpromazine in the horse. Drug Metab Dispos 1981 Jan–Feb; 9(1):30–6

Dewitz TS, McIntire LV, Martin RR, et al: Enzyme release and morphological changes in leukocytes induced by mechanical trauma. Blood Cells 1979 Aug;5(3):499–512

De Wolf MJ, Fridkin M, Kohn LD: Tryptophan residues of cholera toxin and its A and B protomers. Intrinsic fluorescence and solute quenching upon interacting with the ganglioside GM1, oligo-GM1, or dansylated oligo-GM1. J Biol Chem 1981 Jun 10;256(11):5489–96

De Wolf MJ, Fridkin M, Epstein M, et al: Structure-function studies of cholera toxin and its A and B protomers. Modification of tryptophan residues. J Biol Chem 1981 Jun 10;256(11):5481–8

Dextraze PG, Foreman J, Griffiths WC, et al: Comparison of an enzyme immunoassay and a high performance liquid chromatographic method for quantitation of quinidine in serum. Clin Toxicol 1981;18(3):291–7

Dey RD, Echt R, Dinerstein RJ: Morphology, histochemistry, and distribution of serotonin-containing cells in tracheal epithelium of adult rabbit. Anat Rec 1981 Jan;199(1):23–31

DiAugustine RP, Lazarus LH, Jahnke G, et al: Corticotropin/beta-endorphin immunoreactivity in rat mast cells. Peptide or protease? Life Sci 1980 Dec 22–29;27(25–26):2663–8

Diel F, Holz J, Bethge N: Failure of somatostatin and beta-endorphin to affect bovine adrenal cortex cells in vitro. Horm Metab Res 1981 Feb;13(2):95–8

Dierickx K, Goossens N, Vandesande F: The origin of somatostatin fibers in the median eminence and neural lobe of Rana temporaria. Cell Tissue Res 1981;215(1):41–5

Dieter P, Marmé D: Calmodulin-activated plant microsomal Ca2+ uptake and purification of plant NAD kinase and other proteins by calmodulin-Sepharose chromatography. Ann NY Acad Sci 1980; 356:371–3

Di Giorgio RM, Nicoletti F, Amico-Roxas M, et al: Influenza del sistema dopaminergico central sull'attività GABAerigica del cervelletto. Primi risultati. Acta Neurol (Napoli) 1981 Feb;36(1):302–4 (Eng. Abstr.) **(Ita)**

DiLella AG, Roe BA, Steggles AW: Alterations in rabbit liver protein synthesis as a result of phenobarbital treatment. Biochem Biophys Res Commun 1981 Feb 12;98(3):628–34

DiMaio J, Schiller PW: A cyclic enkephalin analog with high in vitro opiate activity. Proc Natl Acad Sci USA 1980 Dec;77(12):7162–6

Di Marcotullio A, Di Marcotullio ML, Pancrazio F, et al: Atrofia testicolare e attività gonadotropa in ratti con anastomosi porto-cava. Minerva Chir 1980 Oct 15;35(19):1449–54 (Eng. Abstr.) **(Ita)**

Ditirro FJ, Ho RH, Martin GF: Immunohistochemical localization of substance-P, somatostatin, and methionine-enkephalin in the spinal cord and dorsal root ganglia of the North American opossum, Didelphis virginiana. J Comp Neurol 1981 May 10;198(2):351–63

Divoll M, Greenblatt DJ: Plasma concentrations of temazepam, a 3-hydroxy benzodiazepine, determined by electron-capture gas-liquid chromatography. J Chromatogr 1981 Jan 2;222(1):125–8

Doell RG, Dallman MF, Clayton RB, et al: Dissociation of adrenal corticosteroid production from ACTH in water–restricted female rats. Am J Physiol 1981 Jul;241(1):R21–4

Dominguez AE, Fernández BE, Seeber AM: Effect of SQ 14225 and SQ 20881 on the norepinephrine contents of the central nervous system. Arch Int Physiol Biochim 1981 Feb;89(1):89–90

Donaldson IA, Hart IC, Heitzman RJ: Growth hormone, insulin, prolactin and total thyroxine in the plasma of sheep implanted with the anabolic steroid trenbolone acetate alone or with oestradiol. Res Vet Sci 1981 Jan;30(1):7–13

Doneen BA: Effects of hypophysectomy and corticosterone acetate treatment on hepatic lipid composition in the chick (Gallus domesticus) embryo. Gen Comp Endocrinol 1981 Mar;43(3):284–91

Donnelly MI, Cooper RA: Succinic semialdehyde dehydrogenases of Escherichia coli: their role in the degradation of p–hydroxyphenylacetate and gamma–aminobutyrate. Eur J Biochem 1981 Jan;113(3):555–61

Donovick PJ, Burright RG, Fanelli RJ, et al: Septal lesions and avoidance behavior: genetic, neurochemical and behavioral considerations. Physiol Behav 1981 Mar;26(3):495–507

Dore M, Atzori L: Influenza del fenobarbital sui livelli di glutatione e sulla attivita' della GSH–S–transferasi del fegato di ratto. Boll Soc Ital Biol Sper 1980 Nov 15;56(21):2213–7 (Eng. Abstr.) (Ita)

Dotson MJ, Chu SH, Hillman GR: Selective inhibition of schistosome acetylcholinesterase by dansylated acetylcholine analogs. Comp Biochem Physiol [C] 1981;68C(2):229–30

Downie JW, Larsson C: Prostaglandin involvement in contractions evoked in rabbit detrusor by field stimulation and by adenosine 5'–triphosphate. Can J Physiol Pharmacol 1981 Mar;59(3):253–60

Downing RW, Rickels K: Responders and nonresponders to chlordiazepoxide and placebo: a discriminant function analysis. Prog Neuropsychopharmacol 1980;4(4–5):405–15

Driscoll CM, McKinlay AF: Particle size effects in thermoluminescent lithium fluoride. Phys Med Biol 1981 Mar;26(2):321–7

Drouva SV, Epelbaum J, Hery M, et al: Ionic channels involved in the LHRH and SRIF release from rat mediobasal hypothalamus. Neuroendocrinology 1981 Mar;32(3):155–62

Drouva SV, Epelbaum J, Tapia–Arancibia L, et al: Opiate receptors modulate LHRH and SRIF release from mediobasal hypothalamic neurons. Neuroendocrinology 1981 Mar;32(3):163–7

Drucker H: Psychotrope et détention en hôpital psychiatrique pour causes politiques. Acta Med Leg Soc (Liege) 1980;30(1):189–210 (Fre)

Dudley MW, Butcher LL, Kammerer RC, et al: The actions of xylamine on central noradrenergic neurons. J Pharmacol Exp Ther 1981 Jun;217(3):834–40

Dudley RD Jr: In defense of 'Limbitrol' [letter] Minn Med 1980 Oct;63(10):713

Dugas M, Zarifian E, Leheuzey MF, et al: Preliminary observations of the significance of monitoring tricyclic antidepressant plasma levels in the pediatric patient. Ther Drug Monit 1980;2(4):307–14

Duhault J, Beregi L, Roman F: Substituted phenethylamines and anorexia. Prog Neuropsychopharmacol 1980;4(4–5):341–9

Al–Dujaili EA, Williams BC, Edwards CR: The development and application of a direct radioimmunoassay for corticosterone. Steroids 1981 Feb;37(2):157–76

Al–Dujaili EA, Hope J, Estivariz FE, et al: Circulating human pituitary pro–gamma–melanotropin enhances the adrenal response to ACTH. Nature 1981 May 14;291(5811):156–9

Dullaart J: Gonadotrophin release in vitro, in the presence and absence of luteinizing hormone releasing hormone, by pituitary glands from ovariectomized and sham–operated immature female rats of various ages. J Endocrinol 1981 Mar;88(3):375–9

Dumont P, Poupaert JH, De Laey P, et al: Anticonvulsant potency of two deuterated analogues of phenytoin: 'DPH–pd and DPH–d5'. J Pharm Belg 1981 Jan–Feb;36(1):21–6

Dun NJ, Karczmar AG: Evidence for a presynaptic inhibitory action of 5–hydroxytryptamine in a mammalian sympathetic ganglion. J Pharmacol Exp Ther 1981 Jun;217(3):714–8

Dunn DL, Scott BS, Dorsey ED: Analysis of pilocarpine and isopilocarpine in ophthalmic solutions by normal–phase high–performance liquid chromatography. J Pharm Sci 1981 Apr;70(4):446–9

Dunn RJ, Belagaje R, Brown EL, et al: The synthesis and cloning of two tyrosine suppressor tRNA genes with altered promoter sequences. J Biol Chem 1981 Jun 25;256(12):6109–18

Dunnette J, Weinshilboum R: Human plasma dopamine–beta–hydroxylase: oxygen and thermal stability. Experientia 1981 Feb 15;37(2):115–7

Dunzendorfer U: alpha–Difluoromethylornithine (alpha DFMO) and phenoxybenzamine hydrochloride in the treatment of chronic non–suppurative prostatitis. Arzneimittelforsch 1981;31(2):382–5

Dupont A, Di Paolo T, Gagné B, et al: Effects of chronic estrogen treatment on dopamine concentrations and turnover in discrete brain nuclei of ovariectomized rats. Neurosci Lett 1981 Feb 23;22(1):69–74

Dupouy JP: Differentiation of MSH–, ACTH–, endorphin–, and LPH–containing cells in the hypophysis during embryonic and fetal development. Int Rev Cytol 1980;68:197–249 (277 ref.)

Dupuy B, Angibeau R, Mendoza N, et al: Lithium effect on calcitonin secretion in the rat. Biomedicine 1980 Nov;33(7):207–8

Dutt JE: On the clinical response/serum level relationship for antidepressants I: Amitriptyline. Psychopharmacol Bull 1981 Apr;17(2):42–55

Dutt MK: Demonstration of DNA with an extra–sensitive Schiff's reagent and a Schiff–type dye–reagent, toluidine blue O–SO2. Microsc Acta 1981 May;84(3):239–43

Dyck LE: Methylphenidate–like stimulants in vitro release [3H]tyramines but not [14C]dopamine. Eur J Pharmacol 1981 Jan 29;69(3):371–4

Dymecki J, Walski M, Medyńska E: Ultrastructural and morphometric investigations on the mechanism of neurotransmitter release from synaptic vesicles. Acta Neuropathol [Suppl] (Berl) 1981;7:381–5

E

Eastwood R, Stiasny S, Tice S: Estimates of the prevalence of bipolar affective disorder. Methods based on treatment with lithium. Acta Psychiatr Scand 1981 Jan;63(1):83–90

Eberhard A, Burlingame AL, Eberhard C, et al: Structural identification of autoinducer of Photobacterium fischeri luciferase. Biochemistry 1981 Apr 28;20(9):2444–9

Ebersolt C, Perez M, Vassent G, et al: Characteristics of the beta 1–and beta 2–adrenergic–sensitive adenylate cyclases in glial cell primary cultures and their comparison with beta 2–adrenergic–sensitive adenylate cyclase of meningeal cells. Brain Res 1981 May 25;213(1):151–61

Ebersolt C, Perez M, Bockaert J: Neuronal, glial and meningeal localizations of neurotransmitter–sensitive adenylate cyclases in cerebral cortex of mice. Brain Res 1981 May 25;213(1):139–50

Ebner F: The inhibition by (+/-)–propranolol of the positive inotropic effects of (+/–)–isoprenaline and (-)–noradrenaline. Competitive antagonism and saturable uptake. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):96–107

Edelfors S: The effect of chronic lithium treatment on the sialic acid content in rat brain synaptosomes. Acta Pharmacol Toxicol (Copenh) 1981 Jan;48(1):61–4

Edwards AV, Furness PN, Helle KB: Adrenal medullary responses to stimulation of the splanchnic nerve in the conscious calf. J Physiol (Lond) 1980 Nov;308:15–27

Edwards DJ, Rizk M: Conversion of 3, 4–dihydroxyphenylalanine and deuterated 3, 4–dihydroxyphenylalanine to alcoholic metabolites of catecholamines in rat brain. J Neurochem 1981 May;36(5):1641–7

Edwards H, Olafsson O, Hyman AI, et al: Dobutamine in the rejecting transplanted heart. Crit Care Med 1981 Jun;9(6):498–9

Edwards JG, Alexander JR, Alexander MS, et al: Controlled trial of sulpiride in chronic schizophrenic patients. Br J Psychiatry 1980 Dec;137:522–9

Egrie JC, Nagle BW: Are the sea urchin mitotic Ca2+–ATPase and Ca2+–sequestering activities affected by calmodulin? Ann NY Acad Sci 1980;356:376–7

Ehlert FJ, Roeske WR, Braestrup C, et al: gamma–Aminobutyric acid regulation of the benzodiazepine receptor: biochemical evidence for pharmacologically different effects of benzodiazepines and propyl beta–carboline–3–carboxylate. Eur J Pharmacol 1981 Apr 9;70(4):593–5

Eichelman B: Drug regimens facilitating aggression: behavior, amine, and receptor alterations [proceedings] Psychopharmacol Bull 1981 Jan;17(1):58–60

Eipper BA, Mains RE: Structure and biosynthesis of pro–adrenocorticotropin/endorphin and related peptides. Endocr Rev 1980 Winter;1(1):1–27 (186 ref.)

Eipper BA, Mains RE: Further analysis of post–translational processing of beta–endorphin in rat intermediate pituitary. J Biol Chem 1981 Jun 10;256(11):5689–95

Eisenburger R, Hampel H, Hofrichter G, et al: Vergleichende pharmakologische Studie über d,l–Adrenalindipivalat–hydrochlorid und l–Adrenalinhydrochlorid nach lokaler und oraler Applikation. Arzneimittelforsch 1981;31(2):325–34 (Eng. Abstr.) (Ger)

Ekholm C, Hillensjö T, Isaksson O: Gonadotropin releasing hormone agonists stimulate oocyte meiosis and ovulation in hypophysectomized rats. Endocrinology 1981 May;108(5):2022–4

Elaev NR: Aktivatsiia Na,K–ATPazy mikrosom nervnykh kletok atsetilkholinom v model'noi sisteme. Biokhimiia 1980 Oct;45(10):1749–54 (Eng. Abstr.) (Rus)

Elaev NR: Noradrenalin kak reguliator sinteza RNK i Na, K–ATF–azy v nervnykh kletkakh. Probl Endokrinol (Mosk) 1981 Jan–Feb;27(1):58–62 (Eng. Abstr.) (Rus)

Eldefrawi ME, Eldefrawi AT, Aronstam RS, et al: [3H]Phencyclidine: a probe for the ionic channel of the nicotinic receptor. Proc Natl Acad Sci USA 1980 Dec;77(12):7458–62

Eliot RJ, Klein AH, Glatz TH, et al: Plasma norepinephrine, epinephrine, and dopamine concentrations in maternal and fetal sheep during spontaneous parturition and in premature sheep during cortisol–induced parturition. Endocrinology 1981 May;108(5):1678–82

AUTHOR SECTION

Elizur A, Segal Z, Yeret A, et al: Effect of propranolol treatment on serum prolactin level in schizophrenic patients.
Commun Psychopharmacol 1980;4(3):203–6

Elsass P, Mellerup ET, Rafaelsen OJ, et al: Effect of lithium on reaction time—a study of diurnal variations. Psychopharmacology (Berlin) 1981; 72(3):279–82

Emilsson A, Gudbjarnason S: Changes in fatty acyl chain composition of rat heart phospholipids induced by noradrenaline.
Biochim Biophys Acta 1981 Apr 23;664(1):82–8

Engberg G, Svensson TH: Mianserin: direct activation of brain norepinephrine neurons by blocking alpha 2–receptors.
Commun Psychopharmacol 1980;4(3):233–9

Engelberg–Kulka H, Dekel L, Israeli–Reches M: Regulation of the escherichia coli tryptophan operon by readthrough of UGA termination codons. Biochem Biophys Res Commun 1981 Feb 27;98(4):1008–15

Enger–Valk BE, van Rotterdam J, Pouwels PH: The construction of new vehicles for the cloning of transcription termination signals.
Nucleic Acids Res 1981 Apr 24;9(8):1973–89

Enna SJ: GABA receptor pharmacology. Functional considerations.
Biochem Pharmacol 1981 May 1;30(9):907–13

Ennis C, Cox B: GABA enhancement of [3H]dopamine release from slices of rat striatum: dependence on slice size. Eur J Pharmacol 1981 Mar 26;70(3):417–20

Epelbaum J, Drouva SV, Tapia–Arancibia L, et al: Interactions entre neuromédiateurs et neuropeptides impliqués dans le contrôle de la neurosécrétion hypothalamique in vitro. Ann Endocrinol (Paris) 1980 Nov–Dec;41(6):478–86 (35 ref.) (Eng. Abstr.) **(Fre)**

Ercan ZS, Türker RK: Alternation by histamine receptor agonists of the release of adrenergic transmitter in the isolated perfused rabbit kidney. Arch Int Pharmacodyn Ther 1981 Feb;249(2):203–12

Eroğlu L, Hizal A, Koyuncuoğlu H: The effect of long–term concurrent administration of chlorpromazine and lithium on the striatal and frontal cortical dopamine metabolism in rats. Psychopharmacology (Berlin) 1981;73(1):84–6

Ervin GN, Birkemo LS, Nemeroff CB, et al: Neurotensin blocks certain amphetamine–induced behaviours. Nature 1981 May 7;291(5810):73–6

Eskay RL, Furness JF, Long RT: Substance P activity in the bullfrog retina: localization and identification in several vertebrate species.
Science 1981 May 29;212(4498):1049–50

Esler M, Skews H, Leonard P, et al: Age–dependence of noradrenaline kinetics in normal subjects. Clin Sci 1981 Feb;60(2):217–9

Esposito R, Manzo M, Cocco F, et al: Utilizzazione della fenilalanina e tirosina nei linfociti di pazienti uremici. Minerva Nefrol 1980 Jul–Sep; 27(3):417–9 (Eng. Abstr.) **(Ita)**

Estanove S, du Grès B, Gressier M: Pharmacologie de la dopamine.
Ann Anesthesiol Fr 1981;22(1):75–83 (36 ref.) **(Fre)**

Ettenberg A, Koob GF, Bloom FE: Response artifact in the measurement of neuroleptic–induced anhedonia. Science 1981 Jul 17;209(4505):357–9

Etzold G, Büttner D, Welfle H: Determination of the N–terminal amino acids of ribosomal proteins after gel electrophoretical purification.
Acta Biol Med Ger 1980;39(11–12):1143–6

Evans BL, Knopp JA, Horton HR: Effect of hydroxynitrobenzylation of tryptophan–177 on reactivity of active site cysteine–25 in papain.
Arch Biochem Biophys 1981 Feb;206(2):362–71

Evans L, Moore G: The treatment of phobic anxiety by zimelidine.
Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):342–5

Evans RH, Watkins JC: Pharmacological antagonists of excitant amino acid action. Life Sci 1981 Mar 23;28(12):1303–8

Evemy KL, Cummins P, Littler WA: The effect of prolonged administration of propranolol and timolol on the growth and the heart of growing rabbits. Clin Sci 1981 Jan;60(1):33–40

F

Fabre LF, McLendon DM, Stephens AG: Comparison of the therapeutic effect, tolerance and safety of ketazolam and diazepam administered for six months to out–patients with chronic anxiety neurosis.
J Int Med Res 1981;9(3):191–8

Fadda F, Liguori G: Effect of stress and ACTH on dopamine metabolism in the nucleus accumbens and frontal cortex.
Boll Soc Ital Biol Sper 1981 Feb 28;57(4):454–8

Faingold CL, Stittsworth JD Jr: Phenytoin: plasma levels and behavioral changes associated with suppression of auditory evoked potentials in the cat. Neuropharmacology 1981 May;20(5):445–9

Famiglietti EV Jr, Vaughn JE: Golgi–impregnated amacrine cells and GABAergic retinal neurons: a comparison of dendritic, immunocytochemical and histochemical stratification in the inner plexiform layer of rat retina. J Comp Neurol 1981 Mar 20;197(1):129–39

Fan CC, Ho RJ: Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 1. Correlation of cyclic AMP levels and initial rates of lipolysis. Mol Cell Biochem 1981 Jan 20;34(1):35–41

Fan CC, Ho RJ: Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 2. Stability and restoration of activity of hormone–sensitive adenylate cyclase of adipocyte plasma membrane. Mol Cell Biochem 1981 Jan 20;34(1):43–50

Fan CC, Ho RJ: Response of white adipocyte of mouse and rabbit to catecholamines and ACTH. 3. Modified binding properties of beta–adrenoreceptor and its decreased coupling efficiency for adenylate cyclase. Mol Cell Biochem 1981 Jan 20;34(1):51–8

Fang VS, Shian LR: A serotonergic mechanism of the prolactin–stimulating action of metoclopramide. Endocrinology 1981 May;108(5):1622–7

Fanimo O, Tayo FM: Responses of the rat anococcygeus muscle to sympathomimetics. Gen Pharmacol 1981;12(3):205–8

Fanjul LF, Ruiz de Galarreta CM, Meites J: Interaction of morphine with the cholinergic system on prolactin release.
Proc Soc Exp Biol Med 1981 Apr;166(4):542–5

Farabollini F, di Prisco CL, Carli G: Neuroendocrine changes following habituation of animal hypnosis in male rabbits. Behav Brain Res 1981 May;2(3):363–72

Farese RV, Sabir MA, Larson RE: Kinetic aspects of cycloheximide–induced reversal of adrenocorticotropin effects on steroidogenesis and adrenal phospholipids in vivo.
Proc Natl Acad Sci USA 1980 Dec;77(12):7189–93

Fariello RG, Shug AL: Competitive inhibition by 3–aminopropanesulfonic acid and gamma–aminobutyric acid of carnitine transport in rat brain slices. Biochem Pharmacol 1981 May 1;30(9):1012–3

Farre ER, Cohen Y: Binding of noradrenaline to bovine serum albumin.
Int J Nucl Med Biol 1981;8(1):65–75

Faustman W, Fowler S, Walker C: Time course of chronic haloperidol and clozapine upon operant rate and duration. Eur J Pharmacol 1981 Mar 5;70(1):65–70

Favorova OO, Madoyan IA, Drutsa VL: 'Half–site' affinity modification of tryptophanyl–tRNA synthetase leads to 'freezing' of the free subunit.
FEBS Lett 1981 Jan 26;123(2):161–4

Feibel JH: Reduced catecholamine excretion at onset of brain death [letter] Lancet 1981 Apr 18;1(8225):890–1

Fekete J, del Castilho P, Kraak JC: Reversed–phase liquid chromatography for the separation of chloropromazine, imipramine and some of their metabolites. J Chromatogr 1981 Jan 16;204:319–27

Fekete M, Kádár T, Penke B, et al: Influence of cholecystokinin octapeptide sulfate ester on brain monoamine metabolism in rats.
J Neural Transm 1981;50(2–4):81–8

Felder W: Aspekte der Psychopharmakotherapie im Kindesalter.
Praxis 1981 Apr 21;70(17):752–6 **(Ger)**

Feldon J, Gray JA: The partial reinforcement extinction effect after treatment with chlordiazepoxide. Psychopharmacology (Berlin) 1981; 73(3):269–75

Ferguson HB, Pappas BA, Trites RL, et al: Plasma free and total tryptophan, blood serotonin, and the hyperactivity syndrome: no evidence for the serotonin deficiency hypothesis. Biol Psychiatry 1981 Mar;16(3):231–8

Ferland L, Marchetti B, Séguin C, et al: Dissociated changes of pituitary luteinizing hormone–releasing hormone (LHRH) receptors and responsiveness to the neurohormone induced by 17 beta–estradiol and LHRH in vivo in the rat. Endocrinology 1981 Jul;109(1):87–93

Fernandez LA, MacSween JM: Lithium and T cell colonies.
Scand J Haematol 1980 Nov;25(5):382–4

Fernstrom JD: Dietary precursors and brain neurotransmitter formation.
Annu Rev Med 1981;32:413–25 (49 ref.)

Fernstrom JD: Effects of precursors on brain neurotransmitter synthesis and brain functions. Diabetologia 1981 Mar;20 Suppl:281–9 (43 ref.)

Feste A, Gan JC: Selective loss of elastase inhibitory activity of alpha 1–proteinase inhibitor upon chemical modification of its tyrosyl residues.
J Biol Chem 1981 Jun 25;256(12):6374–80

Feuerstein G, Adelberg SA, Kopin IJ, et al: Cardiovascular and sympathetic responses to PGF2 alpha injection into hypothalamic nuclei. Brain Res Bull 1981 Mar;6(3):203–7

Feuerstein G, Kopin IJ: Effect of PGD2, PGE2 PGF2 alpha and PGI on blood pressure, heart rate and plasma catecholamine responses to spinal cord stimulation in the rat. Prostaglandins 1981 Feb;21(2):189–206

Feuerstein G, Yamaguchi I, Kopin IJ: Effect of GABA agonist and antagonists on cardiovascular and sympathetic responses in SHR and WKY rats. Clin Exp Hypertens 1981;3(2):207–18

Feurle GE, Wirth A, Diehm C, et al: Exercise–induced release of pancreatic polypeptide and its inhibition by propranolol: evidence for adrenergic stimulation. Eur J Clin Invest 1980 Jun;10(3):249–51

Fex J, Altschuler RA: Enkephalin–like immunoreactivity of olivocochlear nerve fibers in cochlea of guinea pig and cat.
Proc Natl Acad Sci USA 1981 Feb;78(2):1255–9

Fichtl B, Gerdsmeier W: Increased plasma protein binding of propranolol in rabbits with acute renal failure. Life Sci 1981 Jan 5;28(1):31–5

Fichtl B, Doering W: The digoxin–quinidine interaction: serum protein binding unlikely to be involved. Br J Clin Pharmacol 1981 Jan;11(1):94–6

Fier M: Agoraphobia: the 'what if' syndrome. J Med Soc NJ 1981 Apr; 78(4):286–8

Fleve RR: The lithium clinic for treatment and prevention of manic depression: a cost benefit approach. Egypt J Psychiatry 1979 Oct; 2(2):166–90

File SE: Rapid development of tolerance to the sedative effects of lorazepam and triazolam in rats. Psychopharmacology (Berlin) 1981;

73(3):240–5

Filibeck U, Castellano C, Oliverio A: Cross-tolerance between D-amino acids and morphine in mice. Brain Res 1981 May 11;212(1):227–9

Fillenz M, Stanford SC: Vesicular noradrenaline stores in peripheral nerves of the rat and their modification by tranylcypromine.
Br J Pharmacol 1981 Jun;73(2):401–4

Findley WE: The antigonadotropic activity of Lithospermum ruderale. II. The inhibition of LRF-induced gonadotropin release in vitro.
Contraception 1981 Feb;23(2):157–62

Fink M: An objective classification of psychoactive drugs.
Prog Neuropsychopharmacol 1980;4(4–5):495–502

Fink M: Convulsive and drug therapies of depression.
Annu Rev Med 1981;32:405–12 (71 ref.)

Fink M, Irwin P: EEG and behavioral effects of pirenzepine in normal volunteers. Scand J Gastroenterol [Suppl] 1980;15(66):39–46

Firestone P, Kelly MJ, Goodman JT, et al: Differential effects of parent training and stimulant medication with hyperactives: A progress report.
J Am Acad Child Psychiatry 1981 Winter;20(1):135–47

Fischer-Cornelssen KA: Methods of multicenter trials in psychiatry. Part I: Review. Prog Neuropsychopharmacol 1980;4(6):545–60

Fischman MW, Schuster CR: Acute tolerance to cocaine in humans.
Natl Inst Drug Abuse Res Monogr Ser 1980;(34):241–2

Fisher A, Abraham S, Lachman C, et al: Does rigidity in structure of muscarinic agonists and antagonists reflect drug specificity?
Monogr Neural Sci 1980;7:41–54

Fisher S, Maxsbridge B: Public judgments on the importance of valium information [proceedings] Psychopharmacol Bull 1981 Jan;17(1):134

Flach AJ, Peterson JS, Wood I, et al: Degeneration of nerve terminals in cats following systemic epinephrine: depletion of tissue norepinephrine correlated with ultrastructural changes.
Exp Eye Res 1981 Apr;32(4):389–94

Flatt PR, Gylfe E, Hellman B: Thulium binding to the pancreatic beta-cell membrane. Endocrinology 1981 Jun;108(6):2258–63

Fleckman A, Erlichman J, Schubart UK, et al: Effect of trifluoperazine, D600, and phenytoin on depolarization- and thyrotropin-releasing hormone-induced thyrotropin release from rat pituitary tissue.
Endocrinology 1981 Jun;108(6):2072–7

Fleming WJ: Recovery of brain and plasma cholinesterase activities in ducklings exposed to organophosphorus pesticides.
Arch Environ Contam Toxicol 1981;10(2):215–29

Fletcher SM, Hancock VS: Potential errors in benzoylecgonine and cocaine analysis. J Chromatogr 1981 Feb 6;206(1):193–5

Flint AP, Renfree MB: Bromocriptine-induced implantation during lactation in the rat. J Reprod Fertil 1981 May;62(1):181–3

Flint DJ, Clegg RA, Vernon RG: Prolactin and the regulation of adipose-tissue metabolism during lactation in rats.
Mol Cell Endocrinol 1981 May;22(2):265–75

Flora KP, Cradock JC, Davignon JP: Determination of delta 9-tetrahydrocannabinol in pharmaceutical vehicles by high-performance liquid chromatography. J Chromatogr 1981 Feb 6; 206(1):117–23

Fobes JL, Olds ME: Effects of neonatal 6-hydroxydopamine treatment on catecholamine levels and behavior during development and adulthood. Psychopharmacology (Berlin) 1981;73(1):27–30

Fonnum F, Storm-Mathisen J, Divac I: Biochemical evidence for glutamate as neurotransmitter in corticostriatal and corticothalamic fibres in rat brain. Neuroscience 1981;6(5):863–73

Forman LJ, Sonntag WE, Miki N, et al: Maintenance by L-DOPA treatment of estrous cycles and LH response to estrogen in aging female rats. Exp Aging Res 1980 Dec;6(6):547–54

Forman LJ, Just JJ: Cellular quantitation of hemoglobin transition during natural and thyroid-hormone-induced metamorphosis of the bullfrog, Rana catesbeiana. Gen Comp Endocrinol 1981 May;44(1):1–12

Foster DO, Depocas F, Frydman ML: Noradrenaline-induced calorigenesis in warm- and cold-acclimated rats: relations between concentration of noradrenaline in arterial plasma, blood flow to differently located masses of brown adipose tissue, and calorigenic response.
Can J Physiol Pharmacol 1980 Aug;58(8):915–24

Foster DO, Depocas F: Evidence against noradrenergic regulation of vasodilation in rat brown adipose tissue. Can J Physiol Pharmacol 1980 Dec;58(12):1418–25

Foster SD: Dopamine in pediatric therapy. MCN 1981 Jul–Aug;6(4):279

Frances A, Brown RP, Kocsis JH, et al: Psychotic depression: a separate entity? Am J Psychiatry 1981 Jun;138(6):831–3

Franchimont P: Les cybernines intragonadiques.
J Gynecol Obstet Biol Reprod (Paris) 1980;9(8):825–34 (Eng. Abstr.) **(Fre)**

Fraser HM, Clarke IJ, McNeilly AS: Effect of oestrogen and an LH-RH agonist on the release of gonadotrophins in ovariectomized ewes deprived of LH-RH. J Reprod Fertil 1981 May;62(1):131–40

Fraser J, Nadeau J, Robertson D, et al: Regulation of human leukocyte beta receptors by endogenous catecholamines: relationship of leukocyte beta receptor density to the cardiac sensitivity to isoproterenol.
J Clin Invest 1981 Jun;67(6):1777–84

Fredricsson B, Carlström K, Björk G, et al: Effects of prolactin and bromocriptine on the luteal phase in infertile women.
Eur J Obstet Gynaecol Reprod Biol 1981 Apr;11(5):319–33

Freedman DX, Belendiuk K, Belendiuk GW, et al: Blood tryptophan metabolism in chronic schizophrenics. Arch Gen Psychiatry 1981 Jun; 38(6):655–9

Freeman RW, Harbison RD: Hepatic periportal necrosis induced by chronic administration of cocaine. Biochem Pharmacol 1981 Apr 1; 30(7):777–83

Freund D, Freund JL, Kahlau F: Zur Frage der Wirkung von Imipramin auf das Blutbild, den Glukosespiegel und die Aktivität der alkalischen Leukozyten-Phosphatase nichtemotiver Wistar-Ratten und Tiere des Inzuchtstammes TMB (Tryon-Maze-Bright). Arzneimittelforsch 1981; 31(3):425–8 (Eng. Abstr.) **(Ger)**

Freund LG: Severe meprobamate intoxication treated by hemoperfusion over amberlite resin. Artif Organs 1981 Feb;5(1):80–1

Friebele E, Shimoyama A, Hare PE, et al: Adsorption of amino acid entantiomers by Na-montmorillonite. Orig Life 1981 Mar–Jun; 11(1–2):173–84

Fried G, Thureson-Klein A, Lagercrantz H: Noradrenaline content correlated to matrix density in small noradrenergic vesicles from rat seminal ducts. Neuroscience 1981;6(4):787–800

Friedhoff AJ, Miller JC: Nongenetic factors affecting human platelet monoamine oxidase [proceedings] Psychopharmacol Bull 1981 Jan; 17(1):101–3

Friedman PA, Figueiredo JF, Maack T, et al: Sodium-calcium interactions in the renal proximal convoluted tubule of the rabbit.
Am J Physiol 1981 Jun;240(6):F558–68

Fritsch WP, Schacht U, Scholten T, et al: Effects of cimetidine and pirenzepine on peroperative electrical vagal stimulation of gastric acid secretion. Scand J Gastroenterol [Suppl] 1980;15(66):95–100

Frohlich J, Pudek MR, Cormode EJ, et al: Further studies on plasma proteins, lipids, and dye- and drug-binding in a child with analbuminemia. Clin Chem 1981 Jul;27(7):1213–6

Frolkis VV, Shevchuk VG, Golovchenko SF, et al: The effect of hormones on the haemodynamics in animals of different age groups.
Exp Gerontol 1981;16(1):1–12

Froscio M, Guy GR, Murray AW: Calmodulin inhibitors modify cell surface changes triggered by a tumor promoter.
Biochem Biophys Res Commun 1981 Feb 12;98(3):829–35

Frowein HW: Selective effects of barbiturate and amphetamine on information processing and response execution. Acta Psychol (Amst) 1981 Feb;47(2):105–15

Frumkes TE, Miller RF, Slaughter M, et al: Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. III. Amacrine-mediated inhibitory influences on ganglion cell receptive-field organization: a model. J Neurophysiol 1981 Apr;45(4):783–804

Fry BW, Ciarlone AE: Effects of phenytoin on mouse cerebellar 5-hydroxytryptamine and norepinephrine. Neuropharmacology 1981 Jun;20(6):623–5

Fujii S, Akasaka K, Hatano H: Proton magnetic resonance study of Streptomyces subtilisin inhibitor. pH titration and assignments of individual tyrosyl resonances. Biochemistry 1981 Feb 3;20(3):518–23

Fujimoto D, Horiuchi K, Hirama M: Isotrityrosine, a new crosslinking amino acid isolated from Ascaris cuticle collagen.
Biochem Biophys Res Commun 1981 Mar 31;99(2):637–43

Fujimoto M, Okabayashi T: Effect of picrotoxin on benzodiazepine receptors and GABA receptors with reference to the effect of Cl-ion. Life Sci 1981 Feb 23;28(8):895–901

Fujita Y, Anzai M, Inui M, et al: Utilization of N-acetyl-L-tryptophan given intravenously to unrestrained adult rats.
J Nutr Sci Vitaminol (Tokyo) 1980;26(4):381–8

Fuller RW, Hemrick-Luecke SK: Elevation of epinephrine concentration in rat brain by LY51641, a selective inhibitor of type A monoamine oxidase. Res Commun Chem Pathol Pharmacol 1981 May;32(2):207–21

Fundarò A, Cassone MC: Azione degli olii essenziali di camomilla, cannella, assenzio, magis e origano su un comportamento operativo nel ratto. Boll Soc Ital Biol Sper 1980 Nov 30;56(22):2375–80 (Eng. Abstr.) **(Ita)**

Fundarò A, Cassone MC: Sull'associazione di cloropromazina e olio essenziale di assenzio e macis su un comportamento operativo nel ratto.
Boll Soc Ital Biol Sper 1980 Nov 30;56(22):2370–4 (Eng. Abstr.) **(Ita)**

G

Gabrielian ES, Matevosian RSh, Amroian EA: Izmeneniia morfofunktsional'nogo sostoianiia kapilliarnoi sistemy kory golovnogo mozga koshek pod vliianiem adrenergicheskikh vozdeistvii v usloviiakh tormozheniia biosinteza prostaglandinov. Biull Eksp Biol Med 1981 Feb; 91(2):173–5 (Eng. Abstr.) **(Rus)**

Gabryelewicz A, Prokopowicz J, Hnidec O, et al: The effect of somatostatin on haemostasis in dogs. Folia Haematol (Leipz) 1981;108(1):125–31

Gale K: Relationship between the presence of dopaminergic neurons and GABA receptors in substantia nigra: effects of lesions. Brain Res 1981 Apr 6;210(1–2):401–6

AUTHOR SECTION

Gall C, Brecha N, Karten HJ, et al: Localization of enkephalin-like immunoreactivity to identified axonal and neuronal populations of the rat hippocampus. J Comp Neurol 1981 May 10;198(2):335-50

Gallagher JP, Inokuchi H, Nakamura J, et al: Effects of anticonvulsants on excitability and GABA sensitivity of cat dorsal root ganglion cells. Neuropharmacology 1981 May;20(5):427-33

Gallo RV: Effect of electrical stimulation of the dorsomedial hypothalamic nucleus on pulsatile LH release in ovariectomized rats. Neuroendocrinology 1981 Mar;32(3):134-8

Gallo RV: Further studies on dopamine-induced suppression of pulsatile LH release in ovariectomized rats. Neuroendocrinology 1981 Mar; 32(3):187-92

Galster AD, Clutter WE, Cryer PE, et al: Epinephrine plasma thresholds for lipolytic effects in man: measurements of fatty acid transport with [l-13C]palmitic acid. J Clin Invest 1981 Jun;67(6):1729-38

Galzigna L, Manani G, Bianchi M, et al: Some experimental effects with trazodone. Agressologie 1979;20(4):211-6

Gamse R, Wax A, Zigmond RE, et al: Immunoreactive substance P in sympathetic ganglia: distribution and sensitivity towards capsaicin. Neuroscience 1981;6(3):437-41

Ganguly P, Fossett NG: Induction of serotonin secretion by cross-linking of surface receptors of a derivative of wheat germ agglutinin on human platelets. Biochem Biophys Res Commun 1981 Mar 16;99(1):176-82

Gapparov MM, Liapkov BG: Metabolizm lipidperenosiashchikh belkov pecheni krys v norme i pri vvedenii fenobarbitala. Biokhimiia 1980 Oct; 45(10):1744-8 (Eng. Abstr.) **(Rus)**

Gard TG, Bernstein B, Larsen PR: Studies on the mechanism of 3,5,3'-triiodothyronine-induced suppression of secretagogue-induced thyrotropin release in vitro. Endocrinology 1981 Jun;108(6):2046-53

Gardey-Levassort C, Richard MO, de Lauture D, et al: I. Catecholamines in developing rat lung. Life Sci 1981 Jan 26;28(4):331-7

Garg LC, Knepper MA, Burg MB: Mineralocorticoid effects on Na-K-ATPase in individual nephron segments. Am J Physiol 1981 Jun; 240(6):F536-44

Garson A Jr, Gillette PC, McNamara DG: Propranolol: the preferred palliation for tetralogy of Fallot. Am J Cardiol 1981 May;47(5):1098-104

Garverick HA, Elmore RG, Vaillancourt DH, et al: Ovarian response to gonadotropin-releasing hormone in postpartum dairy cows. Am J Vet Res 1980 Oct;41(10):1582-5

Garzarelli S, Cattaneo A, Nicorelli G, et al: Significato clinico della prolattina nelle amenorree. Minerva Ginecol 1981 Apr;33(4):315-20 (Eng. Abstr.) **(Ita)**

Gasson JC: Forms and activity of high molecular weight adrenocorticotropin in guinea pig. Peptides (Fayetteville) 1980 Fall; 1(3):223-9

Gastpar M: Therapie der Depressionen mit Psychopharmaka. Praxis 1981 Feb 3;70(6):215-9 (Eng. Abstr.) **(Ger)**

Gauron EF, Rowley VN: Critical periods for diphenylhydantoin and phenobarbital administration during gestation. Psychol Rep 1980 Dec; 47(3 Pt 2):1163-6

Gauthier P: Pressor responses and adrenomedullary catecholamine release during brain stimulation in the rat. Can J Physiol Pharmacol 1981 May; 59(5):485-92

Gavin M, Blair S: Modification of the macaque's vestibulo-ocular reflex by picrotoxin. Arch Otolaryngol 1981 Jun;107(6):372-6

Gavish M, Snyder SH: gamma-Aminobutyric acid and benzodiazepine receptors: copurification and characterization. Proc Natl Acad Sci USA 1981 Mar;78(3):1939-42

Gawel MJ, Glover V, Burkitt M, et al: The specific activity of platelet monoamine oxidase varies with platelet count during severe exercise and noradrenaline infusion. Psychopharmacology (Berlin) 1981; 72(3):275-7

Geisler CD: A model for discharge patterns of primary auditory-nerve fibers. Brain Res 1981 May 11;212(1):198-201

Geister R, Seifert R, Zorn E: Beurteilung der psychischen Belastung von Seelotsen mittels Urinkatecholaminuntersuchungen. Zentralbl Arbeitsmed Arbeitsschutz Prophyl Ergonomie 1980 Dec; 30(12):458-63 **(Ger)**

Genot G, Morfin R, Peyraud C: Blood-brain barrier for serotonin in the eel (Anguilla anguilla L.). Comp Biochem Physiol [C] 1981; 68C(2):247-50

Gentleman S, Parenti M, Commissiong JW, et al: Dopamine-activated adenylate cyclase of spinal cord: supersensitivity following transection of the cord. Brain Res 1981 Apr 6;210(1-2):271-5

George JR, Fitzgerald JW: Stimulation of bacterial arylsulfatase activity by arylamines: evidence for substrate activation. J Bacteriol 1981 Jul; 147(1):69-74

Georgotas A, Mann J, Bush D, et al: Safety data on zimelidine hydrochloride following an overdose. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):257-61

Georgotas A, Gerbino L, Jordan B, et al: A double-blind comparison of trebenzomine and thioridazine in the treatment of schizophrenia. Psychopharmacology (Berlin) 1981;73(3):292-4

Gerardi AU, Miletti S, Miele G: Influenza di alcune sostanze farmacologiche nella sensazione algogena postoperatoria. Minerva Anestesiol 1980 May;46(5):531-40 (Eng. Abstr.) **(Ita)**

Gerber PP, Trimble ER, Wollheim CB, et al: Effect of insulin on glucose- and arginine-stimulated somatostatin secretion from the isolated perfused rat pancreas. Endocrinology 1981 Jul;109(1):279-83

Germain R, Paul B: Traitement symptomatique de l'ichtyosarcotoxisme par l'association dexaméthasone, cobalamine et tiapride. Med Trop (Mars) 1981 Mar-Apr;41(2):173-9 (Eng. Abstr.) **(Fre)**

Gershengorn MC, Hoffstein ST, Rebecchi MJ, et al: Thyrotropin-releasing hormone stimulation of prolactin release from clonal rat pituitary cells: evidence for action independent of extracellular calcium. J Clin Invest 1981 Jun;67(6):1769-76

Ghoneim MM, Korttila K, Chiang CK, et al: Diazepam effects and kinetics in Caucasians and Orientals. Clin Pharmacol Ther 1981 Jun;29(6):749-56

Ghoneim MM, Mewaldt SP, Berie JL, et al: Memory and performance effects of single and 3-week administration of diazepam. Psychopharmacology (Berlin) 1981;73(2):147-51

Giagnoni G, Santagostino A, Grassi A, et al: Role of adrenergic blocking agents and glucocorticoids on the regulation of pituitary opioid peptides levels. Arch Int Pharmacodyn Ther 1980 Dec;248(2):272-9

Giampietro O, Ferdeghini M, Petrini M: Severe leukopenia and mild thrombocytopenia after chronic bromocriptine (CB-154) administration. Am J Med Sci 1981 May-Jun;281(3):169-72

Giannattasio G, De Ferrari ME, Spada A: Dopamine-inhibited adenylate cyclase in female rat adenohypophysis. Life Sci 1981 Apr 6; 28(14):1605-12

Gibson MJ, Krieger DT: Circadian corticosterone rhythm and stress response in rats with adrenal autotransplants. Am J Physiol 1981 Apr; 240(4):E363-6

Gill SK, Guraya SS: Effects of low doses of alpha-chlorohydrin on phosphatases, beta-glucosidase, beta-glucuronidase & hyaluronidase of rat testis & epididymis. Indian J Exp Biol 1980 Nov;18(11):1351-2

Gillis JS, Lipkin JO, Moran TJ: Drug therapy decisions. A social judgment analysis. J Nerv Ment Dis 1981 Jul;169(7):439-47

Gilmour RF Jr, Zipes DP: Electrophysiological characteristics of rodent myocardium damaged by adrenaline. Cardiovasc Res 1980 Oct; 14(10):582-9

Giompres PE, Zimmermann H, Whittaker VP: Changes in the biochemical and biophysical parameters of cholinergic synaptic vesicles on transmitter release and during a subsequent period of rest. Neuroscience 1981;6(4):775-85

Giussi GA, Ballejo G, Bustos R, et al: Effects of bromocriptine administration to pregnant rabbits upon fetal lung maturation. Pediatr Res 1981 May;15(5):850-2

Glasscock GF, Nicoll CS: Hormonal control of growth in the infant rat. Endocrinology 1981 Jul;109(1):176-84

Glatthaar C, Donald RA, Smith R, et al: Pituitary function in normoprolactinaemic infertile men receiving bromocriptine. Clin Endocrinol (Oxf) 1980 Nov;13(5):455-9

Glazer EJ, Basbaum AI: Immunohistochemical localization of leucine-enkephalin in the spinal cord of the cat: enkephalin-containing marginal neurons and pain modulation. J Comp Neurol 1981 Mar 1; 196(3):377-89

Glennon RA, Doot DL, Young R: DOM and related 2,5-dimethoxy-4-alkylphenylisopropylamines: behavioral and serotonin receptor properties. Pharmacol Biochem Behav 1981 Mar;14(3):287-92

Glover WE: Cholinergic effect of 4-aminopyridine and adrenergic effect of 4-methyl-2-aminopyridine in cardiac muscle. Eur J Pharmacol 1981 Apr 24;71(1):21-31

Gnegy M, Treisman G: Effect of calmodulin on dopamine-sensitive adenylate cyclase activity in rat striatal membranes. Mol Pharmacol 1981 Mar;19(2):256-63

Gnegy ME, Lau YS, Treisman G: Role of calmodulin in states of altered catecholamine sensitivity. Ann NY Acad Sci 1980;356:304-18

Godbillon J, Gauron S: Determination of clomipramine or imipramine and their mono-demethylated metabolites in human blood or plasma by high-performance liquid chromatography. J Chromatogr 1981 Jan 16;204:303-11

Godfraind T, Dieu D: The inhibition by flunarizine of the norepinephrine-evoked contraction and calcium influx in rat aorta and mesenteric arteries. J Pharmacol Exp Ther 1981 May;217(2):510-5

Gold PW, Goodwin FK, Post RM, et al: Vasopressin function in depression and mania [proceedings] Psychopharmacol Bull 1981 Jan;17(1):7-9

Goldberg DM, Yu A, Roomi MW, et al: Effects of phenobarbital upon triacylglycerol metabolism in the guinea pig. Can J Biochem 1981 Jan; 59(1):48-53

Goldberg SR, Kelleher RT, Goldberg DM: Fixed-ratio responding under second-order schedules of food presentation or cocaine injection. J Pharmacol Exp·Ther 1981 Jul;218(1):271-81

Goldhamer P: Relapse in schizophrenia [letter] Arch Gen Psychiatry 1981 Jul;38(7):842-3

Goldman-Rakic PS, Brown RM: Regional changes of monoamines in cerebral cortex and subcortical structures of aging rhesus monkeys. Neuroscience 1981;6(2):177-87

Goldstein A: Dynorphin. Nathan B. Eddy memorial award lecture. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):1-10

Goldstein DS, Harris AH, Izzo JL Jr, et al: Plasma catecholamines and renin during operant blood pressure conditioning in baboons.

Physiol Behav 1981 Jan;26(1):33-7

Goldstein RE, Corash LC, Tallman JF Jr, et al: Shortened platelet survival time and enhanced heart rate responses after abrupt withdrawal of propranolol from normal subjects. Am J Cardiol 1981 May; 47(5):1115-22

Golikov PP: Soderzhanie gliukokortikoidnykh retseptorov v tsitoplazme leikotsitov perifericheskoi krovi cheloveka. Probl Gematol Pereliv Krovi 1981 Feb;26(2):22-5 (Eng. Abstr.) (Rus)

Golub MS, Sassenrath EN, Chapman LF: Mother-infant interaction in rhesus monkeys treated clinically with delta-9-tetrahydrocannabinol. Child Dev 1981 Mar;52(1):389-92

González ER: New studies confirm MAO inhibitors' efficacy in treating severe anxiety [news] JAMA 1981 May 8;245(18):1799-801

Gonzalez FJ, Kasper CB: Sequential translocation of two phenobarbital-induced polysomal messenger ribonucleic acids from the nuclear envelope to the endoplasmic reticulum. Biochemistry 1981 Apr 14;20(8):2292-8

Good MI: Pseudodementia and physical findings masking significant psychopathology. Am J Psychiatry 1981 Jun;138(6):811-4

Goodman HM: Separation of early and late responses of adipose tissue to growth hormone. Endocrinology 1981 Jul;109(1):120-9

Gorde JM, Bert J, Gambarelli D, et al: Apomorphine-induced circling behaviour in hamsters following unilateral injection of scrapie gent in the striatum. Neurosci Lett 1981 Mar 10;22(2):201-4

Gordon CJ, Heath JE: Effect of monoamines on firing rate and thermal sensitivity of neurons in the preoptic area of awake rabbits. Exp Neurol 1981 May;72(2):352-65

Gorewit RC: Effect of apomorphine hydrochloride administration on serum concentrations of prolactin and growth hormone in cattle. Experientia 1981 Feb 15;37(2):204-6

Górski A, Iskierko J: Porównawcza analiza bialek pszenicy, żyta i dwóch odmian pszenżyta T275 i T294. III. Zawartość tryptofanu i tyrozyny w gliadynach i gluteninach oraz N-końcowe aminokwasy frakcji gliadynowej. Ann Univ Mariae Curie Sklodowska [Med] 1979;34:311-6 (Eng. Abstr.) (Pol)

Göthert M, Nolte J, Weinheimer G: Preferential blockade of postsynaptic alpha-adrenoceptors by BE 2254. Eur J Pharmacol 1981 Mar 5; 70(1):35-42

Göthert M: Serotonin-receptor-mediated modulation of Ca2+-dependent 5-hydroxytryptamine release from neurones of the rat brain cortex. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):223-30

Goto M, Inomata N, Ono H, et al: Changes of electroretinogram and neurochemical aspects of GABAergic neurons of retina after intraocular injection of kainic acid in rats. Brain Res 1981 May 4;211(2):305-14

Gottesfeld Z, Fuller GN, Wiggins RC: Adrenergic neuroplasticity is maintained in the nutritional rehabilitated adult rat. Experientia 1981 Feb 15;37(2):168-9

Gottfries CG: Influence of depression and antidepressants on weight. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):353-6

Gottfries I, Rüdeberg K: The role of neuroleptics in an integrated treatment program for chronic schizophrenics. Acta Psychiatr Scand [Suppl] 1981; 63(291):44-55

Goubern M, Portet R: Circadian rhythm and hormonal sensitivity of lipoprotein lipase activity in cold acclimated rats. Horm Metab Res 1981 Feb;13(2):73-7

Govoni S, Yang HY: Sex differences in the content of beta-endorphin and enkephalin-like peptides in the pituitary of obese (ob/ob) mice. J Neurochem 1981 May;36(5):1829-33

Grabner P, Donahue PE, Torma Grabner E, et al: The lack of effect of propranolol on the intestinal phase secretion in the dog. Scand J Gastroenterol 1981;16(1):65-70

Graybiel AM, Ragsdale CW Jr, Yoneoka ES, et al: An immunohistochemical study of enkephalins and other neuropeptides in the striatum of the cat with evidence that the opiate peptides are arranged to form mosaic patterns in register with the striosomal compartments visible by acetylcholinesterase staining. Neuroscience 1981;6(3):377-97

Greenberg R, O'Keefe EH, Antonaccio MJ: The effect of captopril and ascorbic acid on nonenzymatic methionine enkephalin inactivation in the guinea-pig ileum. J Pharmacol Exp Ther 1981 Jun;217(3):750-6

Greenberg S, Curro F, Palmer GC, et al: Possible involvement of cyclic AMP and frontal cortex in amitriptyline mediated suppression of the hypotensive effect of clonidine. Life Sci 1980 Dec 22-29; 27(25-26):2669-74

Greenblatt DJ, Laughren TP, Allen MD, et al: Plasma diazepam and desmethyldiazepam concentrations during long-term diazepam therapy. Br J Clin Pharmacol 1981 Jan;11(1):35-40

Greenhill LL, Puig-Antich J, Chambers W, et al: Growth hormone, prolactin, and growth responses in hyperkinetic males treated with d-amphetamine. J Am Acad Child Psychiatry 1981 Winter;20(1):84-103

Greiss KC, Fogari R: Double-blind clinical assessment of alprazolam, a new benzodiazepine derivative, in the treatment of moderate to severe anxiety. J Clin Pharmacol 1980 Nov-Dec;20(11-12):693-9

Griffiths EC, Webster VA: Thyrotrophin releasing hormone and its metabolites as modulators of CNS activity [letter] Lancet 1981 Apr 11;1(8224):834-5

Grill V, Rundfeldt M, Efendic S: Previous exposure to glucose enhances somatostatin secretion from the isolated perfused rat pancreas. Diabetologia 1981 Apr;20(4):495-500

Grinspoon L, Bakalar JB: Coca and cocaine as medicines: an historical review. J Ethnopharmacol 1981 Mar-May;3(2-3):149-59

Groh V, von Mayersbach H: Enzymatic and functional heterogeneity of lysosomes. Cell Tissue Res 1981;214(3):613-21

Grome JJ, McCulloch J: The effects of chloral hydrate anesthesia on the metabolic response in the substantia nigra to apomorphine. Brain Res 1981 Jun 9;214(1):223-8

Gross G: Neurochemie und klinische Psychiatrie. Fortschr Neurol Psychiatr 1981 Jan;49(1):34-42 (Eng. Abstr.) (Ger)

Gross G, Huber G, Schüttler R: Die Beeinflussung des Langzeitverlaufs schizophrener Krankheiten durch somatotherapeutische Massnahmen. Psychiatr Clin (Basel) 1980;13(3-4):179-92 (Eng. Abstr.) (Ger)

Grossman A, Delitala G, Yeo T, et al: GABA and muscimol inhibit the release of prolactin from dispersed rat anterior pituitary cells. Neuroendocrinology 1981 Mar;32(3):145-9

Grossman A, Yeo T, Delitala G, et al: Two new dopamine agonists that are long acting in vivo but short acting in vitro. Clin Endocrinol (Oxf) 1980 Dec;13(6):595-9

Groves JE: Current concepts in psychiatry: borderline personality disorder. N Engl J Med 1981 Jul 30;305(5):259-62

Grue CE, Powell GV, Gladson NL: Brain cholinesterase (ChE) activity in nestling starlings: implications for monitoring exposure of nestling songbirds to ChE inhibitors. Bull Environ Contam Toxicol 1981 Apr; 26(4):544-7

Gruetter CA, Kadowitz PJ, Ignarro LJ: Methylene blue inhibits coronary arterial relaxation and guanylate cyclase activation by nitroglycerin, sodium nitrite, and amyl nitrite. Can J Physiol Pharmacol 1981 Feb; 59(2):150-6

Gruetter CA, Ignarro LJ, Hyman AL, et al: Contractile effects of 5-hydroxytryptamine in isolated intrapulmonary arteries and veins. Can J Physiol Pharmacol 1981 Feb;59(2):157-62

Grünberger J, Saletu B: Determination of pharmacodynamics of psychotropic drugs by psychometric analysis. Prog Neuropsychopharmacol 1980;4(4-5):417-34

Gründig E, Birnbaumer E, Hawrylewicz A: Influence of phenothiazines or reserpine on the formation of 14C-glycine from U-14C-serine. Enzyme 1981;26(1):43-8

Gryglewski RJ: Evolution of ideas on the role of prostaglandins in inflammation. Agents Actions [Suppl] 1980;7:247-51 (24 ref.)

Guarneri P, Corda MG, Concas A, et al: Kainic acid-induced lesion of rat retina: differential effect on cyclic GMP and benzodiazepine and GABA receptors. Brain Res 1981 Mar 23;209(1):216-20

Guensberger E, Adamisová D, Kolibás E: Unsere Erfahrungen mit Rractivan bei Psychiatrischen Patienten. Agressologie 1980;21(A):63-5 (Eng. Abstr.) (Ger)

Guillemant J, Guillemant S: Effect of exogenous and endogenous ACTH on adrenocortical cyclic GMP in the rat. J Steroid Biochem 1981 Jun; 14(6):557-61

Güllner HG: Does substance P participate in water transport and excretion? Med Hypotheses 1981 Mar;7(3):311-4

Gumbiner B, Kelly RB: Secretory granules of an anterior pituitary cell line, AtT-20, contain only mature forms of corticotropin and beta-lipotropin. Proc Natl Acad Sci USA 1981 Jan;78(1):318-22

Gunsalus RP, Yanofsky C: Nucleotide sequence and expression of Escherichia coli trpR, the structural gene for the trp aporepressor. Proc Natl Acad Sci USA 1980 Dec;77(12):7117-21

Gupta RN, Bartolucci G, Molnar G: Analysis of chlorpromazine in plasma: effect of specimen storage. Clin Chim Acta 1981 Feb 5;109(3):351-4

Gurr JA, Potter VR: The significance of differences between fresh cell suspensions and fresh or maintained monolayers. Ann NY Acad Sci 1980;349:57-66

György L, Dóda M: Influence of the dopaminergic agonists bromocriptine, piribedil and nomifensine on the sympathetic neural transmission in the nictitating membrane of the cat. Arch Int Pharmacodyn Ther 1981 Jan; 249(1):4-11

H

Ha HR, Kewitz G, Wenk M, et al: Quinidine determination in serum: enzyme immunoassay (EIA) V HPLC [letter] Br J Clin Pharmacol 1981 Mar;11(3):312-4

Haak WJ, Reineke LM: Isolation and identification of gamma-aminobutyric acid in Streptomyces lincolnensis. Antimicrob Agents Chemother 1981 Mar;19(3):493

Haas HL, Ryall RW: Is excitation by enkephalins of hippocampal neurones in the rat due to presynaptic facilitation or to disinhibition? J Physiol (Lond) 1980 Nov;308:315-30

Haber S, Barchas PR, Barchas JD: A primate analogue of amphetamine-induced behaviors in humans. Biol Psychiatry 1981 Feb; 16(2):181-96

Habibi B, Cartron JP, Bretagne M, et al: Anti-nomifensine antibody

AUTHOR SECTION

causing immune hemolytic anemia and renal failure. Vox Sang 1981 Feb;40(2):79-84

Hadjiioloff AI, Kancheva LS, Martinova YS, et al: Autoradiographic study of catecholamine metabolism in amphibian dermis. Folia Morphol (Praha) 1981;29(1):56-8

Haglund U, Hellman A, Häggendal E, et al: Effects of adrenergic neuron and ganglion blockers on hemodynamics and plasma catecholamine levels after corticosteroids during hemorrhagic shock in the dog. Acta Anaesthesiol Scand 1980 Dec;24(6):444-50

Halaris AE, Stern W, Harto-Truax N: Clinical efficacy of the new antidepressant bupropion (Wellbutrin) [proceedings] Psychopharmacol Bull 1981 Jan;17(1):140-2

Halász N, Parry DM, Blackett NM, et al: [3H]gamma-aminobutyrate autoradiography of the rat olfactory bulb: hypothetical grain analysis of the distribution of silver grains. Neuroscience 1981;6(3):473-9

Halbreich U, Weinberg U, Stewart J, et al: An inverse correlation between serum levels of desmethylimipramine and melatonin-like immunoreactivity in DMI-responsive depressives. Psychiatry Res 1981 Feb;4(1):109-13

Haldar-Misra C, Thapliyal JP: Thyroid in reproduction of reptiles. Gen Comp Endocrinol 1981 Apr;43(4):537-42

Hall H, Ogren SO: Effects of antidepressant drugs on different receptors in the brain. Eur J Pharmacol 1981 Mar 26;70(3):393-407

Hall JB: Debendox in pregnancy [letter] Lancet 1981 Jul 18;2(8238):154-5

Hallberg H, Almgren O, Engel J, et al: Effects of propranolol on the locomotor stimulation induced by activation of postsynaptic catecholamine receptors. Psychopharmacology (Berlin) 1981; 72(3):227-31

Hallberg H, Almgren O, Svensson TH: Increased brain serotonergic and noradrenergic activity after repeated systemic administration of the beta-2 adrenoceptor agonist salbutamol, a putative antidepressant drug. Psychopharmacology (Berlin) 1981;73(3):201-4

Hallemans R, Naeije R, Melot C, et al: Systemic and pulmonary haemodynamic effects of somatostatin [letter] Lancet 1981 Jun 6; 1(8232):1270

Halpaap-Wood K, Horning EC, Horning MG: The effect of phenobarbital and beta-naphthoflavone induction on the metabolism of biphenyl in the rat and mouse. Drug Metab Dispos 1981 Mar-Apr;9(2):97-102

Halpaap-Wood K, Horning EC, Horning MG: The effect of 3-methylcholanthrene, Aroclor 1254, and phenobarbital induction on the metabolism of biphenyl by rat and mouse 9000g supernatant liver fractions. Drug Metab Dispos 1981 Mar-Apr;9(2):103-7

Halpin RA, Hegeman GD, Kenyon GL: Carbon-13 nuclear magnetic resonance studies of mandelate metabolism in whole bacterial cells and in isolated, in vivo cross-linked enzyme complexes. Biochemistry 1981 Mar 17;20(6):1525-33

Hamer R: Correction of drug names [letter] Ann Emerg Med 1981 Jul; 10(7):395

Hanbauer I, Karoum F, Hellstrom S, et al: Effects of hypoxia lasting up to one month on the catecholamine content in rat carotid body. Neuroscience 1981;6(1):81-6

Hanbauer I, Pradhan S, Yang HY: Role of calmodulin in dopaminergic transmission. Ann NY Acad Sci 1980;356:292-303

Hano J, Vetulani J, Sansone M, et al: Changes in action of tricyclic and tetracyclic antidepressants: desipramine and mianserin, on avoidance behavior in the course of the chronic treatment. Psychopharmacology (Berlin) 1981;73(3):265-8

Hansford M: Paranoid schizophrenia. A serpent which licked my eyes... Nurs Mirror 1981 May 7;152(19):30-3

Hanson G, Alphs L, Pradhan S, et al: Response of striatonigral substance P systems to a dopamine receptor agonist and antagonist. Neuropharmacology 1981 Jun;20(6):541-8

Hanson P, Smith JR, Robinson R, et al: A simple chromatographic technique for the estimation of urinary levels of normetadrenaline and metadrenaline. Clin Biochem 1980 Dec;13(6):262-5

Hansson C, Rorsman H, Rosengren E: Pronounced formation of 5-OH-dopa at enzymatic oxidation of DOPA in the presence of ascorbic acid. Acta Derm Venereol (Stockh) 1981;61(2):147-8

Hanumante MM, Fingerman SW, Fingerman M: Antagonism of the inhibitory effect of the polychlorinated biphenyl preparation, aroclor 1242, on color changes of the fiddler crab, Uca pugilator, by norepinephrine and drugs affecting noradrenergic neurotransmission. Bull Environ Contam Toxicol 1981 Apr;26(4):479-84

Haq SM, Buhrich N: Tolerance of daily single compared to space dose of merital. Med J Malaysia 1980 Jun;34(4):358-62

Harada N, Omura T: Selective induction of two different molecular species of cytochrome P-450 by phenobarbital and 3-methylcholanthrene. J Biochem (Tokyo) 1981 Jan;89(1):237-48

Harris E: Antipsychotic medications. Am J Nurs 1981 Jul;81(7):1316-23

Harris E: Psychotropic drugs: lithium. Am J Nurs 1981 Jul;81(7):1311-5

Harris E: Antidepressants: old drugs, new uses. Am J Nurs 1981 Jul; 81(7):1308-9

Harris RA, Schmidt J, Hitzemann BA, et al: Phosphatidate as a molecular link between depolarization and neurotransmitter release in the brain. Science 1981 Jun 12;212(4500):1290-1

Hart DA, Stein-Streilein J: Hamster lymphoid cell responses in vitro. Adv Exp Med Biol 1981;134:7-22

Hart DA: Ability of monovalent cations to replace potassium during stimulation of lymphoid cells. Cell Immunol 1981 Jan 1;57(1):209-18

Hartviksen I: Er diazepinene så uskyldige og forskrivningen blant norske leger så moderat som ekspertisen gir uttrykk for? Tidsskr Nor Laegeforen 1981 Mar 30;101(9-10):595 (Nor)

Harvey AL, Gage PW: Increase of evoked release of acetylcholine at the neuromuscular junction by a fraction from the venom of the eastern green mamba snake (Dendroaspis angusticeps). Toxicon 1981; 19(3):373-81

Harvey S, Bedrak E, Chadwick A: Serum concentrations of prolactin, luteinizing hormone, growth hormone, corticosterone, progesterone, testosterone and oestradiol in relation to broodiness in domestic turkeys (Meleagris gallopavo). J Endocrinol 1981 May;89(2):187-95

Harvey S: What's so special about my specialty? Psychiatric med nursing. J Pract Nurs 1981 Jun;31(6):27, 32

Hasan SS, Mazumdar S, Singh PM, et al: Response of adrenal catecholamine to a newly synthesized chemical radioprotector. Nuklearmedizin 1981 Apr;20(2):82-4

Hasegawa Y, Miyamoto K, Yazaki C, et al: Regulation of the second surge of follicle-stimulating hormone; effects of antiluteinizing hormone-releasing hormone serum and pentobarbital. Endocrinology 1981 Jul;109(1):130-5

Hashimoto K: [Retrospect on catecholamine research in our laboratories (author's transl)] Kokyu To Junkan 1980 Oct;28(10):1096-101 (Jpn)

Hassan RM, Pesce AJ, Sheng P, et al: Correlation of serum pseudocholinesterase and clinical course in two patients poisoned with organophosphate insecticides. Clin Toxicol 1981;18(4):401-6

Hassanyeh F, Davison K: Bipolar affective psychosis with onset before age 16 years: report of 10 cases. Br J Psychiatry 1980 Dec;137:530-9

Haug P, Suzuki M, Moritz J, et al: Changes in acetylcholine in caudate nucleus tissue isolated in situ detected by gas chromatography mass spectrometry selected ion monitoring. Biomed Mass Spectrom 1980 Nov;7(11-12):533-6

Hauger-Klevene JH, Vecsei P: Metyrapone effect on blood pressure and deoxycorticosterone levels in the rat. Acta Physiol Lat Am 1978; 28(4-5):219-21

Hauger-Klevene JH, Rastrilla AM: Effect of bromoergocriptine on aldosterone free endogenous pool in the rat. Acta Physiol Lat Am 1978; 28(2-3):151-3

Haycock DA, Patrick RL: Catecholamine synthesis regulation in hypothalamic synaptosomes. Brain Res 1981 Jun 15;214(2):371-85

Hays SE, Rubin RT: Differential prolactin responses to haloperidol and TRH in normal adult men. Psychoneuroendocrinology 1981;6(1):45-52

Hazum E, Fridkin M, Baram T, et al: Synthesis, biological activity and resistance to enzymic degradation of luteinizing hormone--releasing hormone analogues modified at position 7. FEBS Lett 1981 Jan 26; 123(2):300-2

Hazum E, Fridkin M, Baram T, et al: Degradation of gonadotropin-releasing hormone by anterior pituitary enzymes. FEBS Lett 1981 May 18;127(2):273-6

Heagerty AM, Donovan MA, Castleden CM, et al: Influence of cimetidine on pharmacokinetics of propranolol. Br Med J [Clin Res] 1981 Jun 13;282(6280):1917-9

Healy DP, Jew JY, Black AC Jr, et al: Bradycardia following injection of 6-hydroxydopamine into the intermediate portion of nucleus tractus solitarius medialis. Brain Res 1981 Feb 16;206(2):415-20

Heathcote BV, Parry M: Pirenzepine selectively inhibits gastric acid secretion: a comparative pharmacological study between pirenzepine and seven other antiacetylcholine drugs. Scand J Gastroenterol [Suppl] 1980;15(66):15-26

Heber D, Swerdloff RS: Gonadotropin-releasing hormone analog and testosterone synergistically inhibit spermatogenesis. Endocrinology 1981 May;108(5):2019-21

Hedge GA, Wright KC, Judd A: Factors modulating the secretion of thyrotropin and other hormones of the thyroid axis. Environ Health Perspect 1981 Apr;38:57-63

Hedqvist P: Autoinhibition versus transsynaptic control of noradrenaline secretion in the rabbit kidney. Acta Physiol Scand 1980 Dec; 110(4):441-3

Heel RC, Brogden RN, Speight TM, et al: Temazepam: a review of its pharmacological properties and therapeutic efficacy as an hypnotic. Drugs 1981 May;21(5):321-40 (69 ref.)

Heffner TG, Luttinger D, Hartman JA, et al: Regional changes in brain catecholamine turnover in the rat during performance on fixed ratio and variable interval schedules of reinforcement. Brain Res 1981 Jun 9;214(1):215-8

Hegarty JE, Fairclough PD, Clark ML, et al: Jejunal water and electrolyte secretion induced by L-arginine in man. Gut 1981 Feb;22(2):108-13

Hegstrand LR, Eichelman B: Determination of rat brain tissue catecholamines using liquid chromatography with electrochemical detection. J Chromatogr 1981 Jan 2;222(1):107-11

Heikkila RE, Cabbat FS, Manzino L, et al: Unexpected differences between mazindol and its homologs on biochemical and behavioral responses. J Pharmacol Exp Ther 1981 Jun;217(3):745-9

Heikkila RE, Shapiro BS, Duvoisin RC: The relationship between loss of dopamine nerve terminals, striatal [3H]spiroperidol binding and rotational behavior in unilaterally 6-hydroxydopamine-lesioned rats. Brain Res 1981 May 4;211(2):285–92

Hell T, Etzrodt H, Mattes P, et al: Gastrectomy with and without duodenal transit: release of glucagon, insulin and somatostatin. Scand J Gastroenterol [Suppl] 1981;67:83–7

Helke CJ, O'Donohue TL, Jacobowitz DM: Substance P as a baro- and chemoreceptor afferent neurotransmitter: immunocytochemical and neurochemical evidence in the rat. Peptides (Fayetteville) 1980 Spring; 1(1):1–9

Hemmendinger LM, Garber BB, Hoffmann PC, et al: Target neuron-specific process formation by embryonic mesencephalic dopamine neurons in vitro. Proc Natl Acad Sci USA 1981 Feb; 78(2):1264–8

Hennessy MB, Hollister TA, Levine S: Pituitary-adrenal responsiveness of mothers to pups in mice of two inbred strains. Behav Neural Biol 1981 Mar;31(3):304–13

Henquin JC: The effect of pH on 86Rubidium efflux from pancreatic islet cells. Mol Cell Endocrinol 1981 Feb;21(2):119–28

Herberg LJ, Wishart TB: Self-stimulation and locomotor changes indicating 'latent' anticholinergic activity by an atypical neuroleptic (thioridazine). Neuropharmacology 1981 Jan;20(1):55–60

Heron DS, Shinitzky M, Hershkowitz M, et al: Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. Proc Natl Acad Sci USA 1980 Dec;77(12):7463–7

Héroux O, Roberge AG: Different influences of two types of diets commonly used for rats on a series of parameters related to the metabolism of central serotonin and noradrenaline. Can J Physiol Pharmacol 1981 Feb;59(2):108–12

Herrera AA, Grinnell AD: Contralateral denervation causes enhanced transmitter release from frog motor nerve terminals. Nature 1981 Jun 11;291(5815):495–7

Herrling PL: The membrane potential of cat hippocampal neurons recorded in vivo displays four different reaction-mechanisms to iontophoretically applied transmitter agonists. Brain Res 1981 May 18; 212(2):331–43

Herrmann WM, Kubicki S: Beispiele für die Projektion von Substanzwirkungen typischer Psychopharmaka auf eine elektrophysiologische Messebene. EEG EMG 1981 Mar;12(1):21–32 (Eng. Abstr.) (Ger)

Herrmann WM, Hofmann W, Kubicki S: Psychotropic drug induced changes in auditory averaged evoked potentials: results of a double-blind trial using an objective fully automated AEP analysis method. Int J Clin Pharmacol Ther Toxicol 1981 Feb;19(2):56–62

Hershkowitz N, Ayala GF: Effects of phenytoin on pyramidal neurons of the rat hippocampus. Brain Res 1981 Mar 16;208(2):487–92

Hertz L, Richardson JS, Mukerji S: Doxepin, a tricyclic antidepressant, binds to normal, intact astroglial cells in cultures and inhibits the isoproterenol-induced increase in cyclic AMP production. Can J Physiol Pharmacol 1980 Dec;58(12):1515–9

Hervonen A, Linnoila I, Pickel VM, et al: Localization of [Met5]- and [Leu5]-enkephalin-like immunoreactivity in nerve terminals in human paravertebral sympathetic ganglia. Neuroscience 1981;6(3):323–30

Hervonen H, Spatz M, Bembry J, et al: Studies related to the blood-brain barrier to monoamines and protein in pia-arachnoid cultures. Brain Res 1981 Apr 6;210(1–2):449–54

Herz A: Neuroendokrinologische Aspekte der Endorphine. Verh Dtsch Ges Inn Med 1980;86:4–12 (45 ref.) (Ger)

Hesketh JE: Catecholamine synthesis in the adrenal medulla of cattle and rats deficient in copper. Biochem Soc Trans 1981 Feb;9(1):101–2

Heym C, König R, Schröder H, et al: Immunofluorescent and biochemical studies on dopamine-beta-hydroxylase and catecholamines in SIF cells of the superior cervical ganglion. Acta Histochem [Suppl] (Jena) 1981; 24:123–9

Hidaka H, Howard BV, Ishibashi F, et al: Effect of pH and 3-hydroxybutyrate on insulin binding and action in cultured human fibroblasts. Diabetes 1981 May;30(5):402–6

Hideg Z: A kolinészteráz-aktivitás meghatározása Ellmann módositott módszerével post mortális vérmintákból. Orv Hetil 1981 Jan 25; 122(4):221–2 (Hun)

Hienz RD, Brady JV: Psychophysical profiles differentiate drugs of abuse. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):226–31

Higgins TJ, Bailey PJ, Allsopp D: Mechanism of stimulation of cardiac myocyte beating rate by 5-hydroxytryptamine. Life Sci 1981 Mar 2; 28(9):999–1005

Hinds TR, Raess BU, Vincenzi FF: Plasma membrane Ca2+ transport: antagonism by several potential inhibitors. J Membr Biol 1981 Jan 30; 58(1):57–65

Hintnaus J: Kyselina mléčná v séru jalovic po aplikaci adrenalinu ve vztahu k březosti. Vet Med (Praha) 1981 Feb;26(2):95–100 (Eng. Abstr.) (Cze)

Hirano T: [Protection of the myocardium and coronary artery circulation (5)] Kokyu To Junkan 1980 Oct;28(10):1102 (Jpn)

Hirsch SR, Manchanda R, Weller MP: Dextro-propranolol in schizophrenia. Prog Neuropsychopharmacol 1980;4(6):633–7

Hjorth S, Carlsson A, Wikström H, et al: 3-PPP, a new centrally acting DA-receptor agonist with selectivity for autoreceptors. Life Sci 1981 Mar 16;28(11):1225–38

Ho IK, Onoda K, Flint BA: Effect of chronic administration of phencyclidine on hepatic mixed-function oxidases in the mouse. Biochem Pharmacol 1981 Mar 1;30(5):545–7

Hobi V, Dubach UC, Skreta M, et al: The effect of bromazepam on psychomotor activity and subjective mood. J Int Med Res 1981; 9(2):89–97

Hodge GK, Boyeson MG, Linn RT: Dopaminergic agonists differentially affect open-field activity of rats with A10 lesions. Psychopharmacology (Berlin) 1981;73(1):39–42

Hogarty GE: Natural and therapeutic environmental indicators of maintenance dosage requirements [proceedings] Psychopharmacol Bull 1981 Jan;17(1):36–7

Hogg RJ, Sawyer M, Hecox K, et al: Carbamazepine-induced acute tubulointerstitial nephritis. J Pediatr 1981 May;98(5):830–2

Holaday JW, D'Amato RJ, Faden AI: Thyrotropin-releasing hormone improves cardiovascular function in experimental endotoxic and hemorrhagic shock. Science 1981 Jul 10;213(4504):216–8

Holford NH, Coates PE, Guentert TW, et al: The effect of quinidine and its metabolites on the electrocardiogram and systolic time intervals: concentration—effect relationships. Br J Clin Pharmacol 1981 Feb; 11(2):187–95

Holmberg G: Critical flicker fusion (CFF) test for sedative effect of antidepressants. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):289–301

Holmstedt B, Fredga A: Sundry episodes in the history of coca and cocaine. J Ethnopharmacol 1981 Mar–May;3(2–3):113–47

Holzbecher M, Ellenberger HA: Simultaneous determination of diphenhydramine, methaqualone, diazepam and chlorpromazine in liver by use of enzyme digestion: a comparison of digestion procedures. J Anal Toxicol 1981 Mar–Apr;5(2):62–4

Homan HD, Ziance RJ: The effects of d-amphetamine and potassium on serotonin release and metabolism in rat cerebral cortex tissue. Res Commun Chem Pathol Pharmacol 1981 Feb;31(2):223–40

Honecker H, Fähndrich E, Coper H, et al: Serum DBH and platelet MAO in patients with depressive disorders. Pharmacopsychiatria 1981 Jan;14(1 Suppl):10–4

Hoshino Y, Kumashiro H, Kaneko M, et al: Serum serotonin, free tryptophan and plasma cyclic AMP levels in autistic children -with special reference to their relation to hyperkinesia. Fukushima J Med Sci 1979;26(3–4):79–91

Hosko MJ, Schmeling WT, Hardman HF: Evidence for a caudal brainstem site of action for cannabinoid induced hypothermia. Brain Res Bull 1981 Mar;6(3):251–8

Hösli L, Hösli E, Andrès PF, et al: Evidence that the depolarization of glial cells by inhibitory amino acids is caused by an efflux of K+ from neurones. Exp Brain Res 1981;42(1):43–8

Hrdina PD, Lapierre YD: Clinical response, plasma levels and pharmacokinetics of desipramine in depressed in-patients. Prog Neuropsychopharmacol 1980;4(6):591–600

Hrdina PD, Dubas TC: Brain distribution and kinetics of desipramine in the rat. Can J Physiol Pharmacol 1981 Feb;59(2):163–7

Hsieh WT, Matthews KS: Tetranitromethane modification of the tyrosine residues of the lactose repressor. J Biol Chem 1981 May 25; 256(10):4856–62

Hsu KY, Noda A, Iguchi S: Hydrazine formation from iproniazid. J Pharmacobiodyn 1980 Nov;3(11):620–7

Hsu LK, Meltzer ES, Crisp AH: Schizophrenia and anorexia nervosa. J Nerv Ment Dis 1981 May;169(5):273–6

Huey LY, Janowsky DS, Judd LL, et al: Effects of lithium carbonate on methylphenidate-induced mood, behavior, and cognitive processes. Psychopharmacology (Berlin) 1981;73(2):161–4

Hugonenq H, Uso T: A propos de l'intérêt du sultopride utilisé a faibles doses chez le grand enfant et l'adolescent. Neuropsychiatr Enfance Adolesc 1980 Dec;28(12):593–7 (Fre)

Huidobro-Toro JP, Way EL: Comparative study on the effect of morphine and the opioid-like peptides in the vas deferens of rodents: species and strain differences, evidence for multiple opiate receptors. Life Sci 1981 Mar 23;28(12):1331–6

Huijmans JG, Degenhart HJ, Kortleve DJ, et al: Effects of 22S-hydroxy-cholesterol and other hydroxylated sterols on the ACTH-stimulated steroid production in rat adrenal cells. Acta Endocrinol (Copenh) 1981 Jun;97(2):243–50

Hunt SP, Emson PC, Gilbert R, et al: Presence of avian pancreatic polypeptide-like immunoreactivity in catecholamine and methionine-enkephalin-containing neurones within the central nervous system. Neurosci Lett 1981 Jan 20;21(2):125–30

Huo KJ: [Preliminary observations on immunoglobulins in schizophrenics (author's transl)] Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1979;12(3):161–3 (Chi)

Hurst HE, Jones DR, Jarboe CH, et al: Determination of clovoxamine concentration in human plasma by electron capture gas chromatography. Clin Chem 1981 Jul;27(7):1210–2

Hurst WJ, Toomey PB: High-performance liquid chromatographic determination of four biogenic amines in chocolate. Analyst 1981 Apr;

106(1261):394–402

Hussain MN, Sole MJ: A simple, specific, radioenzymatic assay for picogram quantities of serotonin or acetylserotonin in biological fluids and tissues. Anal Biochem 1981 Feb;111(1):105–10

Husstedt W, Erbersdobler H: Tierexperimentelle Untersuchungen mit abgebundenen Darmsegmenten zur Frage der Resorption von alpha-Aminoisobuttersäure durch die fetale Darmschleimhaut. Zentralbl Gynaekol 1981;103(4):193–7 (Eng. Abstr.) (Ger)

Huszti Z: Additional data on the function of hypothalamic histamine. Agents Actions 1981 Apr;11(1–2):135–42

Hüttel MS, Olesen AS: Diazemuls. Diazepam i nyt vehikel til parenteral anvendelse. Ugeskr Laeger 1981 Jan;143(3):140 (Dan)

Hymowitz N: Effects of diazepam on schedule-controlled and schedule-induced behavior under signaled and unsignaled shock. J Exp Anal Behav 1981 Jul;36(1):119–32

Hyyppä MT: Tiedonvälitys aivoissa askarruttaa neurotieteilijöitä. Duodecim 1980;96(11):769–72 (Fin)

I

Ibata Y, Tani N, Obata HL, et al: Correlative ontogenetic development of catecholamine- and LHRH-containing nerve endings in the median eminence of the rat. Cell Tissue Res 1981;216(1):31–8

Ide H, Nakazawa Y: Effect of chlorpromazine administration on enzyme activity concerning phosphatidic acid metabolism in rat liver. J Pharmacobiodyn 1980 Nov;3(11):612–9

Ientile R, Di Giorgio RM, Rotiroti D, et al: GABA depletion in chick brain-stem after intraventricular injection of cefazolin. Res Commun Chem Pathol Pharmacol 1981 Feb;31(2):241–50

Ikeno T, Dickens G, Lloyd T, et al: The receptor-mediated activation of tyrosine hydroxylation in the superior cervical ganglion of the rat. J Neurochem 1981 May;36(5):1632–40

Illsley NP, Lamartiniere CA: Endocrine regulation of rat serum cholinesterase activity. Endocrinology 1981 May;108(5):1737–43

Imazawa M, Miyamoto K: Purification of phenytoin-binding site from the brain. Folia Psychiatr Neurol Jpn 1980;34(3):362

Imbs JL, Singer L, Danion JM, et al: Effects of indomethacin and methylprednisolone on renal elimination of lithium in the rat. Int Pharmacopsychiatry 1980;15(3):143–9

Imperato A, Porceddu ML, Morelli M, et al: Benzodiazepines prevent kainate-induced loss of GABAergic and cholinergic neurons in the chick retina. Brain Res 1981 May 25;213(1):205–10

Imperatore A, Somma A, Vairo G, et al: Aggregazione delle piastrine e piribedil. Arch Sci Med (Torino) 1980 Apr–Jun;137(2):253–8 (Eng. Abstr.) (Ita)

Imura H: beta-Endorphin and related peptides. Jpn J Pharmacol 1980; 30(Suppl):1P

Ing H, Cross WG, Tymons BJ: The spectrum of neutrons from A238Pu–Li source. Health Phys 1981 Mar;40(3):345–50

Ings R, Pappas B: Neonatal intraspinal 6-hydroxydopamine: depletion of norepinephrine but not dopamine. Eur J Pharmacol 1981 Apr 9; 70(4):577–83

Inoue F, Harrison JV: Folic acid and phenytoin hyperplasia [letter] Lancet 1981 Jul 11;2(8237):86

Inui N, Nishi Y, Hasegawa MM, et al: Induction of 8-azaguanine or ouabain resistant somatic mutation of Chinese hamster lung cells by treatment with tryptophan products. Cancer Lett 1980 May;9(3):185–9

Irace G, Balestrieri C, Parlato G, et al: Tryptophanyl fluorescence heterogeneity of apomyoglobins. Correlation with the presence of two distinct structural domains. Biochemistry 1981 Feb 17;20(4):792–9

Isambert MF, Henry JP: Solubilization and reconstitution of the adenosine 5'-triphosphate dependent noradrenaline uptake system of bovine chromaffin granule membrane. Biochimie 1981 Mar;63(3):211–9

Ishikawa M, Kudo Y, Fukuda H: The effect of diazepam on nystagmus induced by stimulation of the lateral geniculate body in the rabbit. Neuropharmacology 1981 May;20(5):435–9

Ishikawa N, Ichikawa T, Shigei T: Possible embryogenetical differences of the dog venous system in sensitivity to vasoactive substances. Jpn J Pharmacol 1980 Dec;30(6):807–18

Ishimaru T, Mori H, Koh K, et al: [A study on the significance of bromocriptine (CB-154) administration in normoprolactinemic anovulatory women (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1980 Oct;32(10):1583–90 (Eng. Abstr.) (Jpn)

Itakura T, Kasamatsu T, Pettigrew JD: Norepinephrine-containing terminals in kitten visual cortex: laminar distribution and ultrastructure. Neuroscience 1981;6(2):159–75

Itil TM, Schneider SJ, Fredrickson JW: The replicability of the psychophysiological effects of diazepam. Biol Psychiatry 1981 Jan; 16(1):65–70

Ito S, Nakazato Y, Ohga A: Further evidence for the involvement of Na+ channels in the release of adrenal catecholamine: the effect of scorpion venom and grayanotoxin I. Br J Pharmacol 1981 Jan;72(1):61–7

Ito S, Fujita K: Formation of cysteine conjugates from dihydroxyphenylalanine and its S-cysteinyl derivatives by peroxidase-catalyzed oxidation. Biochim Biophys Acta 1981 Jan 21; 672(2):151–7

Itoh S, Katsuura G, Hirota R, et al: Circadian rhythm of plasma corticosterone in vagotomized rats. Experientia 1981 Apr 15;37(4):380–1

Iudaev NA, Utesheva ZF, Novikova TE, et al: Ugnetenie sekretsii prolaktiona pod deĭstviem leitsin-énkefalina. Dokl Akad Nauk SSSR 1981;256(2):500–2 (Rus)

Iuvone PM, Neff NH: Dopamine neurons of the retina: a simple method system for studying synaptic regulatory mechanisms. Essays Neurochem Neuropharmacol 1981;5:75–94 (35 ref.)

Iven H, Zetler G: Failure of peptides (angiotensin, bradykinin, substance P, physalaemin, Met-enkephalin) to influence the cardiac action potential. Pharmacology 1980;21(6):403–6

Iwasa T, Miyagawa Y, Mori N: [Primary amenorrhea possibly due to insufficient LH-RH secretion] Nippon Sanka Fujinka Gakkai Zasshi 1980 Oct;32(10):1647–9 (Jpn)

J

Jackson DM, Bailey RC, Christie MJ, et al: Long-term d-amphetamine in rats: lack of change in post-synaptic dopamine receptor sensitivity. Psychopharmacology (Berlin) 1981;73(3):276–80

Jacob M, Duru M, Duru C: Stabilité et dosage de la pilocarpine dans les collyres. Pharm Acta Helv 1981;56(2):59–63 (Fre)

Jacobs BL, Heym J, Trulson ME: Cats develop tolerance to d-amphetamine's effects upon locomotion and stereotyped behaviors. Eur J Pharmacol 1981 Jan 29;69(3):353–6

Jacobson SB: Psychiatric treatment in the aged. NY State J Med 1981 Apr;81(5):802–4

Jähkel M, Oehler J, Schmidt J: Veränderungen der neuronalen Aktivität im Hippokampus der Ratte unter Lnagzeitbehandlung mit Desipramin. Acta Biol Med Ger 1980;39(10):1083–7 (Eng. Abstr.) (Ger)

Jakubowska-Naziemblo B, Wlodzimierska B, Traczyk WZ: Effect of intracerebroventricular administration of substance P and its hexapeptide fragment on the estrus cycle in female rats. Acta Physiol Pol 1980;31(6):637–45

Janka Z, Szentistvanyi I, Kiraly E, et al: Preferential vulnerability of dendrites to lithium ion in rat brain and in nerve cell culture. Acta Neuropathol [Suppl] (Berl) 1981;7:44–7

Janoff AS, Mazorow DL, Coughlin RT, et al: The modification of human erythrocyte membrane structure by membrane stabilizers: an electron spin resonance study. Am J Hematol 1981;10(2):171–9

Jansen EH, Steenbergen J, de Jong FH, et al: The use of affinity matrices in the purification of inhibin from bovine follicular fluid. Mol Cell Endocrinol 1981 Feb;21(2):109–17

Jansen JB, Lamers CB: The effect of somatostatin on bombesin-stimulated serum gastrin and gastric acid secretion in man. Digestion 1981; 21(4):193–7

Janzarik W: Psychopathologische Aspekte der Verlaufsforschung an idiopathischen Psychosen. Psychiatr Clin (Basel) 1980;13(3–4):139–49 (Eng. Abstr.) (Ger)

Jardin F, Sportiche M, Bazin M, et al: Dobutamine: a hemodynamic evaluation in human septic shock. Crit Care Med 1981 Apr;9(4):329–32

Jarema MA, Arndt KT, Savage M, et al: Genetic insertion of nuclear spin labels in the lac repressor. J Biol Chem 1981 Jul 10;256(13):6544–7

Järhult J, Hamberger B, Lanthén G, et al: The role of catecholamines in the control of gastrin and acid secretion during insulin hypoglycaemia in man. Digestion 1981;21(2):92–7

Jason KM, Cooper TB, Friedman E: Prenatal exposure to imipramine alters early behavioral development and beta adrenergic receptors in rats. J Pharmacol Exp Ther 1981 May;217(2):461–6

Jaup BH, Stockbrügger RW, Dotevall G: Comparison of the action of pirenzepine and L-hyoscyamine on gastric acid secretion and other muscarinic effects. Scand J Gastroenterol [Suppl] 1980;15(66):89–94

Jaup BH, Blomstrand C: Cerebro-spinal fluid concentrations of pirenzepine after therapeutic dosage. Scand J Gastroenterol [Suppl] 1980;15(66):35–7

Jędrzejewska A, Ostenda M: Neuropathological findings in autonomic nervous system of alimentary tract of rat after application of catecholamines. Acta Neuropathol [Suppl] (Berl) 1981;7:273–5

Jessel HJ, Jessel I, Wegener G: Therapie von älteren depressiven Patienten. Lofepramin und Amitriptylin unter Doppelblindbedingungen. ZFA (Stuttgart) 1981 Apr 10;57(10):784–8 (Ger)

Jha RJ, Kelkar VV: Effect of drugs interacting with adrenergic mechanisms and of adrenalectomy on pilocarpine-induced salivation in mice. Indian J Med Res 1980 Dec;72:923–6

Jhamandas K, Dumbrille A: Regional release of [3H]adenosine derivatives from rat brain in vivo: effect of excitatory amino acids, opiate agonists, and benzodiazepines. Can J Physiol Pharmacol 1980 Nov;58(11):1262–78

Jick H, Holmes LB, Hunter JR, et al: First-trimester drug use and congenital disorders. JAMA 1981 Jul 24–31;246(4):343–6

Jimerson DC, Ballenger JC, Lake CR, et al: Plasma and CSF MHPG in normals [proceedings] Psychopharmacol Bull 1981 Jan;17(1):86–7

Jindal SP, Lutz T, Cooper TB: Determination of phenelzine in human plasma with gas chromatography-mass spectrometry using an isotope labeled internal standard. J Chromatogr 1980 Dec 12;221(2):301-8

Johansson O, Lundberg JM: Ultrastructural localization of VIP-like immunoreactivity in large dense-core vesicles of 'cholinergic-type' nerve terminals in cat exocrine glands. Neuroscience 1981;6(5):847-62

Johnson AL, van Tienhoven A: Plasma concentrations and corticosterone relative to photoperiod, oviposition, and ovulation in the domestic hen. Gen Comp Endocrinol 1981 Jan;43(1):10-6

Johnson DA: Depression: treatment compliance in general practice. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):447-53

Johnson GF, Hunt GE, Duggin GG, et al: Lithium nephrotoxicity [letter] Med J Aust 1981 Apr 4;1(7):376

Johnson KM, Oeffinger KC: The effect of phencyclidine on dopamine metabolism in the mouse brain. Life Sci 1981 Jan 26;28(4):361-9

Johnson MR, Althuis TH, Bindra JS, et al: Potent analgetics derived from 9-nor-9 beta-hydroxyhexahydrocannabinol. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):68-74

Johnson RG, Carty SE, Scarpa A: Proton: substrate stoichiometries during active transport of biogenic amines in chromaffin ghosts. J Biol Chem 1981 Jun 10;256(11):5773-80

Johnstone EC, Bourne RC, Crow TJ, et al: The relationships between clinical response, psychophysiological variables and plasma levels of amitriptyline and diazepam in neurotic outpatients. Psychopharmacology (Berlin) 1981;72(3):233-40

Johnstone M: Effect of maternal lorazepam on the neonate [letter] Br Med J [Clin Res] 1981 Jun 13;282(6280):1973-4

Jolicoeur FB, Rondeau DB, Belanger F, et al: Influence of substance P on the behavioral changes induced by haloperidol in rats. Peptides (Fayetteville) 1980 Spring;1(1):103-7

Jonderko G, Sobczyk P, Gabryel A, et al: Einige endokrinologische Aspekte der Lithium-Langzeittherapie. Z Gesamte Inn Med 1981 Feb 1;36(3):79-82 (Eng. Abstr.) (Ger)

Jonderko G, Sobczyk P, Gabryel A, et al: Długotrwałe stosowanie soli litu - aspekty endokrynologiczne i biochemiczne. Pol Tyg Lek 1981 Jan 5;36(1):23-5 (Eng. Abstr.) (Pol)

Jones DL, Mogenson GJ, Wu M: Injections of dopaminergic, cholinergic, serotoninergic and GABAergic drugs into the nucleus accumbens: effects on locomotor activity in the rat. Neuropharmacology 1981 Jan;20(1):29-37

Jones RS: Specific enhancement of neuronal responses to catecholamine by p-tyramine. J Neurosci Res 1981;6(1):49-61

Jones RS: High-affinity uptake of choline in slices of rat cerebral cortex: effects of antidepressant and anticholinergic drugs. Can J Physiol Pharmacol 1981 Apr;59(4):392-6

Jones RS: In vivo pharmacological studies on the interactions between tryptamine and 5-hydroxytryptamine. Br J Pharmacol 1981 Jun;73(2):485-93

Jones SB: Myocardial norepinephrine turnover during induced hypothermia and rewarming. J Appl Physiol 1981 May;50(5):962-6

Joó I, Wollemann M: The effect of catecholamines and their inhibitors on the solubilized adenylate cyclase activity of bovine retina. Exp Eye Res 1980 Dec;31(6):659-63

Jope RS: Acetylcholine turnover and compartmentation in rat brain synaptosomes. J Neurochem 1981 May;36(5):1712-21

Jorde R, Waldum HL, Burhol PG, et al: The effect of somatostatin on fasting and postprandial plasma GIP, serum insulin, and blood glucose in man. Scand J Gastroenterol 1981;16(1):113-9

Jukofsky D, Kramer A, Mulé SJ: Evaluation of the TRI 'dipstick' test for the detection of drugs of abuse in urine. J Anal Toxicol 1981 Jan-Feb;5(1):14-9

Juorio AV, Jones RS: The effect of mesencephalic lesions on tyramine and dopamine in the caudate nucleus of the rat. J Neurochem 1981 Jun;36(6):1898-903

Jürgens R, Becker W, Kornhuber HH: Natural and drug-induced variations of velocity and duration of human saccadic eye movements: evidence for a control of the neural pulse generator by local feedback. Biol Cybern 1981;39(2):87-96

Jürgensen HJ, Christensen NJ, Ladefoged S, et al: Lack of effect of intravenous LHRH on plasma noradrenaline in man. Clin Endocrinol (Oxf) 1980 Sep;13(3):249-52

Juvancz P: The effect of p-bromomethamphetamine (V-111) on sleep on the rat. Eur J Pharmacol 1981 Apr 9;70(4):461-6

K

Kabra PM, Mar NA, Marton LJ: Simultaneous liquid chromatographic analysis of amitriptyline, nortriptyline, imipramine, desipramine, doxepin, and nordoxepin. Clin Chim Acta 1981 Apr 9;111(2-3):123-32

Kafka MS, Wirz-Justice A, Naber D, et al: Circadian acetylcholine receptor rhythm in rat brain and its modification by imipramine. Neuropharmacology 1981 May;20(5):421-5

Kahn E: Genetics and schizophrenic behavior. Psychiatr Q 1980 Winter;52(4):251-69 (124 ref.)

Kajiwara N, Murakami A, Hashida J, et al: [Evaluation of catecholamine measurement of high performance liquid chromatography with electronic detector (author's transl)] Horumon To Rinsho 1980 Oct;28(10):1205-10 (Jpn)

Kakudo K, Paull WK Jr, Vacca LL: Immunocytochemical study of substance P containing nerve terminals in rat spinal cord. Technical considerations. Histochemistry 1981;71(1):17-32

Kalacheva GS, Vysotskii ES, Rodicheva EK, et al: Lipidy svetiashchikhsia bakterii Photobacterium mandapamensis. Mikrobiologiia 1981 Jan-Feb;50(1):79-83 (Eng. Abstr.) (Rus)

Kalcheim C, Szechtman H, Koch Y: Bisexual behavior in male rats treated neonatally with antibodies to luteinizing hormone-releasing hormone. J Comp Physiol Psychol 1981 Feb;95(1):36-44

Kaloyanova F, Bainova A, Zaprianov Z: Inhibition of monoamine oxidase activity after combined action of chlordimeform with the antidepressant nialamide. Arch Environ Contam Toxicol 1981;10(1):1-8

Kalra SP, Kalra PS: A dopamine agonist stimulates progesterone secretion from adrenal gland. Life Sci 1981 Mar 30;28(13):1467-9

Kalsner S: The role of calcium in the effects of noradrenaline and phenoxybenzamine on adrenergic transmitter release from atria: no support for negative feedback of release. Br J Pharmacol 1981 Jun;73(2):363-71

Kamer RS, Turi AR, Solomon PR, et al: Increased mesolimbic dopamine binding following chronic haloperidol treatment. Psychopharmacology (Berlin) 1981;72(3):261-3

Kamlana SH, Kerry RJ, Khan IA: Lithium: some drug interactions. Practitioner 1980 Dec;224(1350):1291-2

Kamp CW, Morgan WW: GABA antagonists enhance dopamine turnover in the rat retina in vivo. Eur J Pharmacol 1981 Jan 29;69(3):273-9

Kampf D, Huempel M, Lerche U, et al: Effects of uremia and hemodialysis on lormetazepam disposition. Clin Pharmacol Ther 1981 Jul;30(1):77-85

Kanatsuka A, Makino H, Matsushima Y, et al: Effect of calcium on the secretion of somatostatin and insulin from pancreatic islets. Endocrinology 1981 Jun;108(6):2254-7

Kane JM, Quitkin FM, Rifkin A, et al: Prophylactic lithium with and without imipramine for bipolar I patients: a double-blind study [proceedings] Psychopharmacol Bull 1981 Jan;17(1):144-5

Kane JM, Cooper TB, Sachar EJ, et al: Clozapine: plasma levels and prolactin response. Psychopharmacology (Berlin) 1981;73(2):184-7

Kaneko M, Kaneko K, Shinsako J, et al: Adrenal sensitivity to adrenocorticotropin varies diurnally. Endocrinology 1981 Jul;109(1):70-5

Kangawa K, Minamino N, Chino N, et al: The complete amino acid sequence of alpha-neo-endorphin. Biochem Biophys Res Commun 1981 Apr 15;99(3):871-8

Karasek M: Influence of TRH and TSH on the ultrastructure of rat pineal gland. Acta Med Pol 1980;21(4):347-8

Karawya E, Mostafa MH, Osman N: The kinetic mechanism of inhibition of liver pyridoxal kinase with tryptophan metabolites. Biochim Biophys Acta 1981 Jan 15;657(1):153-8

Kärkkäinen S, Seppälä E: Gas chromatographic analysis of therapeutic concentrations of maprotiline in serum, using flame-ionization detection. J Chromatogr 1980 Dec 12;221(2):319-26

Karl RC: Evidence for a role of calmodulin in insulin release from pancreatic islets. J Surg Res 1981 May;30(5):478-81

Karle IL: Comparison of stereospecific conformations for threo and erythro beta-hydroxy-N-acetyl-tryptophanamide. Int J Pept Protein Res 1980 Nov;16(5):471-6

Karobath M, Drexler G, Supavilai P: Modulation by picrotoxin and IPTBO of 3H-flunitrazepam binding to the GABA/benzodiazepine receptor complex of rat cerebellum. Life Sci 1981 Jan 19;28(3):307-13

Karoum F, Commissiong JC, Neff NH, et al: Regional differences in catecholamine formation and metabolism in the rat spinal cord. Brain Res 1981 May 18;212(2):361-6

Karson CN, Staub RA, Kleinman JE, et al: Drug effect on blink rates in rhesus monkeys: preliminary studies. Biol Psychiatry 1981 Mar;16(3):249-54

Karson CN, Staub RA, Kleinman JE, et al: Blink rates and receptor supersensitivity. Neuropharmacology 1981 Jan;20(1):91-3

Karsten W, Müller A: Radical formation in single crystals of aromatic amines and radical transformation by light. Int J Radiat Biol 1981 Mar;39(3):235-52

Kárteszi M, Stark E, Rappay G, et al: Corticoliberin activity of rat neurohypophysis is distinct from vasopressin. Am J Physiol 1981 Jun;240(6):E689-93

Katikineni M, Davies TF, Catt KJ: Regulation of adrenal and testicular prolactin receptors by adrenocorticotropin and luteinizing hormone. Endocrinology 1981 Jun;108(6):2367-74

Kato Y, Shiraki S, Hamada Y, et al: Chemicals which promote survival of ultraviolet-irradiated lon and ruv mutants of Escherichia coli K12. Can J Microbiol 1980 Dec;26(12):1518-22

Katsos A, Philippidis H, Palaiologos G: Effect of L-tryptophan injection in rats on some enzymes of amino acid metabolism in liver. I. In vitro studies of the effect of L-tryptophan and its metabolites on the extramitochondrial L-alanine: 2-ketoglutaric aminotransferase. Horm Metab Res 1981 Feb;13(2):85-8

Katz MS, Partilla JS, Piñeyro MA, et al: Essential role of GTP in epinephrine stimulation of human fat cell adenylate cyclase. J Lipid Res 1981 Jan;22(1):113-21

AUTHOR SECTION

Katz RJ, Schmaltz K: Dopaminergic involvement in attention. A novel animal model. Prog Neuropsychopharmacol 1980;4(6):585–90

Katz Z, Lancet M: Inadvertent intrauterine injection of methylene blue in early pregnancy [letter] N Engl J Med 1981 Jun 4;304(23):1427

Katzorke T, Propping D, Tauber PF: Zyklusstörungen während konsekutiver artefizieller Inseminationstherapie und ihre Behandlung. Fortschr Med 1981 Apr 2;99(13):471–4 (Eng. Abstr.) (Ger)

Kaufman EE, Nelson T: Kinetics of coupled gamma-hydroxybutyrate oxidation and D-glucuronate reduction by an NADP+-dependent oxidoreductase. J Biol Chem 1981 Jul 10;256(13):6890–4

Kaufmann SH, Hofmann HP, Kreiskott H: Induction of hyperphagia in rats by intracerebroventricular infusion of sodium pentobarbital. A method for testing anorexigenic compounds. Arzneimittelforsch 1981; 31(2):335–7

Kawamura T, Itaoka T, Nakata S, et al: [Measurement of deep body temperature difference after open heart surgery: correlations with hemodynamics, endogenous catecholamine and renin activity (author's transl)] Nippon Kyobu Geka Gakkai Zasshi 1981 Feb;29(2):211–7 (Eng. Abstr.) (Jpn)

Kayama Y, Hsiao CF, Fukuda Y, et al: Sensitivity to GABA of neurons of the dorsal and ventral lateral geniculate nuclei in the rat. Brain Res 1981 Apr 27;211(1):202–5

Kędryna T, Gumińska M, Eckstein M: The effect of Craviten, a new antiarrhythmic drug, its 2R, 2'R isomer, quinidine and procaine amide on human platelet aggregation. Pol J Pharmacol Pharm 1980 Nov–Dec; 32(6):883–8

Kehr W: 3-Methoxytyramine and normetanephrine as indicators of dopamine and noradrenaline release in mouse brain in vivo. J Neural Transm 1981;50(2–4):165–78

Kelly PA, McCulloch J: Heterogeneous depression of glucose utilization in the caudate nucleus by GABA agonists. Brain Res 1981 Mar 30; 209(2):458–63

Kenakin TP: A pharmacological method to estimate the pKi of competitive inhibitors of agonist uptake processes in isolated tissues. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):89–95

Kennett GA, Joseph MH: The functional importance of increased brain tryptophan in the serotonergic response to restraint stress. Neuropharmacology 1981 Jan;20(1):39–43

Kent S: Drugs to boost sexual potency. Geriatrics 1981 Jul;36(7):158–66

Kerdelhue B, Palkovits M, Karteszi M, et al: Circadian variations in substance P, luliberin (LH-RH) and thyroliberin (TRH) contents in hypothalamic and extrahypothalamic brain nuclei of adult male rats. Brain Res 1981 Feb 16;206(2):405–13

Kerdelhue B, Weisman AS, Weiner RI: A dopaminergic binding site in the high speed supernatant of steer anterior pituitary homogenates. Endocrinology 1981 Jul;109(1):307–9

Kessler KM, Perez GO: Decreased quinidine plasma protein binding during hemodialysis. Clin Pharmacol Ther 1981 Jul;30(1):121–6

Kestenbaum CJ: Adolescents at risk for manic-depressive illness. Adolesc Psychiatry 1980;8:344–66

Khachaturian H, Sladek JR Jr: Simultaneous monoamine histofluorescence and neuropeptide immunocytochemistry: III. Ontogeny of catecholamine varicosities and neurophysin neurons in the rat supraoptic and paraventricular nuclei. Peptides (Fayetteville) 1980 Spring;1(1):77–95

Khan AU: A comparison of the therapeutic and cardiovascular effects of a single nightly dose of Prothiaden (dothiepin, dosulepin) and Lentizol (sustained-release amitriptyline) in depressed elderly patients. J Int Med Res 1981;9(2):108–12

Kielholz P, Terzani S, Gastpar M, et al: Behandlung therapieresistenter Depressionen ohne Elektroschock. Dtsch Med Wochenschr 1981 May 22;106(21):671–3 (Eng. Abstr.) (Ger)

Kijne B, Rasmussen H, Kirk L: Lithiumdosis og alder. Ugeskr Laeger 1981 Jan;143(3):119–20 (Eng. Abstr.) (Dan)

Kilbinger H, Wessler I: Pre- and postsynaptic effects of muscarinic agonists in the guinea-pig ileum. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):259–66

Kilbinger H, Kruel R: Choline inhibits acetylcholine release via presynaptic muscarine receptors. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):131–4

Kim DH, Akera T, Brody TM: Effects of quinidine on the cardiac-glycoside sensitivity of guinea-pig and rat heart. J Pharmacol Exp Ther 1981 Jun;217(3):559–65

Kim DH, Akera T, Brody TM: Interactions between quinidine and cardiac glycosides involving mutual binding sites in the guinea pig. J Pharmacol Exp Ther 1981 Jul;218(1):108–14

Kim JS, Uchimura H, Hirano M, et al: Type B monoamine oxidase activities toward beta-phenylethylamine in discrete hypothalamic and circumventricular nuclei of the rat. Biochem Pharmacol 1981 Apr; 30(8):893–5

Kim PS, Hess GP: Acetylcholine receptor-controlled ion flux in electroplax membrane vesicles: identification and characterization of membrane properties that affect ion flux measurements. J Membr Biol 1981 Feb 28;58(3):203–11

Kim RA, Lukacs J, Tanaka RD, et al: Effects of hycanthone and praziquantel on monoamine oxidase and cholinesterases in Schistosoma mansoni. J Parasitol 1981 Feb;67(1):20–3

Kimball CD, Chang CM, Huang SM, et al: Immunoreactive endorphin peptides and prolactin in umbilical vein and maternal blood. Am J Obstet Gynecol 1981 May 15;140(2):157–64

Kimoto Y, Tohyama M, Satoh K, et al: Fine structure of rat cerebellar noradrenaline terminals as visualized by potassium permanganate 'in situ perfusion' fixation method. Neuroscience 1981;6(1):47–58

Kimura T, Share L, Wang BC, et al: The role of central adrenoreceptors in the control of vasopressin release and blood pressure. Endocrinology 1981 May;108(5):1829–36

King JA, Millar RP: TRH, GH-RIH, and LH-RH in metamorphosing Xenopus laevis. Gen Comp Endocrinol 1981 May;44(1):20–7

King JA, Millar RP: Radioimmunoassay of methionine(5)-enkephalin sulphoxide: phylogenetic and anatomical distribution. Peptides (Fayetteville) 1980 Fall;1(3):211–6

Kishimoto T, Urakawa N: The inhibitory effect of lithium of high-K induced contraction in guinea-pig taenia coli. Naunyn Schmiedebergs Arch Pharmacol 1980;315(1):69–76

Kitchen I, Hart SL: Differential loss of biological activity of the enkephalins induced by current. Eur J Pharmacol 1981 Jan 29; 69(3):393–6

Kleinrok Z, Ossowska G: Wpływ trójheksyfenidylu na antyamfetaminowe dzialanie flufenazyny. Ann Univ Mariae Curie Sklodowska [Med] 1979; 34:341–5 (Eng. Abstr.) (Pol)

Kline NS: Classification of drugs and patients to achieve maximum therapeutic response. Prog Neuropsychopharmacol 1980;4(4–5):491–4

Kline NS: Anxiety and/or the depressive syndromes. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):271–6

Klotz U: Determination of bromazepam by gas-liquid chromatography and its application for pharmacokinetic studies in man. J Chromatogr 1981 Mar 13;222(3):501–6

Knoth J, Isaacs JM, Njus D: Amine transport in chromaffin granule ghosts. pH dependence implies cationic form is translocated. J Biol Chem 1981 Jul 10;256(13):6541–3

Knox JM, Orr MW, Allen R, et al: The reliability of 5-hydroxytryptamine induced platelet aggregation responses in schizophrenic patients treated with neuroleptic drugs. Br J Clin Pharmacol 1981 Mar;11(3):261–3

Kobayashi H, Yuyama A, Imajo S, et al: Effects of acute and chronic administration of DDVP (dichlorvos) on distribution of brain acetylcholine in rats. J Toxicol Sci 1980 Nov;5(4):311–9

Kobayashi S, Kyui S, Yoshida T, et al: Absorption, distribution and excretion of 14C-pirenzepine in rats. Accumulation characteristics after multiple dose regimen. Arzneimittelforsch 1981;31(4):679–90

Koch B, Sakly M, Lutz-Bucher B: Modulation by transcortin-like binding sites of uptake and distribution of glucocorticoids by dispersed pituitary cells. Mol Cell Endocrinol 1981 May;22(2):169–78

Kocián J, Kociánová J, Brodan V: Vliv kombinovaného geriatrického přípravku na sérové bílkoviny a jaterní zkoušky. Cesk Gastroenterol Vyz 1981 Mar;35(2):49–53 (Eng. Abstr.) (Cze)

Kocsis JH, Frances A, Kalman TP, et al: The effect of psychobiological research on treatment outcome. A controlled study. Arch Gen Psychiatry 1981 May;38(5):511–5

Koczkas S, Holmberg G, Wedin L: A pilot study of the effect of the 5-HT-uptake inhibitor, zimelidine, on phobic anxiety. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):328–41

Koek W, Slangen JL: Habituation of the head-poke response: effects of an amphetamine-barbiturate mixture, PLG and fenfluramine. Psychopharmacology (Berlin) 1981;72(3):251–6

Koga Y, Downes H, Taylor SM: Direct and indirect actions of dopamine on tracheal smooth muscle. Naunyn Schmiedebergs Arch Pharmacol 1980;315(1):15–20

Koide T, Matsushita H: An enhanced sensitivity of muscarinic cholinergic receptor associated with dopaminergic receptor subsensitivity after chronic antidepressant treatment. Life Sci 1981 Mar 9;28(10):1139–45

Kojima H, Fukushima S, Hirono T, et al: Biochemical and histochemical studies on catecholamines in bullfrog spinal ganglia. J Neurochem 1981 Jun;36(6):2106–9

Kojima M, Kim JS, Uchimura H, et al: Effect of thyroidectomy on choline acetyltransferase in rat hypothalamic nuclei. Brain Res 1981 Mar 23; 209(1):227–30

Kolakowska T, Fraser S, Franklin M, et al: Neuroendocrine tests during treatment with neuroleptic drugs: I. Plasma prolactin response to chlorpromazine challenge. Psychopharmacology (Berlin) 1981; 72(3):283–5

Kolinová M, Mares P, Fischer J: Effect of pentobarbital on thalamo- and hippocampocortical processes in rats. Physiol Bohemoslov 1981; 30(2):139–48

Komiskey HL, Cook TM, Lin CF, et al: Impairment of learning or memory in the mature and old rat by diazepam. Psychopharmacology (Berlin) 1981;73(3):304–5

Konevskii AG, Gavrikov KV, Dvoretskaia MN: O znachenii neiroreguliatornykh vzaimootnoshenii v transplantogii. Vestn Khir 1980 Dec;125(12):88–91 (Eng. Abstr.) (Rus)

König L: Die Lithiumdosis in Relation zu Körpergewicht und Alter bei der Recidivprophylaxe phasischer psychosen. Agressologie 1980; 21(A):15–7 (Eng. Abstr.) (Ger)

AUTHOR SECTION

Koninckx PR, Brosens IA, Verhoeven G, et al: Increased postovulatory plasma follicle stimulating hormone levels in the luteinized unruptured follicle syndrome: a role for inhibin? Br J Obstet Gynaecol 1981 May; 88(5):525–9

Konturek SJ, Jaworek J, Tasler J, et al: Effect of substance P and its C–terminal hexapeptide on gastric and pancreatic secretion in the dog. Am J Physiol 1981 Jul;241(1):G74–81

Konturek SJ, Tasler J, Jaworek J, et al: Gastrointestinal secretory, motor, circulatory, and metabolic effects of prosomatostatin. Proc Natl Acad Sci USA 1981 Mar;78(3):1967–71

Korcok M: Tranquilizers not overprescribed for anxiety [news] JAMA 1981 Jul 3;246(1):14

Korkach VI: Sostoianie zhelez vnutrennel sekretsii pri gipodinamii (obzor literatury). Vrach Delo 1981 Feb;(2):11–6 (73 ref.) (Rus)

Kornetsky C, Esposito RU: Reward and detection thresholds for brain stimulation: dissociative effects of cocaine. Brain Res 1981 Mar 30; 209(2):496–500

Korneyev AY, Factor MI: Increase of benzodiazepine binding to the membranes isolated in the presence of diazepam. Eur J Pharmacol 1981 Apr 24;71(1):127–30

Koroscil TM, Gallant S: The phosphorylation of adrenal proteins in response to adrenocorticotropic hormone. J Biol Chem 1981 Jul 10; 256(13):6700–7

Kosaki G, Nomura T, Kambayashi J: The mechanism of the inhibitory effect of protease inhibitors on platelet aggregation and cellular synthesis of prostaglandins. I. The effect on the release of arachidonic acid from phospholipids. Thromb Res 1980 Dec 1–15;20(5–6):587–98

Kostellow AB, Ziegler D, Morrill GA: Regulation of Ca2+ and cyclic AMP during the first meiotic division in amphibian oocytes by progesterone. J Cyclic Nucleotide Res 1980;6(5):347–58

Kostowski W, Plaznik A, Pucilowski O, et al: Lesion of serotonergic neurons antagonizes clonidine induced suppression of avoidance behavior and locomotor activity in rats. Psychopharmacology (Berlin) 1981;73(3):261–4

Kovács GL, Versteeg DH, de Kloet ER, et al: Passive avoidance performance correlates with catecholamine turnover in discrete limbic brain regions. Life Sci 1981 Mar 9;28(10):1109–16

Kovács GL, Bohus B, De Wied D: Retention of passive avoidance behavior in rats following alpha– and gamma–endorphin administration: effects of post–learning treatments. Neurosci Lett 1981 Feb 23;22(1):79–82

Kow LM, Paden CM, Pfaff DW: Dispensability of spinal monoaminergic systems in mediating the lordosis reflex of the female rat. Pharmacol Biochem Behav 1981 May;14(5):707–11

Kowalska MA, Szweda–Lewandowska Z, Puchala M, et al: Changes in the tryptophan fluorescence in gamma–irradiated human haemoglobin. Int J Radiat Biol 1981 Jan;39(1):21–30

Kozlov IA, Milgrom YM, Tsybovski IS: Isolation of alpha–subunits of factor F1 from submitochondrial particles and the reconstitution of active ATPase from isolated alpha–subunits and beta–subunits bound to the mitochondrial membrane. Biochem J 1980 Nov 15;192(2):483–8

Kozlov VK, Markosian RA, Filatova LV: Gradient pH na membranakh serotoninovykh granul trombotsitov: printsipy izucheniia s pomoshch'iu fliuorestsentnykh aminoproizvodnykh akridina. Biull Eksp Biol Med 1981 Feb;91(2):155–7 (Eng. Abstr.) (Rus)

Kozlovskaia MM, Kharlamov AN, Raevskii KS, et al: Rol'GAMK–ergicheskogo zvena v razvitii trankviliziruiushchego éffekta u koshek. Biull Eksp Biol Med 1981;91(1):45–8 (Eng. Abstr.) (Rus)

Kozlowski GP, Chu L, Hostetter G, et al: Cellular characteristics of immunolabeled luteinizing hormone releasing hormone (LHRH) neurons. Peptides (Fayetteville) 1980 Spring;1(1):37–46

Kraemer GW, Breese GR, Prange AJ Jr, et al: Use of 6–hydroxydopamine to deplete brain catecholamines in the rhesus monkey: effects on urinary catecholamine metabolites and behavior. Psychopharmacology (Berlin) 1981;73(1):1–11

Kraeuchi K, Gentsch C, Feer H: Individually reared rats: alteration in noradrenergic brain functions. J Neural Transm 1981;50(2–4):103–12

Krall A, Spring–Mills E: Effects of bromocriptine and perphenazine on male accessory sex glands. I. The seminal vesicles. Arch Androl 1981 Jun;6(4):295–300

Krall JF, Connelly M, Weisbart R, et al: Age–related elevation of plasma catecholamine concentration and reduced responsiveness of lymphocyte adenylate cyclase. J Clin Endocrinol Metab 1981 May;52(5):863–7

Kraus–Friedmann N, Zimniak P: Glucagon and epinephrine–stimulated phospholipid methylation in hepatic microsomes. Life Sci 1981 Mar 30;28(13):1483–8

Krausz LM, Hitz JB, Buckler RT, et al: Substrate–labeled fluorescent immunoassay for phenobarbital. Ther Drug Monit 1980;2(3):261–72

Křepela E: Možnost biodegradace prolinových exorfinu v gastrointestinálním ústrojí. Cesk Gastroenterol Vyz 1981 Mar; 35(2):68–71 (Eng. Abstr.) (Cze)

Krivosheev OG, Syutkin EA, Antonov AS, et al: Interrelationship between pineal gland and hypothalamic–hypophyseal complex. IV. Effect of pinealectomy on luteinizing function of rat hypophysis. Neurosci Behav Physiol 1980 Nov–Dec;10(6):480–4

Kriwaczek VM, Schwyzer R, Gillan MG, et al: Tobacco mosaic virus–enkephalin conjugates: potentiation of opioid activity. Peptides (Fayetteville) 1981 Spring;2(1):89–92

Kršiak M, Sulcová A, Tomasiková Z, et al: Drug effects on attack defense and escape in mice. Pharmacol Biochem Behav 1981;14 Suppl 1:47–52

Krstulovic AM, Friedman MJ, Sinclair PR, et al: Complementary use of amperometric and spectrophotometric detection for concurrent monitoring of serum tryptophan metabolites by reversed–phase liquid chromatography. Clin Chem 1981 Jul;27(7):1291–5

Kruszewska A, Langwiński R: Wpływ rezerpiny na objawy abstynencji morfinowej u myszy. Ann Univ Mariae Curie Sklodowska [Med] 1979; 34:133–9 (Pol)

Kryzhanovsky GN, Aliev MN: The stereotyped behavior syndrome: a new model and proposed therapy. Pharmacol Biochem Behav 1981 Mar; 14(3):273–81

Kuba K, Kato E, Kumamoto E, et al: Sustained potentiation of transmitter release by adrenaline and dibutyryl cyclic AMP in sympathetic ganglia. Nature 1981 Jun 25;291(5817):654–6

Kudo Y, Ajioka H, Fukuda H: Antagonistic action of baclofen on substance P–induced depolarization in the isolated spinal cord of the frog. Gen Pharmacol 1981;12(3):145–9

Kudriavtseva GV, Denisova II: Opredelenie periova poluzhizni kliuchevykh fermentov pentozofosfatnogo puti––gliukozo–6–fosfatdegidrogenazy i transketolazy. Biokhimiia 1980 Jan;45(1):118–23 (Eng. Abstr.) (Rus)

Kuhn CM, Vogel RA, Mailman RB, et al: Effect of 5,7–dihydroxytryptamine on serotonergic control of prolactin secretion and behavior in rats. Psychopharmacology (Berlin) 1981;73(2):188–93

Kuhn DM, O'Callaghan JP, Lovenberg W: The role of calmodulin in the activation of tryptophan hydroxylase by phosphorylating conditions. Ann NY Acad Sci 1980;356:399

Kuhn E, Hozák R: Psychometric studies of pirenzepine. Scand J Gastroenterol [Suppl] 1980;15(66):47–53

Kühne GE, Grünes JU: Zur Psychopathologischen Befunddokumentation in der Psychopharmakotherapie. Agressologie 1980;21(A):1–5 (Eng. Abstr.) (Ger)

Kulay MN, Simões M de J, Novo NF, et al: Comportamento do número de lisossomos na placenta de ratas prenhes submetidas ao stress agudo e previamente tratadas com o cloridrato de 1–isopropilamino–3–(1–naftil–oxi)–2–propranolol. Rev Paul Med 1980 Nov–Dec;96(5–6):96–9 (Eng. Abstr.) (Por)

Kulkosky PJ, Gray L, Gibbs J, et al: Feeding and selection of saccharin after injections of bombesin, LiCl, and NaCl. Peptides (Fayetteville) 1981 Spring;2(1):61–4

Kümpel Q: Psychopharmakologie in der Gerontopsychiatrie. Agressologie 1980;21(A):67–9 (Eng. Abstr.) (Ger)

Kuo JF, Andersson RG, Wise BC, et al: Calcium–dependent protein kinase: widespread occurrence in various tissues and phyla of the animal kingdom and comparison of effects of phospholipid, calmodulin, and trifluoperazine. Proc Natl Acad Sci USA 1980 Dec;77(12):7039–43

Kuramoto T, Haber B: The K+ liquid ion exchange electrode system: responses to drugs and neurotransmitters. J Neurosci Res 1981; 6(1):37–48

Kurland AA, Nagaraju A, Hanlon TE, et al: A comparison of dopamine receptor blocking assay with plasma drug levels of haloperidol in schizophrenic patients. J Clin Pharmacol 1981 Jan;21(1):42–7

Kurland AA, Nagaraju A: Viloxazine and the depressed schizophrenic––methodological issues. J Clin Pharmacol 1981 Jan; 21(1):37–41

Kuruvilla A, Uretsky N: The interaction of chlordiazepoxide and sodium valproate in the nucleus accumbens of the rat. Life Sci 1981 Jan 26; 28(4):393–9

Kuss HJ, Feistenauer E: Quantitative high–performance liquid chromatographic assay for the determination of maprotiline and oxaprotiline in human plasma. J Chromatogr 1981 Jan 16;204:349–53

Kwok YH, Mitchelson F: Comparison of the antimuscarinic activity of mianserin and amitriptyline in the cat superior cervical ganglion. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):161–4

L

Laborit G, Baron C, Topal G, et al: Intérêt du gamma hydroxybutyrate de Na dans la protection cérébrale au cours des hypoxies sévères chez le lat. Agressologie 1980;21(4):189–97 (Eng. Abstr.) (Fre)

Labrie F, Ferland L, Veilleux R, et al: Influence of estrogens on tuberoinfundibular and striatal dopaminergic systems in the rat. Acta Psychiatr Belg 1980 Sep–Oct;80(5):658–73

Labech B, Heins J, Hilse H, et al: Die Aktivität der Dipeptidyl–Peptidase IV in verschiedenen Organen und Geweben der Ratte und ihre mögliche Beziehung zum Substanz–P–Metabolismus. Pharmazie 1981;36(2):161–3 (Ger)

Lackovic Z, Parenti M, Neff NH: Simultaneous determination of femtomole quantities of 5–hydroxytryptophan, serotonin and 5–hydroxyindoleacetic acid in brain using HPLC with electrochemical detection. Eur J Pharmacol 1981 Jan 29;69(3):347–52

Lader SR: A radioreceptor assay for neuroleptic drugs in plasma.

AUTHOR SECTION

J Immunoassay 1980;1(1):57–75

Laemmel K: Psychopharmaka in der Praxis. Praxis 1981 Feb 3;70(6):192–9 (Eng. Abstr.) (Ger)

Lagacé L, Labrie F, Antakly T, et al: Sensitivity of rat adenohypophyseal cells to estradiol and LHRH during long-term culture. Am J Physiol 1981 Jun;240(6):E602–8

Lagerspetz KY: Comparative psychopharmacology. Curr Dev Psychopharmcol 1981;6:1–43 (182 ref.)

Lakoski JM, Mohrland JS, Gebhart GF: The effect of morphine on the content of serotonin, 5-hydroxyindole acetic acid and substance-P in the nuclei raphe magnus and reticularis gigantocellularis. Life Sci 1980 Dec 22–29;27(25–26):2639–44

Lakowicz JR, Cherek H: Resolution of heterogeneous fluorescence from proteins and aromatic amino acids by phase-sensitive detection of fluorescence. J Biol Chem 1981 Jun 25;256(12):6348–53

Lam DM, Hollyfield JG: Localization of putative amino acid neurotransmitters in the human retina. Exp Eye Res 1980 Dec; 31(6):729–32

Lambert MA, Moss CW: Production of p-hydroxyhydrocinnamic acid from tyrosine by Peptostreptococcus anaerobius. J Clin Microbiol 1980 Aug;12(2):291–3

Lambertini F, Re G, Cavalli G: Effetto del fenobarbital sulla attività antimitotica della vincristina e della colchicina. Arch Sci Med (Torino) 1980 Jul–Sep;137(3):405–10 (Eng. Abstr.) (Ita)

Lambie DG, Johnson RH: The effects of phenytoin on phenobarbitone and primidone metabolism. J Neurol Neurosurg Psychiatry 1981 Feb; 44(2):148–51

Lambrecht G: Struktur–und Konformations–Wirkungs–Beziehungen heteroxyklischer Acetylcholin–analoga. 12. Mitteilung: Synthese und cholinerge Eigenschaften stereoisomerer 3–Acetoxythiacyclohexame). Arzneimittelforsch 1981;31(4):634–40 (Eng. Abstr.) (Ger)

LaMotte CC, de Lanerolle NC: Human spinal neurons: innervation by both substance P and enkephalin. Neuroscience 1981;6(4):713–23

Lampe RM, Weir MR, McLeod HL, et al: A clinical trial of antihistamine, decongestant, or placebo in antibiotic-treated acute otitis media followed with pneumatic otoscopy and impedance tympanometry. Milit Med 1981 Apr;146(4):259–61

Lane DE: Self-medication of psychiatric patients. J Psychiatr Nurs 1981 May;19(5):27–8

Lane MJ, Reece PA, Schapel GJ: Excessive frequency of phenytoin dosage [letter] Med J Aust 1981 Feb 21;1(4):191–2

Lanfumey L, Adrien J: Récepteurs beta-adrénergiques et sommeil paradoxal chez le Rat. C R Acad Sci [D] (Paris) 1981 Mar 2;292(9):645–7 (Eng. Abstr.) (Fre)

Lanfumey L, Arluison M, Adrien J: Destruction of noradrenergic cell bodies by intracerebral 6-hydroxydopamine in the newborn rat. Brain Res 1981 Jun 15;214(2):445–50

Lange E, König L, Eymann B: Besonderheiten und Schwierigkeiten beim gezielten medikamentösen Einsatz in der Behandlung von chronisch Schizophrenen (schizophrener 'Defekt'). Psychiatr Neurol Med Psychol (Leipz) 1981 Jan;33(1):34–8 (Eng. Abstr.) (Ger)

Langer G, Pühringer W: Haloperidol and droperidol treatment in schizophrenics. Clinical application of the 'prolactin-model'. Acta Psychiatr Belg 1980 Sep–Oct;80(5):574–83

Langmoen IA, Segal M, Andersen P: Mechanisms of norepinephrine actions on hippocampal pyramidal cells in vitro. Brain Res 1981 Mar 16;208(2):349–62

Lanoir J, Ternaux JP, Pons C, et al: Long-term effects of a tryptophan-free diet on serotonin metabolism and sleep-waking balance in rats. Exp Brain Res 1981;41(3–4):346–57

Lapin A, Karobath M: A sensitive and specific method for the determination of chlorimipramine and desmethylchlorimipramine in plasma using selected ion monitoring with chemical ionization. Biomed Mass Spectrom 1980 Nov;7(11–12):588–91

Larking P: Gas chromatographic determination of clonazepam. J Chromatogr 1980 Dec 12;221(2):399–402

Laskowska-Klita T, Bong M: The effect of unilateral nephrectomy and sham operation on tyrosine content and activity of tyrosine aminotransferase in the rat. Horm Metab Res 1981 Mar;13(3):155–7

Laufer R, Chorev M, Gilon C, et al: Persistent action of N-methylated analogs of substance P on rat parotid slices. FEBS Lett 1981 Jan 26; 123(2):291–4

Laurberg P, Orskov H: Release of somatostatin-like immunoreactivity from the perfused canine thyroid. Selective stimulatory effect of calcium ions. J Clin Invest 1981 May;67(5):1451–6

Lavallée M, de Champlain J, Nadeau RA: Reflexly induced inhibition of catecholamine release through a peripheral muscarinic mechanism. Can J Physiol Pharmacol 1980 Nov;58(11):1334–41

Laven R, Schäfer EA: Freisetzung von Norfenefrin-HCl aus Depotpräparaten in einem In-vitro-Lösemodell. Rechnerische Simulation von Wirkstoffprofilen mit Hilfe pharmakokinetischer Parameter und Vergleich mit In-vivo-Wirkungsverläufen. Arzneimittelforsch 1981;31(2):353–6 (Eng. Abstr.) (Ger)

Lavielle S, Ling NC, Guillemin RC: Solid-phase synthesis of two glycopeptides containing the amino acid sequence 5 to 9 of somatostatin. Carbohydr Res 1981 Mar 2;89(2):221–8

Lavielle S, Ling NC, Saltman R, et al: Synthesis of a glycotripeptide and a glycosomatostatin containing the 3-O-(2-acetamido-2-deoxy-beta-D-glucopyranosyl)-L-serine residue. Carbohydr Res 1981 Mar 2;89(2):229–36

Lavretskaia EF, Klusha VE, Svirskis ShV, et al: O spektre deistviia nekotorykh tripeptidov na tsentral'nuiu nervnuiu sistemu. Dokl Akad Nauk SSSR 1981;257(3):741–5 (Rus)

Law FC: Metabolic disposition and irreversible binding of phencyclidine in rats. Toxicol Appl Pharmacol 1981 Feb;57(2):263–72

Law FC, So EM: Induction studies of delta 1-tetrahydrocannabinol metabolism by rat and rabbit lungs. Comp Biochem Physiol [C] 1981; 69C(1):19–23

Lawrence JM, Hamill RW, Cochard P, et al: Effects of spinal cord transection on synapse numbers and biochemical maturation in rat lumbar sympathetic ganglia. Brain Res 1981 May 11;212(1):83–8

Le Fur G, Mizoule J, Burgevin MC, et al: Multiple benzodiazepine receptors: evidence of dissociation between anticonflict and anticonvulsant properties by PK 8165 and PK 9084 (two quinoline derivatives). Life Sci 1981 Mar 30;28(13):1439–48

Leander S, Håkanson R, Sundler F: Nerves containing substance P, vasoactive intestinal polypeptide, enkephalin or somatostatin in the guinea-pig taenia coli. Distribution, ultrastructure and possible functions. Cell Tissue Res 1981;215(1):21–39

Lechin F, van der Dijs B, Gomez F, et al: Pharmacomanometric studies of colonic motility as a guide to the chemotherapy of schizophrenia. J Clin Pharmacol 1980 Nov–Dec;20(11–12):664–71

Lecrubier Y, Puech AJ, Frances H, et al: Beta-adrenergic stimulation and antidepressant activity. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):173–8

Lederman E, Lederman RP, Work BA Jr, et al: Maternal psychological and physiologic correlates of fetal-newborn health status. Am J Obstet Gynecol 1981 Apr 15;139(8):956–8

Lee KS, Hume JR, Giles W, et al: Sodium current depression by lidocaine and quinidine in isolated ventricular cells. Nature 1981 May 28; 291(5813):325–7

Lees G, Chubb I, Freeman C, et al: Effect of nerve activity on transport of nerve growth factor and dopamine beta-hydroxylase antibodies in sympathetic neurones. Brain Res 1981 Jun 9;214(1):186–9

Lees GJ, Geffen LB, Rush RA: Phentolamine increases neuronal binding and retrograde transport of dopamine beta-hydroxylase antibodies. Neurosci Lett 1981 Mar 10;22(2):115–8

Leff S, Adams L, Hyttel J, et al: Kainate lesion dissociates striatal dopamine receptor radioligand binding sites. Eur J Pharmacol 1981 Mar 5;70(1):71–5

Legrand J, Soulier J: Le syndrome confusionnel consécutif aux opérations endoculaires. J Fr Ophtalmol 1981;4(2):143–6 (Eng. Abstr.) (Fre)

Lehy T, Peranzi G, Cristina ML: Correlative immunocytochemical and electron microscopic studies: identification of (entero)glucagon-somatostatin- and pancreatic polypeptide-like-containing cells in the human colon. Histochemistry 1981;71(1):67–80

Leighton HJ, Waggoner WG: Measurement of tyrosine hydroxylase activity in nerve terminals of rat hippocampus, hypothalamus, and striatum using an improved assay for tyrosine hydroxylase. Life Sci 1981 Jan 26;28(4):385–91

Lejeune J, Maunoury C, Réthoré MO, et al: Site fragile Xq27 et métabolisme des monocarbonés. Diminution significative de la fréquence de la lacune chromosomique par traitement in vitro et in vivo. C R Acad Sci [D] (Paris) 1981 Feb 16;292(7):491–3 (Eng. Abstr.) (Fre)

Lemaire S, Derome G, Tseng R, et al: Distinct regulations by calcium of cyclic GMP levels and catecholamine secretion in isolated bovine adrenal chromaffin cells. Metabolism 1981 May;30(5):462–8

Lemke HD, Oesterhelt D: The role of tyrosine residues in the function of bacteriorhodopsin. Specific nitration of tyrosine 26. Eur J Biochem 1981 Apr,115(3):595–604

Lemoine P, Achaintre A, Balvay G, et al: Double-blind trial of amineptine and clomipramine in the treatment of depression. Curr Med Res Opin 1981;7(4):234–40

Lenehan T, Omer LM, Darragh A: Effects of Ro 11-2465, a new psychotropic agent on the uptake of serotonin by human platelets—in vitro determination of the IC50. Arch Int Pharmacodyn Ther 1981 Jan; 249(1):147–52

Lenoir L, Lavoine JR, Ostapzeff G: Le marquage médical du corps. Ou quand le médecin se fait stigmatiseur. Acta Med Leg Soc (Liege) 1980; 30(1):43–69 (Fre)

León CA: The temporo-spatial context. A neglected aspect of the depressive response. Acta Psychiatr Scand 1981 Feb;63(2):129–46

Leonardi R, Toffoli C, Rigamonti L, et al: Il vasoactive intestinal polypeptide (VIP). Suo ruolo nella fisiologia dell'apparato digerente. Minerva Med 1981 Apr 2;72(13):801–5 (Eng. Abstr.) (Ita)

LeRoith D, Liel Y, Sack J, et al: The TSH response to TRH is exaggerated in primary testicular failure and normal in the male castrate. Acta Endocrinol (Copenh) 1981 May;97(1):103–8

Lesse H: Prolonged effects of cocaine on hippocampal activity.

AUTHOR SECTION

Commun Psychopharmacol 1980;4(3):247-54

Lesser IM, Friedmann CT: Attitudes toward medication change among chronically impaired psychiatric patients. Am J Psychiatry 1981 Jun; 138(6):801-3

Levandowsky M: Endosymbionts, biogenic amines, and a heterodyne hypothesis for circadian rhythms. Ann NY Acad Sci 1981;361:369-75

Levick SE, Jalali B, Strauss JS: With onions and tears: a multidimensional analysis of a counter-ritual. Fam Process 1981 Mar;20(1):77-83

Lewis DV Jr, Zbicz KL, Nepp ME, et al: Diphenylhydantoin enhances early adaptation in Aplysia giant neurons. J Pharmacol Exp Ther 1981 Jul;218(1):41-5

Lewis JW, Ryan SM, Arnold AP, et al: Evidence for a catecholaminergic projection to area X in the zebra finch. J Comp Neurol 1981 Feb 20; 196(2):347-54

Lewis PJ, Lowing RK, Gompertz D: Automated discrete kinetic method for erythrocyte acetylcholinesterase and plasma cholinesterase. Clin Chem 1981 Jun;27(6):926-9

Lhuguenot JC, Maume BF: A method for the analysis of catecholamines by selected ion monitoring and 14C isotope dilution in adrenal medullary cell culture. Biomed Mass Spectrom 1980 Nov;7(11-12):529-32

Lichtenberger LM, Shaw LS, Bailey RB: Release of somatostatin from rodent antral mucosae maintained in organ culture. Am J Physiol 1981 Jul;241(1):G59-66

Lieberman J: Cholinergic rebound in neuroleptic withdrawal syndromes. Psychosomatics 1981 Mar;22(3):253-4

Liebowitz MR, Klein DF: Interrelationship of hysteroid dysphoria and borderline personality disorder. Psychiatr Clin North Am 1981 Apr; 4(1):67-87

Liebowitz MR, Klein DF: Differential diagnosis and treatment of panic attacks and phobic states. Annu Rev Med 1981;32:583-99 (46 ref.)

Lim BT, Kimura T: Conformation prediction and spectral studies on adrenodoxin. The accessibility of the tyrosine residue at position 82 in the polypeptide. J Biol Chem 1981 May 10;256(9):4400-6

Lin MT, Chandra A, Chern YF, et al: Intracerebroventricular injection of sympathomimetic drugs inhibits both heat production and heat loss mechanisms in the rat. Can J Physiol Pharmacol 1980 Aug;58(8):896-902

Lin MT: The catecholamine precursor L-3,4-dihydroxyphenylalanine inhibits both heat production and heat loss mechanisms in the rabbit. Can J Physiol Pharmacol 1980 Aug;58(8):956-64

Lin MT, Chandra A, Chern YF, et al: Effects of intracerebroventricular injection of d-amphetamine on metabolic, respiratory, and vasomotor activities and body temperatures in the rat. Can J Physiol Pharmacol 1980 Aug;58(8):903-8

Lin MT, Chandra A, Chern YF, et al: Effects of DL-propranolol on the thermoregulatory responses of rats at different ambient temperatures. Experientia 1981 Apr 15;37(4):370-1

Lin MT, Chandra A, Chen YM: Lesions in the substantia nigra of rats induce thermoregulatory deficit in the cold. Experientia 1981 Mar 15; 37(3):284-6

Lin XT: [Human thyrotropin radioimmunoassay (heterogenous system) and its clinical application (author's transl)] Chung Hua Nei Ko Tsa Chih 1979;18(3):192-6 **(Chi)**

Lindbom LO, Forsberg T: Cardiovascular effects of zimelidine and other antidepressant in conscious rats. Acta Psychiatr Scand [Suppl] 1981; 63(Suppl 290):380-4

Lindeke B, Brötell H, Karlén B, et al: Determination of oxybutynin (4-diethylaminobut-2-ynyl 2-cyclohexyl-2-phenylglycolate) in serum and urine by gas chromatography/mass spectrometry with single ion detection. Acta Pharm Suec 1981;18(1):25-34

Linden W: Exposure treatments for focal phobias. A review. Arch Gen Psychiatry 1981 Jul;38(7):769-75 (49 ref.)

Lindgren JE: Guide to the analysis of cocaine and its metabolites in biological material. J Ethnopharmacol 1981 Mar-May;3(2-3):337-51 (81 ref.)

Lindström P: Further studies on 5-hydroxytryptamine transport in pancreatic islets and isolated beta-cells. Br J Pharmacol 1981 Jun; 73(2):385-91

Lindvall O, Ingvar M, Stenevi U: Effects of methamphetamine on blood flow in the caudate-putamen after lesions of the nigrostriatal dopaminergic bundle in the rat. Brain Res 1981 Apr 27;211(1):211-6

Linkowski P, Mendlewicz J: 1. Les neuroleptiques et les mono-amines cerebrales. Acta Psychiatr Belg 1980 Sep-Oct;80(5):559-73 (38 ref.) **(Fre)**

Linnoila M, George L, Guthrie S, et al: Effect of alcohol consumption and cigarette smoking on antidepressant levels of depressed patients. Am J Psychiatry 1981 Jun;138(6):841-2

Lipcsey A: A schizophrenia biokémiai megközelítése. Orv Hetil 1980 Nov 23;121(47):2863-70 **(Hun)**

Lippton HL, Chapnick BM, Kadowitz PJ: Influence of prostaglandins on vasoconstrictor responses in the hindquarters vascular bed of the cat. Prostaglandins Med 1981 Feb;6(2):183-202

Lipshultz S, Shanfeld J, Chacko S: Emergence of beta-adrenergic sensitivity in the developing chicken heart. Proc Natl Acad Sci USA 1981 Jan;78(1):288-92

List SJ, Seeman P: Resolution of dopamine and serotonin receptor components of [3H]spiperone binding to rat brain regions. Proc Natl Acad Sci USA 1981 Apr;78(4):2620-4

Lisý V, Dutton GR, Currie DN: Cerebellar specific gamma-glutamyltranspeptidase activation by GABA and taurine in postnatal mouse brain. Life Sci 1980 Dec 22-29;27(25-26):2615-20

Liu TC, Jackson GL: Differential effects of cyclic nucleotide analogues and GnRH on LH synthesis and release. Am J Physiol 1981 Jul; 241(1):E6-13

Lo Dico G, Milia S, Firinu C, et al: Impiego di farmaci dopaminergici (piridossina, 2-bromo-alfa-ergocriptina, piribedil) nel blocco della lattazione. Minerva Ginecol 1980 Sep;32(9):771-9 (Eng. Abstr.) **(Ita)**

Lobley GE, Robins SP, Palmer RM, et al: Measurement of the rates of protein synthesis in rabbits. A method for the estimation of rates of change in the specific radioactivities of free amino acids during continuous infusions. Biochem J 1980 Nov 15;192(2):623-9

Loewy AD, McKellar S: Serotonergic projections from the ventral medulla to the intermediolateral cell column in the rat. Brain Res 1981 Apr 27;211(1):146-52

Löffelholz K: Release of acetylcholine in the isolated heart. Am J Physiol 1981 Apr;240(4):H431-40 (101 ref.)

Logue JN, Sachais BA: Factors which affect antidepressant drug responses in a multicenter controlled trial [proceedings] Psychopharmacol Bull 1981 Jan;17(1):138-9

Loh YP, Jenks BG: Evidence for two different turnover pools of adrenocorticotropin, alpha-melanocyte-stimulating hormone, and endorphin-related peptides released by the frog pituitary neurointermediate lobe. Endocrinology 1981 Jul;109(1):54-61

Lolova I: Histochemical study of the cholinesterase activity in cat myenteric ganglia during postnatal development. J Neural Transm 1981; 50(2-4):297-310

Loney J, Whaley-Klahn MA, Ponto LB, et al: Predictors of adolescent height and weight in hyperkinetic boys treated with methylphenidate [proceedings] Psychopharmacol Bull 1981 Jan;17(1):132-4

Lonky SA, Gochman N, Smith S, et al: Amino acid analysis of elastin hydrolysates using a lithium citrate gradient: quantification of elastin from whole lung. Clin Chim Acta 1981 Mar 5;110(2-3):227-33

Loonen AJ, Soe-Agnie CJ, Soudijn W: Effects of halopemide on GABA receptor binding, uptake and release. Brain Res 1981 Apr 6; 210(1-2):485-92

Lorez H: Fluorescence histochemistry indicates damage of striatal dopamine nerve terminals in rats after multiple doses of methamphetamine. Life Sci 1981 Feb 23;28(8):911-6

Löscher W: Anticonvulsant activity of metabolites of valproic acid. Arch Int Pharmacodyn Ther 1981 Jan;249(1):158-63

Löscher W: Zum Wirkungsmechanismus der Antiepileptika. Tierexperimentelle Befunde zur Bedeutung von Neurotransmittern. Nervenarzt 1981 Feb;52(2):61-7 **(Ger)**

Löscher W, Schmidt D: Stability of gamma-aminobutyric acid in human cerebrospinal fluid and plasma [letter] Ther Drug Monit 1981;3(1):109

Lotter EC, Krinsky R, McKay JM, et al: Somatostatin decreases food intake of rats and baboons. J Comp Physiol Psychol 1981 Apr; 95(2):278-87

Loudon JB, Tiplady B, Ashcroft GW, et al: Zimelidine and amitriptyline in the treatment of depressive illness in general practice. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):454-63

Loughlin JS, Badger TM, Crowley WF Jr: Perifused pituitary cultures: a model for LHRH regulation of LH secretion. Am J Physiol 1981 Jun;240(6):E591-6

Louis JC, Vincendon G, Massarelli R, et al: Development of dopaminergic properties in cultured neurons from chick embryo cerebral hemispheres. Biochem Soc Trans 1981 Feb;9(1):104-5

Lowe TL, Cohen DJ, Miller S, et al: Folic acid and B12 in autism and neuropsychiatric disturbances of childhood. J Am Acad Child Psychiatry 1981 Winter;20(1):104-11

Lowy MT, Yim GK: Selective reduction by dexamethasone of stress-related hyperphagias. Life Sci 1980 Dec 22-29;27(25-26):2553-8

Lucas A, Aynsley-Green A, Blackburn AM, et al: Plasma neurotensin in term and preterm neonates. Acta Paediatr Scand 1981 Mar;70(2):201-6

Luchins DJ, Gillin JC, Wagner RL, et al: Piperidine in chronic schizophrenic patients: a controlled double-blind study. Biol Psychiatry 1981 Jan;16(1):91-5

Lucot JB, Horwitz J, Seiden LS: The effects of p-chloroamphetamine administration on locomotor activity and serotonin in neonatal and adult rats. J Pharmacol Exp Ther 1981 Jun;217(3):738-44

Luisi M, Franchi F, Kicovic PM: A group-comparative study of effects of Ovestin cream versus Premarin cream in post-menopausal women with vaginal atrophy. Maturitas 1980 Dec;2(4):311-9

Lundström J, Högberg T, Gesztonyi T, et al: Metabolism of zimelidine in rat, dog and man. Identification and synthesis of the principal metabolites. Arzneimittelforsch 1981;31(3):486-94

Lymangrover JR, Martin RA: Effects of extracellular potassium and 4-aminopyridine on corticosteroid secretion. Mol Cell Endocrinol 1981 Mar;21(3):199-210

AUTHOR SECTION

M

Maayan ML, Volpert EM, From A: Calcium depletion stimulates thyrozine release from the thyroid. Endocrinology 1981 May;108(5):1987–8

McAinsh J, Baber NS, Holmes BF, et al: Bioavailability of sustained release propranolol formulations. Biopharm Drug Dispos 1981 Jan–Mar; 2(1):39–48

McCalden TA, Rose L: Differential sensitivity of the two phases of ear artery contraction to intimal and adventitial norepinephrine. Experientia 1981 Mar 15;37(3):268–9

McCaleb ML, Myers RD: Cholecystokinin acts on the hypothalamic 'noradrenergic system' involved in feeding. Peptides (Fayetteville) 1980 Spring;1(1):47–9

McCarty R, Kvetnansky R, Kopin IJ: Plasma catecholamines in rats: daily variations in basal levels and increments in response to stress. Physiol Behav 1981 Jan;26(1):27–31

McDermott JR, Smith AI, Biggins JA, et al: Characterization and determination of neuropeptides by high-performance liquid chromatography and radioimmunoassay. J Chromatogr 1981 Mar 13; 222(3):371–9

McEvoy RC, Leung PE, Goggins JA: Tissue culture of fetal rat islets: corticosterone promotes D cell maintenance and function. Endocrinology 1981 Jun;108(6):2277–82

McEwen BS, Stephenson BS, Krey LC: Radioimmunoassay of brian tissue and cell nuclear corticosterone. J Neurosci Methods 1980 Oct;3(1):57–65

McGilveray IJ, Midha KK, Rowe M, et al: Bioavailability of 11 quinidine formulations adn pharmacokinetic variation in humans. J Pharm Sci 1981 May;70(5):524–9

McGrath PJ, Quitkin FJ, Stewart JW, et al: Novel antidepressants: a clinical trial of mianserin [proceedings] Psychopharmacol Bull 1981 Jan; 17(1):21–3

McIntosh CH, Pederson RA, Koop H, et al: Gastric inhibitory polypeptide stimulated secretion of somatostatinlike immunoreactivity from the stomach: inhibition by acetylcholine or vagal stimulation. Can J Physiol Pharmacol 1981 May;59(5):468–72

McIntyre HB, Firemark HM, Cho AK, et al: Computer analyzed EEG in amphetamine-responsive hyperactive children. Psychiatry Res 1981 Apr;4(2):189–97

McKauge L, Tyrer JH, Eadie MJ: Factors influencing simultaneous concentrations of carbamazepine and its epoxide in plasma. Ther Drug Monit 1981;3(1):63–70

McKearney JW: Individual differences in effects of tricyclic antidepressants and anticholinergic drugs on operant behavior in the squirrel monkey. Life Sci 1981 May 4;28(18):2049–54

McKinney WT Jr: Discussion of paper by Dr. Klaus Miczek [proceedings] Psychopharmacol Bull 1981 Jan;17(1):62–3

McKnew DH, Cytryn L, Buchsbaum MS, et al: Lithium in children of lithium-responding parents. Psychiatry Res 1981 Apr;4(2):171–80

McLean AJ, Isbister C, Bobik A, et al: Reduction of first-pass hepatic clearance of propranolol by food. Clin Pharmacol Ther 1981 Jul; 30(1):31–4

McLendon MH: Development of occupational and environmental health criteria for the F-16. Aviat Space Environ Med 1981 Mar;52(3):145–7

McLennan H, Liu J: The postexcitatory effects of acidic amino acids on spinal neurones. Can J Physiol Pharmacol 1981 Mar;59(3):239–43

McLoughlin L, Lowry PJ, Ratter SJ, et al: Characterisation of the pro opiocortin family of peptides in human cerebrospinal fluid. Neuroendocrinology 1981 Apr;32(4):209–12

MacMahon B: More on Bendectin [editorial] JAMA 1981 Jul 24–31; 246(4):371–2

McNeill TH, Scott DE, Sladek JR Jr: Simultaneous monoamine histofluorescence and neuropeptide immunocytochemistry: I. Localization of catecholamines and gonadotropin-releasing hormone in the rat median eminence. Peptides (Fayetteville) 1980 Spring; 1(1):59–68

McRae MA, Hanegan JL: The effect of para-chlorophenylalanine of thermoregulation in the Mongolian gerbil (Meriones unguiculatus). Comp Biochem Physiol [C] 1981;68C(2):181–6

MacVicar BA, Weir G, Riexinger K, et al: Paradoxical effects of lithium on field potentials of dentate granule cells in slices of rat hippocampus. Neuropharmacology 1981 May;20(5):489–96

Madoyan IA, Favorova OO, Kovaleva GK, et al: Affinity labelling of tryptophanyl-tRNA synthetase with mesitoyl-AMP. FEBS Lett 1981 Jan 26;123(2):156–60

Maeda K, Frohman LA: Neurotensin release by rat hypothalamic fragments in vitro. Brain Res 1981 Apr 6;210(1–2):261–9

Magnusson O, Nilsson LB, Westerlund D: Simultaneous determination of dopamine, DOPAC and homovanillic acid. Direct injection of supernatants from brain tissue homogenates in a liquid chromatography—electrochemical detection system. J Chromatogr 1980 Dec 12;221(2):237–47

Maguire KP, Norman TR, Burrows GD, et al: Simultaneous measurement of dothiepin and its major metabolites in plasma and whole blood by gas chromatography-mass fragmentography. J Chromatogr 1981 Mar 13;222(3):399–408

Magun BE, Fennie CW: Effects of hyperthermia on binding, internalization, and degradation of epidermal growth factor. Radiat Res 1981 Apr;86(1):133–46

Maigret B, Premilat S, Fournie-Zaluski MC, et al: Proposals for conformation of enkephalins related to opiate mu-pharmacophore. Biochem Biophys Res Commun 1981 Mar 16;99(1):267–74

Mains RE, Eipper BA: Differences in the post-translational processing of beta-endorphin in rat anterior and intermediate pituitary. J Biol Chem 1981 Jun 10;256(11):5683–8

Mairbäurl H, Humpeler E: The influence of adrenaline on the metabolism of erythrocytes in vitro. Biochem Soc Trans 1981 Feb;9(1):99–100

Makara GB, Stark E, Kárteszi M, et al: Effects of paraventricular lesions on stimulated ACTH release and CRF in stalk-median eminence of the rat. Am J Physiol 1981 Apr;240(4):E441–6

Makarov IA, Makarenko KI, Desiatnikova NV: Ob izmeneniiakh gormonal'nogo i lipidnogo obmenov pri khronicheskoi profintoksikatsii metilmetakrilatom. Gig Tr Prof Zabol 1981 Apr;(4):20–2 (Eng. Abstr.) (Rus)

Maksay G, Pálosi E, Tegyey Z, et al: Oxazepam esters. 3. Intrinsic activity, selectivity, and prodrug effect. J Med Chem 1981 May;24(5):499–502

Malanga CJ, Yong MC, O'Donnell JP: Pharmacological characterization of the dopaminergic stimulation of mucociliary particle transport by Mytilus edulis gill. Gen Pharmacol 1981;12(3):139–44

Malatino LS, Calandra C, Costa M, et al: Modificazioni giornaliere dei livelli di triptofano plasmatico in soggetti con depressione endogena. Riv Patol Nerv Ment 1979 Nov–Dec;100(6):340–6 (Eng. Abstr.) (Ita)

Malhotra RK, Ostrander JM, Hurley LH, et al: Chemical conversion of anthramycin 11-methyl ether to didehydroanhydroanthramycin and its utilization in studies of the biosynthesis and mechanism of action of anthramycin. J Nat Prod 1981 Jan–Feb;44(1):38–44

Mallet J, Privat A, Samolyk D, et al: Synthèse in vitro de la tyrosine hydroxylase. C R Acad Sci [D] (Paris) 1981 Feb 9;292(6):455–60 (Eng. Abstr.) (Fre)

Malm L: Propranolol as cause of watery nasal secretion [letter] Lancet 1981 May 2;1(8227):1006

Malt U: Litium. En praktisk klinisk oversikt. Tidsskr Nor Laegeforen 1981 Mar 30;101(9–10):549–54 (Eng. Abstr.) (Nor)

Maltaverne S: Psychotrope et détention. Acta Med Leg Soc (Liege) 1980; 30(1):185–8 (Fre)

Mandarino L, Stenner D, Blanchard W, et al: Selective effects of somatostatin-14, -25 and -28 on in vitro insulin and glucagon secretion. Nature 1981 May 7;291(5810):76–7

Mann M, Michael SD, Svare B: Ergot drugs suppress plasma prolactin and lactation but not aggression in parturient mice. Horm Behav 1980 Dec;14(4):319–28

Männistö PT: Purification and properties of thyrotrophin releasing hormone (TRH)-containing particles from the rat hypothalamus. Med Biol 1980 Dec;58(6):310–8

Männistö PT, Mattila J, Tuomisto J: Further evidence of the dual role of noradrenaline in regulation of thyrotrophin secretion in male rats. Acta Endocrinol (Copenh) 1981 Jun;97(2):213–20

Mantovani P, Pepeu G: Interactions between ionophores, Mg2+ and Ca2+ on acetylcholine formation and release in brain slices. Pharmacol Res Commun 1981 Feb;13(2):175–64

Manunta G, Naitana S: Induzione ormonale della lattazione dopo trattamento breve negli ovini. Nota terza. Boll Soc Ital Biol Sper 1981 Jan 30;57(2):165–71 (Eng. Abstr.) (Ita)

Manunta G, Naitana S: Sull'induzione della lattazione nei bovini dopo trattamento ormonale breve. Boll Soc Ital Biol Sper 1981 Jan 30; 57(2):172–8 (Eng. Abstr.) (Ita)

Marcus DJ, Swift TR, McDonald TF: Acute effects of phenytoin on peripheral nerve function in the rat. Muscle Nerve 1981 Jan–Feb; 4(1):48–50

Margherita S, Guilford J: Composition and efficacy of iodothyronine immunogens and host responsiveness in radioimmunoassay (RIA) for serum thyroxine (T4). Experientia 1981 Mar 15;37(3):314–5

Margolis-Kazan H, Peute J, Schreibman MP, et al: Ultrastructural localization of gonadotropin and luteinizing hormone releasing hormone in the pituitary gland of a teleost fish (the platyfish). J Exp Zool 1981 Jan;215(1):99–102

Marín J, Salaices M, Sánchez CF, et al: Vasoconstrictor effects of tyramine and noradrenaline on goat brain vessels. Gen Pharmacol 1981; 12(3):187–91

Markianos M, Lykouras L: Circadian rhythms of dopamine-beta-hydroxylase and c-AMP in plasma of controls and patients with affective disorders. J Neural Transm 1981;50(2–4):149–55

Marks IM: Review of behavioral psychotherapy, I: Obsessive-compulsive disorders. Am J Psychiatry 1981 May;138(5):584–92 (45 ref.)

Marnane WG, Tai YH, Decker RA, et al: Methylprednisolone stimulation of guanylate cyclase activity in rat small intestinal mucosa: possible role in electrolyte transport. Gastroenterology 1981 Jul;81(1):90–100

Marquez MT, de Mikulic LE, Aramendia P: Differential beta-adrenergic sensitivity of atrial tissue assessed by chronotropic and inotropic responses to several sympathomimetic amines. Acta Physiol Lat Am 1978;28(4–5):193–9

Marriott P, Pansa M, Hiep A: Depot fluphenazine maintenance treatment and associated weight changes. Compr Psychiatry 1981 May–Jun;

22(3):320-5

Marsafy YM, Hafez ES: Effect of adrenoceptor blocker and MAOI on postcoital utero-oviductal contractility, sperm transport, and sperm attachment to eggs in rabbits. Arch Androl 1981 Jun;6(4):307-16

Marsden CA: Effect of L-tryptophan on mouse brain 5-hydroxytryptamine: comparison of values obtained using a fluorimetric assay and a liquid Chromatographic assay with electrochemical detection. J Neurochem 1981 May;36(5):1621-6

Marsh HC, George EM, Koehler KA, et al: Tryptophan exposure in various conformational isomers of bovine prothrombin fragment 1. An acrylamide quenching study. Biochim Biophys Acta 1981 Jan 30; 667(1):35-43

Marshall JF, Critchfield JW, Kozlowski MR: Altered succinate dehydrogenase activity of basal ganglia following to mesotelencephalic dopaminergic projection. Brain Res 1981 May 18;212(2):367-77

Marshall JM: Effects of ovarian steroids and pregnancy on adrenergic nerves of uterus and oviduct. Am J Physiol 1981 May;240(5):C165-74 (83 ref.)

Marshall TC, Clark CR, Brewster DW, et al: Toxicological assessment of heat transfer fluids proposed for use in solar energy applications, II. Toxicol Appl Pharmacol 1981 Mar 30;58(1):31-8

Marshall WS, Bern HA: Active chloride transport by the skin of a marine teleost is stimulated by urotensin I and inhibited by urotensin II. Gen Comp Endocrinol 1981 Apr;43(4):484-91

Marshburn PB, Iuvone PM: The role of GABA in the regulation of the dopamine/tyrosine hydroxylase-containing neurons of the rat retina. Brain Res 1981 Jun 15;214(2):335-47

Marston FA, Dickson AJ, Pogson CI: Factors affecting induction of tyrosine aminotransferase in isolated rat liver cells. Mol Cell Biochem 1981 Jan 20;34(1):59-64

Martens GJ, Jenks BG, van Overbeeke AP: Microsuperfusion of neurointermediate lobes of Xenopus laevis: concomitant and coordinately controlled release of newly synthesized peptides. Comp Biochem Physiol [C] 1981;69C(1):75-82

Martin C, Martin A, Varset B: Pharmacologie comparée de l'adrénaline et de la noradrénaline. Ann Anesthesiol Fr 1981;22(1):85-96 (16 ref.) **(Fre)**

Martines G, Copponi V, Cagnetta G: Aspetti del danno epatico dopo somministrazione sperimentale di alcuni farmaci. Nota preliminare. Arch Sci Med (Torino) 1980 Jul-Sep;137(3):367-86 (Eng. Abstr.) **(Ita)**

Martinet M, Fonlupt P, Pacheco H: Activation of soluble striatal tyrosine hydroxylase in the rat brain after CDPcholine administration. Biochem Pharmacol 1981 Mar 1;30(5):539-41

Martínez D, Giménez MP: Determination of benzodiazepines by derivative spectroscopy. J Anal Toxicol 1981 Jan-Feb;5(1):10-3

Martinez JL Jr, Vasquez BJ, Jensen RA, et al: L-dopa enhances acquisition of an inhibitory avoidance response. Commun Psychopharmacol 1980;4(3):215-8

Martinez JL Jr, Vasquez BJ, Messing RB, et al: Age-related changes in the catecholamine content of peripheral organs in male and female F344 rats. J Gerontol 1981 May;36(3):280-4

Martinez JR, Martinez AM: Stimulatory and inhibitory effects of substance P on rat submandibular secretion. J Dent Res 1981 Jun; 60(6):1031-8

Martínez-Aguirre E: Antagonism of 4-aminopyridine to ketamine-diazepam anesthesia in children. Acta Anaesthesiol Belg 1980; 31(4):289-91

Marusarz TZ, Wolpert EA, Koh SD: Memory processing with lithium carbonate. J Clin Psychiatry 1981 May;42(5):190-2

Maruyama S, Makino K, Kim T, et al: [Studies on the mechanism of the hypertropic action of hydrocortisone on the secretory tubules of the mouse submandibular glands. 3) Effect of hydrocortisone acetate on the noradrenaline stimulation to submandibular glands (author's transl)] Josai Shika Daigaku Kiyo 1980;1(9):29-34 (Eng. Abstr.) **(Jpn)**

Marwaha J, Freedman R, Hoffer B: Electrophysiological changes at a central noradrenergic synapse during thallium toxicosis. Toxicol Appl Pharmacol 1980 Dec;56(3):345-52

Marwaha J, Palmer M, Hoffer B, et al: Differential electrophysiological and behavioral responses to optically active derivatives of phencyclidine. Naunyn Schmiedebergs Arch Pharmacol 1981 Jan; 315(3):203-9

Marwaha J, Palmer M, Hoffer B, et al: Phencyclidine inhibition of cerebellar Purkinje neurons. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):187-92

Marwaha J, Hoffer BJ, Geller HM, et al: Electrophysiologic interactions of antipsychotic drugs with central noradrenergic pathways. Psychopharmacology (Berlin) 1981;73(2):126-33

Mary PL, Rao JP: Type of adrenoceptors involved in induction by adrenaline of hepatic alkaline phosphatase in mice in vivo. Br J Pharmacol 1981 Jan;72(1):8-9

Mas-Chamberlin C, Gillet G, André J, et al: The metabolism and kinetics of tiflorex in the rat. Drug Metab Dispos 1981 Mar-Apr;9(2):150-5

Mashkovskii MD, Gorkin VZ, Verevkina IV, et al: Izbiratel'noe ingibirovanie pirazidolom monoaminoksidazy tipa A. Biull Eksp Biol Med 1981 Feb;91(2):169-71 (Eng. Abstr.) **(Rus)**

Masini E, Blandina P, Fantozzi R, et al: Correlation between cholinergic histamine release and quinuclidinyl-benzilate ([3H]-QNB) binding in mast cell membranes. Agents Actions 1981 Apr;11(1-2):55-9

Masini-Repiso AM, Coleoni AH: Effect of epinephrine and 5-hydroxytryptamine on in vitro thyroid iodine organification. Acta Endocrinol (Copenh) 1981 Jun;97(2):207-12

Maślińska D, Lewandowska I, Prokopczyk J: Effect of prolonged acetylcholinesterase inhibition on postnatal brain development in rabbit. I. Level of serotonin in different brain regions. Acta Neuropathol [Suppl] (Berl) 1981;7:52-5

Massicotte J, Borgus JP, Lachance R, et al: Inhibition of HCG-induced cyclic AMP accumulation and steroidogenesis in rat luteal cells by an LHRH agonist. J Steroid Biochem 1981 Mar;14(3):239-42

Masterton G, Main CJ, Lever AF, et al: Low blood pressure in psychiatric inpatients. Br Heart J 1981 Apr;45(4):442-6

Masuda Y, Utsui Y, Shiraishi Y, et al: Evidence for a synergistic interaction between phenytoin and phenobarbital in experimental animals. J Pharmacol Exp Ther 1981 Jun;217(3):805-11

Matcovich A: Azione dei farmaci narcotici ed oppioidi naturali sulla secrezione dell'ormone somatotropo. Clin Ter 1981 Apr 30;97(2):121-36 (172 ref.) **(Ita)**

Mathew RJ, Ho BT, Kralik P, et al: Catecholamines and monoamine oxidase activity in anxiety. Acta Psychiatr Scand 1981 Mar;63(3):245-52

Matsui M: [Effect of endotoxin shock on endocrine function and carbohydrate metabolism (author's transl)] Masui 1981 Jan;30(1):39-46 (Eng. Abstr.) **(Jpn)**

Matthews WD, Intoccia AP, Osborne VL, et al: Correlation of [14C]muscimol concentration in rat brain with anticonvulsant activity. Eur J Pharmacol 1981 Jan 29;69(3):249-54

Matthews WD, McCafferty GP, Setler PE: An electrophysiological model of GABA-mediated neurotransmission. Neuropharmacology 1981 Jun; 20(6):561-5

Mattingly BA, Zolman JF: The effect of para-chlorophenylalanine and scopolamine on passive avoidance in chicks. Pharmacol Biochem Behav 1981 May;14(5):669-76

Matussek N: Psychopharmaka und Neuroendokrinium. Verh Dtsch Ges Inn Med 1980;86:100-6 **(Ger)**

Matussek N: Entwicklung der biologisch-psychiatrischen Depressionsforschung. MMW 1981 May 8;123(19):793-4 (Eng. Abstr.) **(Ger)**

Matussek N, Laakmann G: Growth hormone response in patients with depression. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):122-6

Maurel D, Boissin J: Plasma thyroxine and testosterone levels in the red fox (Vulpes vulpes L.) during the annual cycle. Gen Comp Endocrinol 1981 Mar;43(3):402-4

Maurer H, Pfleger K: Determination of 1,4- and 1,5-benzodiazepines in urine using a computerized gas chromatographic-mass spectrometric technique. J Chromatogr 1981 Mar 13;222(3):409-19

May PR, Van Putten T, Jenden DJ, et al: Prognosis in schizophrenia: individual differences in psychological response to a test dose of antipsychotic drug and their relationship to blood and saliva levels and treatment outcome. Compr Psychiatry 1981 Mar-Apr;22(2):147-52

May PR, Tuma AH, Dixon WJ, et al: Schizophrenia. A follow-up study of the results of five forms of treatment. Arch Gen Psychiatry 1981 Jul;38(7):776-84

Mazurkiewicz-Kwilecki IM: Effect of diazepam on stress induced changes in brain histamine. Pharmacol Biochem Behav 1981 Mar;14(3):333-8

Mefford IN, Roth KA, Gilberg M, et al: In vivo intraneuronal MAO inhibition in rat brain SKF 64139, comparison to other potent PNMT inhibitors. Eur J Pharmacol 1981 Mar 26;70(3):345-53

Mefford IN: Application of high performance liquid chromatography with electrochemical detection to neurochemical analysis: measurement of catecholamines, serotonin and metabolites in rat brain. J Neurosci Methods 1981 Feb;3(3):207-24 (47 ref.)

Mehrotra SN, Liu L, Srivastava JR, et al: Evaluation of various methods in treatment of enuresis. Indian Pediatr 1980 Jun;17(6):519-22

Meites J, Sonntag WE: Hypothalamic hypophysiotropic hormones and neurotransmitter regulation: current views. Annu Rev Pharmacol Toxicol 1981;21:295-322 (160 ref.)

Mellerup ET, Dam H, Plenge P, et al: Lithium effects on citrate metabolism in humans and rats. Psychopharmacology (Berlin) 1981; 73(1):75-6

Mellerup ET, Rafaelsen OJ: Depression and cerebrospinal fluid citrate. Acta Psychiatr Scand 1981 Jan;63(1):57-60

Melloni GF, Minoja GM, Scorazzati G, et al: Renal effect of SB 7505: a double-blind study. Eur J Clin Pharmacol 1981 Feb;19(3):177-80

Meltzer HY, Simonovic M, Sturgeon RD, et al: Effect of antidepressants, lithium and electroconvulsive treatment on rat serum prolactin levels. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):100-21

Memo M, Lucchi L, Spano PF, et al: Dose-dependent and reversible effects of lead on rat dopaminergic system. Life Sci 1981 Feb 16; 28(7):795-9

Mendelsohn FA, Kachel CD: Stimulation by serum of aldosterone production from rat adrenal glomerulosa cells in vitro: relationships to K+, serotonin and angiotensin II. Acta Endocrinol (Copenh) 1981 Jun;97(2):231-42

AUTHOR SECTION

Mendis N, Pare CM, Sandler M, et al: Is the failure of (-)deprenyl, a selective monoamine oxidase B inhibitor, to alleviate depression related to freedom from the cheese effect? Psychopharmacology (Berlin) 1981; 73(1):87–90

Menitove JE, Rassiga AL, McLaren GD, et al: Antigranulocyte antibodies and deranged immune function associated with phenytoin-induced serum sickness. Am J Hematol 1981;10(3):277–84

Menon M, Peegel H, Menon KM: In vitro effect of danazol on luteinizing hormone-releasing hormone-stimulated luteinizing hormone release in rat anterior pituitary cell cultures in vitro. Endocrinology 1981 Jul; 109(1):191–6

Meola JM, Rosano TG, Swift T: Thin-layer chromatography, with fluorescence detection, of benzodiazepines and tricyclic antidepressants in serum from emergency-room patients. Clin Chem 1981 Jul; 27(7):1254–5

Merault G, Labouesse J, Graves PV, et al: Kinetics of formation of tryptophanyl-adenylate by tryptophanyl-tRNA synthetase from beef pancreas. FEBS Lett 1981 Jan 26;123(2):165–8

Merrigan MD, Lais LT: The effect of cold stress on the modulation of vascular adrenergic transmission by acetylcholine.
J Pharmacol Exp Ther 1981 Jul;218(1):142–7

Metcalfe SA, Colley PJ, Neal GE: A comparison of the effects of pretreatment with phenobarbitone and 3-methylcholanthrene on the metabolism of aflatoxin B1 by rat liver microsomes and isolated hepatocytes in vitro. Chem Biol Interact 1981 May;35(2):145–57

Metz J, Busch DA, Meltzer HY: Des-tyrosine-gamma-endorphin: H-reflex response similar to neuroleptics. Life Sci 1981 May 4; 28(18):2003–8

Meyers CA, Kastin AJ, Schally AV, et al: Use of the mouse vas deferens assay to evaluate the action of somatostatin peptides on gastric acid secretion. Digestion 1981;21(1):21–4

Meyerson LR, Sano MC, Critchett DJ, et al: Lateral olfactory tract lesions reveal neuronal localization of benzodiazepine recognition sites.
Eur J Pharmacol 1981 Apr 24;71(1):147–50

Miceli JN, Bowman DB, Aravind MK: An improved method for the quantitation of phencyclidine (PCP) in biological samples utilizing nitrogen-detection gas chromatography. J Anal Toxicol 1981 Jan–Feb; 5(1):29–32

Michaelis ML, Michaelis EK: Ca++ fluxes in resealed synaptic plasma membrane vesicles. Life Sci 1981 Jan 5;28(1):37–45

Michaelson DM, Angel I: Saturable acetylcholine transport into purified cholinergic synaptic vesicles. Proc Natl Acad Sci USA 1981 Apr; 78(4):2048–52

Miczek KA: Pharmacological evidence for catecholamine involvement in animal aggression [proceedings] Psychopharmacol Bull 1981 Jan; 17(1):60–2

Miczek KA, Woolley J, Schlisserman S, et al: Analysis of amphetamine effects on agonistic and affiliative behavior in squirrel monkeys (Saimiri sciureus). Pharmacol Biochem Behav 1981;14 Suppl 1:103–7

Midha KK, Mackonka C, Cooper JK, et al: Radioimmunoassay for perphenazine in human plasma. Br J Clin Pharmacol 1981 Jan;11(1):85–8

Midha KK, Cooper JK, Bailey K, et al: The metabolism of 3-methoxyamphetamine in dog, monkey and man. Xenobiotica 1981 Feb;11(2):137–46

Mikeska J, Pospíšil M: Erythrocytic and granulocytic differentiation of transplanted bone marrow cells in mice treated with thyroid hormones.
Folia Biol (Praha) 1981;27(2):126–34

Mikkelsen E, Lake CR, Brown GL, et al: The hyperactive child syndrome: peripheral sympathetic nervous system function and the effect of d-amphetamine. Psychiatry Res 1981 Apr;4(2):157–69

Miller D: Treatment of the seriously disturbed adolescent.
Adolesc Psychiatry 1980;8:469–81

Miller RF, Frumkes TE, Slaughter M, et al: Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. I. Receptors, horizontal cells, bipolars, and G-cells.
J Neurophysiol 1981 Apr;45(4):743–63

Miller RF, Frumkes TE, Slaughter M, et al: Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. II. Amacrine and ganglion cells. J Neurophysiol 1981 Apr;45(4):764–82

Miller RS, Wiedeman GH, Linn L: Prescribing psychotropic drugs: whose responsibility? Soc Work Health Care 1980 Fall;6(1):51–61

Millhorn DE, Eldridge FL, Waldrop TG: Prolonged stimulation of respiration by endogenous central serotonin. Respir Physiol 1980 Dec; 42(3):171–88

Millicovsky G, Johnston MC: Maternal hyperoxia greatly reduces the incidence of phenytoin-induced cleft lip and palate in A/J mice.
Science 1981 May 8;212(4495):671–2

Minamino N, Kangawa K, Chino N, et al: Beta-neo-endorphin, a new hypothalamic 'big' Leu-enkephalin of porcine origin: its purification and the complete amino acid sequence.
Biochem Biophys Res Commun 1981 Apr 15;99(3):864–70

Mineeva MF, Darinskii NV, Robak Ia: Vliianie indometatsina i nonakhlazina na aktivnost' tirozingidroksilazy v miokarde i golovnom mozge krys. Biull Eksp Biol Med 1981 Feb;91(2):181–4 (Eng. Abstr.) **(Rus)**

Minnema DM, Hudson CG, Jones JD: A comparison of GE(Li) detectors with different efficiencies for low-level general purpose counting.
Health Phys 1981 Jan;40(1):55–61

Miquelis R, Simon C: The thyroid lysosomal system: dynamic state of the organelles in relation to iodine release. Eur J Cell Biol 1981 Apr; 24(1):70–3

Mirro MJ, Watanabe AM, Bailey JC: Electrophysiological effects of the optical isomers of disopyramide and quinidine in the dog. Dependence on stereochemistry. Circ Res 1981 Jun;48(6 Pt 1):867–74

Mirzoian SA, Movsesian TG, Karagian AT, et al: Vliianie arzninkikh uglekislykh minerral'nykh vann na zakhvat mechennogo noradrenalina srezami miokarda i aktivnost' mitokhondrial'noi monoaminoksidazy.
Vopr Kurortol Fizioter Lech Fiz Kult 1981 Mar–Apr;(2):42–5 **(Rus)**

Misra AL, Pontani RB, Bartolomeo JG: Disposition of [3H] phencyclidine in the rat after single and multiple doses. Life Sci 1980 Dec 22–29; 27(25–26):2501–8

Mitkevich SP, Koliaskina GI: Vliianie aminazina i mazheptila na proliferatsiiu limfotsitov perifericheskoi krovi v usloviiakh kul'tivirovaniia s fitogemaggliutininom. Zh Nevropatol Psikhiatr 1981; 81(2):115–7 (Eng. Abstr.) **(Rus)**

Mittel NS, Gardner GH 3d, Rose BW: Computerized monitoring of psychotropic drug orders: some trends and revelations.
Hosp Community Psychiatry 1981 Apr;32(4):277–8

Miura Y, Tomioka H, Adachi M, et al: [Plasma catecholamine concentration as an index for evaluating cardiac sympathetic nerve activity (author's transl)] Kokyu To Junkan 1980 Oct;28(10):1111–7 **(Jpn)**

Miwa BJ, Garland WA, Blumenthal P: Determination of flurazepam in human plasma by gas chromatography-electron capture negative chemical ionization mass spectrometry. Anal Chem 1981 May; 53(6):793–7

Miyano K, Ota T, Toki S: Stereoselective formation of glucuronides in metabolism of hexobarbital enantiomers in vivo: isolation and quantitation of glucuronides in rabbit urine. Drug Metab Dispos 1981 Jan–Feb;9(1):60–4

Miyata M, Imai H, Ishikawa S, et al: Change in human electroretinography associated with thioridazine administration.
Ophthalmologica 1980;181(3–4):175–80

Mkheidze MO, Pekarskaia NA, Shaposhnikov AM: Issledovaniia aktivnosti kholinesterazy dlia preduprezhdeniia lekarstvennykh oslozhnenii.
Lab Delo 1981;(2):97–100 (Eng. Abstr.) **(Rus)**

Modigh K, Balldin J, Edén S, et al: Electroconvulsive therapy and receptor sensitivity. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):91–9

Moen KA, Wisnes AR, Elsayed EA, et al: The effect of adrenaline on peripheral vascular resistance at different temperatures in a hind part preparation of rainbow trout (Salmo gairdnerii R.).
Comp Biochem Physiol [C] 1981;69C(1):157–9

Möhler H, Richards JG, Wu JY: Autoradiographic localization of benzodiazepine receptors in immunocytochemically identified gamma-aminobutyrergic synapses. Proc Natl Acad Sci USA 1981 Mar; 78(3):1935–8

Moir AJ, Perry SV: Phosphorylation of rabbit cardiac-muscle troponin I by phosphorylase kinase. The effect of adrenaline. Biochem J 1980 Nov 1;191(2):547–54

Moises HC, Hoffer BJ, Woodward DJ: GABA facilitation by noradrenaline shows supersensitivity in cerebellum after 6-hydroxydopamine. Naunyn Schmiedebergs Arch Pharmacol 1980; 315(1):37–46

Moises HW, Beckmann H: Antidepressant efficacy of tranylcypromine isomers: a controlled study. J Neural Transm 1981;50(2–4):185–92

Molcan J, Rakús A, Motýlová A: Pharmakokinetische Studie des Lithium-retard bei affektiven Psychosen. Agressologie 1980;21(A):11–4 (Eng. Abstr.) **(Ger)**

Monmaur P: Phasic hippocampal activity during paradoxical sleep in the rat: selective suppression after diazepam administration. Experientia 1981 Mar 15;37(3):261–2

Montanaro N, Dall'Olio R, Gandolfi O, et al: Behavioral supersensitivity to methamphetamine following chronic treatment with (—)-sulpiride in the rat. Boll Soc Ital Biol Sper 1981 Feb 28;57(4):401–6

Monteverde R, Rossi G, Lattere M: Studio endocrinologico della beta-talassemia maior. Minerva Pediatr 1980 Dec 15;32(23):1335–42 (Eng. Abstr.) **(Ita)**

Montgomery C, Vore M: The effect of diethylstilbestrol treatment on the metabolism and biliary excretion of [14C]phenytoin in the isolated perfused rat liver. Toxicol Appl Pharmacol 1981 May;58(3):510–9

Montgomery SA, Rani SJ, McAuley R, et al: The antidepressant efficacy of zimelidine and maprotiline. Acta Psychiatr Scand [Suppl] 1981; 63(Suppl 290):219–24

Montgomery SA, McAuley R, Rani SJ, et al: A double blind comparison of zimelidine and amitriptyline in endogenous depression.
Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):314–27

Moody JP, Smith AH, Naylor GJ: The effect of mianserin on urinary catecholamine excretion in psychiatric patients.
Br J Clin Pharmacol 1981 Jan;11(1):103–5

Moore DP: Methylphenidate in depression and states of apathy.
South Med J 1981 Mar;74(3):347–8

AUTHOR SECTION

Morel N, Meunier FM: Simultaneous release of acetylcholine and ATP from stimulated cholinergic synaptosomes. J Neurochem 1981 May;36(5):1766–73

Morgan AA, Hughes JP: An investigation into the value of cholinesterase estimations of workers in a plant manufacturing tri-aryl phosphate plasticizers. J Soc Occup Med 1981 Apr;31(2):69–75

Morgane PJ: Monoamine theories of sleep: the role of serotonin—a review [proceedings] Psychopharmacol Bull 1981 Jan;17(1):13–7 (27 ref.)

Möricke R, Marek H: Der Einfluss der beta-Rezeptorenblocker Propranolol und Talinolol auf die glukose-orziprenalinduzierte Insulinsekretion, die Glukosetoleranz und das Verhalten der unveresterten freien Fettsäuren bei stoffwechselgesunden Probanden. Z Gesamte Inn Med 1981 Mar;36(5):263–7 (Eng. Abstr.) (Ger)

Morimoto K, Okamura H, Kanzaki H, et al: The adrenergic nerve supply to bovine ovarian follicles. Int J Fertil 1981;26(1):14–9

Morishima T, Hanawa S: Urinary excretion of 5-S-cysteinyldopa in healthy Japanese. Acta Derm Venereol (Stockh) 1981;61(2):149–50

Morley JE, Brammer GL, Sharp B, et al: Neurotransmitter control of hypothalamic-pituitary-thyroid function in rats. Eur J Pharmacol 1981 Mar 26;70(3):263–71

Moroni F, Bianchi C, Tanganelli S, et al: The release of gamma-aminobutyric acid, glutamate, and acetylcholine from striatal slices: a mass fragmentographic study. J Neurochem 1981 May;36(5):1691–9

Morre MC, Wurtman RJ: Characteristics of synaptosomal tyrosine uptake in various brain regions: effect of other amino acids. Life Sci 1981 Jan 5;28(1):65–75

Morris MD, Virus RM, Gebhart GF: Dorsal tegmental bundle destruction: effects on operant behavior, brain catecholamine levels, and behavioral suppression produced by adrenergic agonists. Life Sci 1980 Dec 22–29;27(25–26):2621–6

Morton CR, Chahl LA: Indirect evidence for the importance of axonal transport in maintenance of stores of the mediator of neurogenic oedema. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):277–80

Mory G, Ricquier D, Hémon P: Effects of chronic treatments upon the brown adipose tissue of rats. II. Comparison between the effects of catecholamine injections and cold adaptation. J Physiol (Paris) 1980;76(8):859–64

Mörz R, Hengl G, Prager J, et al: Hemmung der Glukose und Leucin-Resorption durch Somatostatin beim Hund.
Res Exp Med (Berl) 1981;178(3):241–6 (Eng. Abstr.) (Ger)

Moss DE, Rogers JB, Deutsch JA, et al: Time dependent changes in anterograde scopolamine-induced amnesia in rats.
Pharmacol Biochem Behav 1981 Mar;14(3):321–3

Mostert JW: Die Halcion-affère. S Afr Med J 1981 Jun 27;59(27):967 (Afr)

Motles E, Ely Y, Elazar Z: Role of the pulvinar-lateral posterior nucleus complex in turning behavior. Physiol Behav 1980 Dec;25(6):921–9

Mould GP, Clough J, Morris BA, et al: A propranolol radioimmunoassay and its use in the study of its pharmacokinetics following low doses. Biopharm Drug Dispos 1981 Jan–Mar;2(1):49–57

Moulds RF, Jauernig RA, Shaw J: A comparison of the effects of hydrallazine, diazoxide, sodium nitrite and sodium nitroprusside on human isolated arteries and veins. Br J Clin Pharmacol 1981 Jan;11(1):57–61

Mounié J, Goudonnet H, Dumas M, et al: Facteurs nutritionnels lipidiques de l'induction enzymatique par le phénobarbital chez le rat. Influence de la composition quantitative et qualitative lipidique du régime alimentaire. J Pharmacol 1981 Jan–Mar;12(1):3–14 (Eng. Abstr.) (Fre)

Mount ME, Dayton AD, Oehme FW: Carbaryl residues in tissues and cholinesterase activities in brain and blood of rats receiving carbaryl. Toxicol Appl Pharmacol 1981 Apr;58(2):282–96

Movshon JA: Cortical effects of monocular deprivation: suppression or deafferentation? [news] Nature 1981 May 28;291(5813):284–5

Moyer JA, Greenberg LH, Frazer A, et al: Subsensitivity of the beta-adrenergic receptor-linked adenylate cyclase system of rat pineal gland following repeated treatment with desmethylimipramine and nialamide. Mol Pharmacol 1981 Mar;19(2):187–93

Mubagwa K, Carmeliet E: Electrophysiological effects of acetylcholine on rabbit cardiac Purkinje Fibers. Arch Int Pharmacodyn Ther 1981 Feb;249(2):326–7

Mueller AL, Hoffer BJ, Dunwiddie TV: Noradrenergic responses in rat hippocampus: evidence for medication by alpha and beta receptors in the in vitro slice. Brain Res 1981 Jun 9;214(1):113–26

Mulas A, Longoni R, Spina L, et al: Ipsiversive turning behaviour after discrete unilateral lesions of the dorsal mesencephalic reticular formation by kainic acid. Brain Res 1981 Mar 16;208(2):468–72

Müller-Oerlinghausen B, Albrecht J, Kampf D: Lithium-Prophylaxe und Nierenfunktion. Zusammenfassende Beurteilung und Richtlinien zur Therapieüberwachung. Nervenarzt 1981 Feb;52(2):113–5 (Ger)

Murai M: [Effects of benzoylcholine on ChE activity in rabbit and rat brain and erythrocytes (author's transl)] Nippon Yakurigaku Zasshi 1981 Feb;77(2):115–22 (Eng. Abstr.) (Jpn)

Murata Y, Martin CB Jr, Miyake K, et al: Effect of catecholamine on fetal breathing activity in rhesus monkeys. Am J Obstet Gynecol 1981 Apr 15;139(8):942–7

Murayama K, Shindo N, Mineki R, et al: Determination of glutamic acid and gamma-aminobutyric acid in Ringer's solution without desalination at the femtomole level by gas chromatography chemical ionization mass spectrometry. Biomed Mass Spectrom 1981 Apr;8(4):165–9

Murdoch GH, Rosenfeld MG: Regulation of pituitary function and prolactin production in the GH4 cell line by vitamin D.
J Biol Chem 1981 Apr 25;256(8):4050–3

Murray TF, Cheney DL: The effect of phencyclidine on the turnover rate of acetylcholine in various regions of rat brain.
J Pharmacol Exp Ther 1981 Jun;217(3):733–7

Murthy VV: Effects of propranolol on the adenylate cyclase activities in the arteries and ventricle of dog. Life Sci 1980 Dec 22–29;27(25–26):2645–8

Musich JR, Behrman SJ, Menon KM: Estrogenic and antiestrogenic effects of danazol administration in studies of estradiol receptor binding. Am J Obstet Gynecol 1981 May 1;140(1):62–9

Myshliakova NV, Klusha VE, Chipens GI: Vliianie fragmentov peptidnykh gormonov i tiroliberina na gomeostaz gliukozy v krovi myshei.
Biokhimiia 1980 Oct;45(10):1761–6 (Eng. Abstr.) (Rus)

N

Naber D, Cohen RM, Pickar D, et al: Episodic secretion of opioid activity in human plasma and monkey CSF: evidence for a diurnal rhythm. Life Sci 1981 Feb 23;28(8):931–5

Nádasdi L, Medzihradszky K: A study of the applicability of QSAR calculation for peptide hormones. Biochem Biophys Res Commun 1981 Mar 31;99(2):451–7

Nagao T, Murata S, Ikezawa K, et al: [Effects of diltiazem on hemodynamics and His bundle electrogram in the anesthetized dog (author's transl)] Nippon Yakurigaku Zasshi 1981 Feb;77(2):195–203 (Eng. Abstr.) (Jpn)

Nagataki S, Brubaker RF: Early effect of epinephrine on aqueous formation in the normal human eye. Ophthalmology (Rochester) 1981 Mar;88(3):278–82

Nagayama H, Takagi A, Takahashi R; Chronopharmacological studies of neuroleptics. Curr Dev Psychopharmcol 1981;6:191–214 (53 ref.)

Naggar VF: An in vitro study of the interaction between diazepam and some antacid or excipients. Pharmazie 1981;36(2):114–7

Nagy BR, Dillman CE Jr: Case report of unusual diazepam abstinence syndrome. Am J Psychiatry 1981 May;138(5):694–5

Naik RB, Mathias CJ, Wilson CA, et al: Cardiovascular and autonomic reflexes in haemodialysis patients. Clin Sci 1981 Feb;60(2):165–70

Nakabayashi H, Sagara H, Usukura N, et al: Effect of somatostatin on the flow rate and triglyceride levels of thoracic duct lymph in normal and vagotomized dogs. Diabetes 1981 May;30(5):440–5

Nakagaki M, Katoh I, Handa T: Surface potential of lipid membrane estimated from the partitioning of methylene blue into liposomes.
Biochemistry 1981 Apr 14;20(8):2208–12

Nakagawa R, Tanaka M, Kohno Y, et al: Regional responses of rat brain noradrenergic neurones to acute intense stress.
Pharmacol Biochem Behav 1981 May;14(5):729–32

Nakahata N, Nakanishi H, Suzuki T: Effect of catecholamine on the contractile responses of rabbit colon and duodenum to vagus nerve stimulation in vivo. Fukushima J Med Sci 1979;26(3–4):71–7

Nakamura T, Noda C, Ichihara A: Two phase regulation of tyrosine aminotransferase activity by insulin in primary cultured hepatocytes of adult rats. Biochem Biophys Res Commun 1981 Apr 15;99(3):775–80

Nakanishi S, Yamazaki H, Nishiguchi K, et al: Effects of pargyline and diethyldithiocarbamate in vivo treatment on aldehyde dehydrogenase activities of submitochondrial fractions. Arch Toxicol 1980 Dec;46(3–4):241–8

Nakashima T, Taurog A, Krulich L: Serum thyroxine, triiodothyronine, and TSH levels in iodine-deficient and iodine-sufficient rats before and after exposure to cold. Proc Soc Exp Biol Med 1981 May;167(1):45–50

Nakata Y, Kusaka Y, Yajima H, et al: Further characterization of the binding of substance P to a fraction from rabbit brain enriched in synaptic membranes. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):211–4

Nandedkar AK, Williamson R, Kutt H, et al: A comparison of plasma phenytoin level determinations by EMIT and gas-liquid chromatography in patients with renal insufficiency.
Ther Drug Monit 1980;2(4):427–30

Narasimhachari N, Friedel RO: Quantitation of biologically important primary amines as their isothiocyanate derivatives by gas chromatography using nitrogen detector and validation by selected ion monitoring. Clin Chim Acta 1981 Mar 5;110(2–3):235–43

Narayanan R, Balaram P: Fluorescence and N.M.R. studies of the binding of cholinergic fluorescent probes to horse serum cholinesterase.
Int J Pept Protein Res 1981 Feb;17(2):170–80

Nauman A, Kamiński T, Herbaczyńska-Cedro K: In vivo and in vitro effects of adrenaline on conversion of thyroxine to triiodothyronine and to reverse-triiodothyronine in dog liver and heart.
Eur J Clin Invest 1980 Jun;10(3):189–92

Nazarova AF: Polimorfizm syvorotochnoĭ kholinésterazy cheloveka v moskovskoi populiatsii. Genetika (Moskva) 1981;17(2):375–61 (Rus)

Nedergaard J: Effects of cations on brown adipose tissue in relation to possible metabolic consequences of membrane depolarisation. Eur J Biochem 1981;114(1):159–67

Negishi M, Jensen NM, Garcia GS, et al: Structural gene products of the murine Ah complex. Differences in ontogenesis and glucosamine incorporation between liver microsomal cytochromes P1–450 and P–448 induced by polycyclic aromatic compounds. Eur J Biochem 1981 Apr; 115(3):585–94

Nekola MV, Pedroza E, Schally AV: Paradoxical effects of D–Trp6–LHRH in immature female rats correlated with changes in ACTH, prolactin, and corticosterone levels. Biol Reprod 1981 Apr; 24(3):505–11

Nestler EJ, Greengard P: Dopamine and depolarizing agents regulate the state of phosphorylation of protein I in the mammalian superior cervical sympathetic ganglion. Proc Natl Acad Sci USA 1980 Dec; 77(12):7479–83

Nestler EJ, Rainbow TC, McEwen BS, et al: Corticosterone increases the amount of protein 1, a neuron–specific phosphoprotein, in rat hippocampus. Science 1981 Jun 5;212(4499):1162–4

Nestoros JN: Benzodiazepines in schizophrenia: a need for reassessment. Int Pharmacopsychiatry 1980;15(3):171–9

Neuhuber W, Groh V, Gottschall J, et al: The cornea is not innervated by substance P–containing primary afferent neurons. Neurosci Lett 1981 Feb 23;22(1):5–9

Neumann HJ, Becher G: Zur Anwendung des beta–Rezeptorenblockers Propranolol (Obsidan) in der chirurgischen Stomatologie. Stomatol DDR 1980 Dec;30(12):908–12 (Eng. Abstr.) (Ger)

Nichols DJ, Chevins PF: Plasma corticosterone fluctuations during the oestrous cycle of the house mouse. Experientia 1981 Mar 15;37(3):319–20

Nielsen HV, Klemp P, Crone P: Et forgiftningstilfaelde med anuri og kredsløbssvigt behandlet med dopamin–infusion. Ugeskr Laeger 1981 13 Apr;143(16):1017–8 (Eng. Abstr.) (Dan)

Nikitina MM: Vliianie sveta na sintez kortikosterona v nadpochechnikakh krys in vitro. Biol Nauki 1981;(4):58–63 (Rus)

Nikolics K, Bieglmayer C, Spona J, et al: Inhibition of LH–release by synthetic analogues of LH–RH in rat pituitary cell culture. Peptides (Fayetteville) 1981 Spring;2(1):65–73

Nimura N, Ishida K, Kinoshita T: Novel post–column derivatization method for the fluorimetric determination of norepinephrine and epinephrine. J Chromatogr 1980 Dec 12;221(2):249–55

Nishimura S, Sorimachi M, Yamagami K: Exocytotic secretion of catecholamines from the cat adrenal medulla by sodium deprivation: involvement of calcium influx mechanism. Br J Pharmacol 1981 Feb; 72(2):305–17

Nistri A: Excitatory and inhibitory action of ibotenic acid on frog spinal motoneurones in vitro. Brain Res 1981 Mar 16;208(2):397–408

Noaillac–Depeyre J, Hollande E: Evidence for somatostatin, gastrin and pancreatic polypeptide–like substances in the mucosa cells of the gut in fishes with and without stomach. Cell Tissue Res 1981;216(1):193–203

Noe BD: Inhibition of islet prohormone to hormone conversion by incorporation of arginine and lysine analogs. J Biol Chem 1981 May 25;256(10):4940–6

Nomura Y, Yotsumoto I, Segawa T: Ontogenetic development of high potassium– and acetylcholine–induced release of dopamine from striatal slices of the rat. Brain Res 1981 Apr;227(2):171–7

Noordam A, Maat L, Beyerman HC: Quantitative determination of pilocarpine, isopilocarpine, pilocarpic acid, and isopilocarpic acid in clinical ophthalmic pilocarpine formulations by reversed–phase liquid chromatography. J Pharm Sci 1981 Jan;70(1):96–7

Nordgren L, von Schéele C: Nortriptyline and pituitary–thyroid function in affective disorder. Pharmacopsychiatria 1981 Mar;14(2):61–5

Nordling J, Meyhoff HH, Christensen NJ: Influence of sympathetic tonus and plasma noradrenaline on urethral pressure. Scand J Urol Nephrol 1981;15(1):1–6

Norman JA: Neuroleptic drugs are nonstereospecific inhibitors of calmodulin–stimulated phosphodiesterase activity. Ann NY Acad Sci 1980;356:415–6

Normand M, Lalonde J, Lavoie M, et al: Adrenocortical responses to adrenocorticotrophin in the rat. Can J Physiol Pharmacol 1980 Nov; 58(11):1279–85

Norqvist A, Fowler CJ, Oreland L: The deamination of monoamines by pig dental pulp. Biochem Pharmacol 1981 Mar 1;30(5):403–9

Novellino E, Ortonne JP, Voulot C, et al: Identification of cysteinyldopa–derived units in eumelanins from mammalian eyes. FEBS Lett 1981 Mar 9;125(1):101–3

Novotná R: Effect of immobilization and of elevation of the 5–hydroxytryptamine concentrations in the brain stem on liver tryptophan pyrrolase activity in a hibernator [the golden hamster]. Physiol Bohemoslov 1981;30(1):27–33

Nowak LM, MacDonald RL: Substance P decreases a potassium conductance of spinal cord neurons in cell culture. Brain Res 1981 Jun 15;214(2):416–23

Nunley WC Jr, Kitchin JD 3d, Thorner MO, et al: Effects of hyperprolactinemia and bromocriptine on the human endometrium. Fertil Steril 1981 Apr;35(4):479–80

Nunn B: Some characteristics of mouse platelet aggregation and a comparison of the activity of a range of compounds in mouse and human platelet–rich plasma in vitro. Thromb Haemost 1981 Feb 23;45(1):1–5

Nyberg G: Pindolol in orthostatic hypotension [letter] Br Med J 1981 May 23;282(6277):1704

O

O'Callaghan JP, Dunn LA, Lovenberg W: Calmodulin–mediated phosphorylation of synaptosomal cytosolic proteins. Ann NY Acad Sci 1980;356:417–21

Ochi R: [Effect of acetylcholine and adrenaline on membrane currents in ventricular muscle (author's transl)] Kokyu To Junkan 1980 Oct; 28(10):1103–9 (Jpn)

Ochs HR, Greenblatt DJ, Roberts GM, et al: Diazepam interaction with antituberculosis drugs. Clin Pharmacol Ther 1981 May;29(5):671–8

Oehlberg SM, Regan DO, Rudrauff ME, et al: A preliminary evaluation of parenting, depression, and violence profiles in methadone–maintained women. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):380–6

Oehler J, Jähkel M, Schmidt J: Der Einfluss sozialer Isolation auf die Transmitter–Sensitivität striataler und hippokampaler Neurone der Ratte. Acta Biol Med Ger 1980;39(10):1089–93 (Eng. Abstr.) (Ger)

Oehler J, Westermann KH: Lokomotorische Aktivität von Ratten nach chronischer Vorbehandlung mit Haloperidol. Acta Biol Med Ger 1980; 39(11–12):1235–9 (Eng. Abstr.) (Ger)

Ogren SO, Cott JM, Hall H: Sedative/anxiolytic effects of antidepressants in animals. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):277–88

Ogren SO, Ross SB, Hall H, et al: The pharmacology of zimelidine: a 5–HT selective reuptake inhibitor. Acta Psychiatr Scand [Suppl] 1981; 63(Suppl 290):127–51

Ogren SO: Studies on the role of serotonin in avoidance learning [proceedings] Psychopharmacol Bull 1981 Jan;17(1):17–9

Ohkura Y, Ohtsubo K, Zaitsu K, et al: Fluorimetric assay for dopamine beta–hydroxylase in rat plasma. Chem Pharm Bull (Tokyo) 1980 Nov; 28(11):3385–8

Ohlsson A, Lindgren JE, Wahlen A, et al: Plasma levels of delta 9–tetrahydrocannabinol after intravenous, oral, and smoke administration. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):250-6

Ohmori K, Yamanami S, Shuto K, et al: Effect of sodium dipropylacetate on conflict behavior in rats. Jpn J Pharmacol 1980 Dec;30(6):925–7

Ohnishi Y, Tanaka M: Effects of pilocarpine and paracentesis on occluding junctions between the nonpigmented ciliary epithelial cells. Exp Eye Res 1981 May;32(5):635–47

Ohrström A: Dose–related interaction between timolol and adrenaline. Albrecht Von Graefes Arch Klin Exp Ophthalmol 1981;216(1):55–9

Oka M, Nagai Y, Okamoto K, et al: Effect gamma–melanotropin (gamma–MSH) on the conditioned behavior. J Pharmacobiodyn 1980 Nov;3(11):628–30

Okabe E, Higashi H, Fujisawa T, et al: Effects of perhexiline on myocardial phosphorylase activity, myocardial catecholamine content and heart rate. Jpn Circ J 1981 Jun;45(6):667–71

Okamoto K, Sakai Y: Inhibitory actions of taurocyamine, hypotaurine, homotaurine, taurine and GABA on spike discharges of Purkinje cells, and localization of sensitive sites, in guinea pig cerebellar slices. Brain Res 1981 Feb 16;206(2):371–86

Okasha A: Classification, biochemistry of depression and the mode of action of antidepressant drugs. Egypt J Psychiatry 1979 Apr;2(1):3–18

Okasha A, Eid SZ, Bishry Z, et al: Levels of HIAA and VMA in C.S.F. of schizophrenics before and after treatment. J Egypt Med Assoc 1978; 61(Suppl 1–2):38–50

Okazaki H: [The hormonal regulation of the hepatic glycogenolysis in the newborn (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1980 May;32(5):541–9 (Eng. Abstr.) (Jpn)

Okuma T, Inanaga K, Otsuki S, et al: A preliminary double–blind study on the efficacy of carbamazepine in prophylaxis of manic–depressive illness. Psychopharmacology (Berlin) 1981;73(1):95–6

Olafsson O, Sigfússon S, Grímsson A: Control of addictive drugs in Iceland 1976—78. J Epidemiol Community Heelth 1980 Dec;34(4):305–8

Olcese J, Figueroa H, Hall TR, et al: Effects of para–chlorophenylalanine, a brain serotonin depletor, on pituitary cyclic AMP levels in the rainbow trout, Salmo gairdneri. Gen Comp Endocrinol 1981 Apr;43(4):462–6

Olds ME, Fobes JL: The central basis of motivation: intracranial self–stimulation studies. Annu Rev Psychol 1981;32:523–74 (246 ref.)

Olds ME, Fobes JL, Albert V: Catecholamine–serotonin interaction effects on activity in rats neonatally treated with 6–hydroxydopamine. Psychopharmacology (Berlin) 1981;73(1):31–3

Olie JP, Gay C, Lebeau P, et al: Intoxication volontaire au datura à partir d'un médicament anti–asthmatique. Nouv Presse Med 1981 Feb 14; 10(6):429 (Fre)

Oliverio A, Castellano C: Behavioral effects of opiates: a pharmacogenetic analysis. Curr Dev Psychopharmcol 1981;6:45–64 (78 ref.)

Olpe HR: Differential effects of clomipramine and clorgyline on the sensitivity of cortical neurons to serotonin: effect of chronic treatment. Eur J Pharmacol 1981 Jan 29;69(3):375–7

Ondrusek MG, Kilts CD, Frye GD, et al: Behavioral and biochemical studies of the scopolamine-induced reversal of neuroleptic activity. Psychopharmacology (Berlin) 1981;73(1):17-22

Ong SB, Lee CT: A double-blind comparison of nomifensine and amitriptyline in the treatment of depression. Acta Psychiatr Scand 1981 Mar;63(3):198-207

Onoda K, Ho IK: The inhibition and potentiation of procarbazine on hepatic mixed-function oxidases in phenobarbital tolerant and nontolerant mice. Drug Chem Toxicol 1980;3(2):185-200

Ooi DS, Poznanski WJ, Smith FM: Effects of contact with vacutainer tube stoppers on the estimation of quinidine in serum and plasma. Clin Biochem 1980 Dec;13(6):297-300

O'Regan S, Collier B: Factors affecting choline transport by the cat superior cervical ganglion during and following stimulation, and the relationship between choline uptake and acetylcholine synthesis. Neuroscience 1981;6(3):511-20

Oreland L, Wiberg A, Asberg M, et al: Platelet MAO activity and monoamine metabolites in cerebrospinal fluid in depressed and suicidal patients and in healthy controls. Psychiatry Res 1981 Feb;4(1):21-9

Orida N, Poo MM: Maintenance and dissolution of acetylcholine receptor clusters in the embryonic muscle cell membrane. Brain Res 1981 Apr; 227(2):293-8

O'Rourke RA, Horwitz LD: Effects of chronic oral quinidine on left ventricular performance. Am Heart J 1981 Jun;101(6):769-73

Orr MW, Knox JM, Allen R, et al: The effects of neuroleptic drugs on 5-hydroxytryptamine induced platelet aggregation in schizophrenic patients. Br J Clin Pharmacol 1981 Mar;11(3):255-9

Orsulak PJ, Gerson B: Therapeutic monitoring of tricyclic antidepressants: quality-control considerations. Ther Drug Monit 1980; 2(3):233-42

O'Shea M, Adams ME: Pentapeptide (proctolin) associated with an identified neuron. Science 1981 Jul 31;213(4507):567-9

Osipovskii SA, Polesskaia MM: Reaktsii identifitsirovannogo neĭrona vinogradnoĭ ulitki na applikatsiiu peptidov, mediatorov, prostaglandinov i tsiklicheskikh nukleotidov. Neirofiziologiia 1981;13(1):80-7 (Eng. Abstr.) (Rus)

Osterrieder W, Yang QF, Trautwein W: The time course of the muscarinic response to ionophoretic acetylcholine application to the S-A node of the rabbit heart. Pfluegers Arch 1981 Mar;389(3):283-91

Otsuki M, Sakamoto C, Yun H, et al: Effect of somatostatin and calcium deprivation on cholecystokinin or caerulein-induced insulin and glucagon release from the isolated perfused rat pancreas. Endocrinol Jpn 1980 Dec;27 Suppl 1:95-102

Ottenweller JE, Hedge GA: Thyroid hormones are required for daily rhythms of plasma corticosterone and prolactin concentration. Life Sci 1981 Mar 2;28(9):1033-40

Oud PS, Zahniser DJ, Vooijs GP, et al: Thionine-Feulgen Congo Red — a new staining technique for automated cytology. Acta Histochem [Suppl] (Jena) 1981;24:199-206

Overhoff H, Strugala G, Forth W: Absorption of 14C-clanobutin-Na in blood-perfused tied-off jejunal segments in vivo of rats. Arzneimittelforsch 1981;31(4):670-4

Owens DR, Jones MK, Hayes TM, et al: Human insulin: study of safety and efficacy in man. Br Med J [Clin Res] 1981 Apr 18;282(6272):1264-6

Oyama H, Martin J, Sussman K, et al: The biological activity of catfish pancreatic somatostatin. Regul Pept 1981 Mar;1(6):387-96

Ozawa S: Biphasic effect of thyrotropin-releasing hormone on membrane K+ permeability in rat clonal pituitary cells. Brain Res 1981 Mar 23; 209(1):240-4

P

Packer JE, Mahood JS, Willson RL, et al: Reactions of the trichloromethylperoxy free radical (Cl3COO) with tryptophan, tryptophanyl-tyrosine and lysozyme. Int J Radiat Biol 1981 Feb; 39(2):135-41

Padmanabhan V, Kesner JS, Convey EM: A priming effect of luteinizing hormone releasing hormone on bovine pituitary cells in vitro. J Anim Sci 1981 May;52(5):1137-42

Palatý V: Release of noradrenaline from the rat tail artery induced by inhibition of the sodium pump in calcium-free solution. Can J Physiol Pharmacol 1981 Apr;59(4):347-50

Palkovits M, Raisman R, Briley M, et al: Regional distribution of [3H]imipramine binding in rat brain. Brain Res 1981 Apr 6; 210(1-2):493-8

Palladini G, Margotta V, Medolago-Albani L, et al: Photosensitization and the nervous system in the planarian Dugesia gonocephala. A histochemical, ultrastructural and behavioral investigation. Cell Tissue Res 1981;215(2):271-9

Palmer GC: Regional distribution of neurohumoral responsive adenylate cyclase in rabbit brain microvessels. Neurosci Lett 1981 Jan 20; 21(2):207-10

Palmore WP, Fregly MJ, Simpson CF: Catecholamine-mediated diuresis in turkeys. Proc Soc Exp Biol Med 1981 May;167(1):1-5

Pals DT, Micalizzi ER: Participation of prostaglandins in the vasodepressor effect of substance P. J Pharm Pharmacol 1981 Feb; 33(2):110-1

Pandey BR, Singh SP, Brumleve SJ, et al: Interrelationship between anticonvulsant and enzyme inhibitory properties of N-methyl-N-2-[1-(1-arylthiocarbamido)] cyclopentyl nitrobenzamides. Pharmacol Res Commun 1981 Jan;13(1):65-74

Pang SF, Yu HS, Tang PL: A diurnal rhythm of N-acetylserotonin in the retina of rats. Neurosci Lett 1981 Jan 20;21(2):197-200

Pao CC, Dyess BT: Regulation of small RNAs in Escherichia coli. Alteration in the intracellular concentrations of small RNAs during amino acid and energy starvation. Biochim Biophys Acta 1981 Mar 26;653(1):1-8

Pardo Y, Wajntraub G: [Advances in the research of the contraceptive action of LH-RH analogs] Harefuah 1980 Oct 15;99(8):229-31 (Heb)

Parent A, Descarries L, Beaudet A: Organization of ascending serotonin systems in the adult rat brain. A radioautographic study after intraventricular administration of [3H]5-hydroxytryptamine. Neuroscience 1981;6(2):115-38

Parker CR Jr, Winkel CA, Rush AJ Jr, et al: Plasma concentrations of 11-deoxycorticosterone in women during the menstrual cycle. Obstet Gynecol 1981 Jul;58(1):26-30

Parvez H, Parvez S: Influence of the hypophysio-adrenocortical system on the metabolism of 3H-adrenaline in the hypothalamus, hypophysis and the rest of the brain of rats. Horm Metab Res 1981 Feb;13(2):98-102

Pasich J, Drobnicka B, Kasprzyk A: Dynamik der Arzneimittelabagabe aus Suppositorien. 5. Mitteilung: Liberation von Chlorpromazin aus Zäpfchengrundlagen. Pharmazie 1981;36(1):20 (Eng. Abstr.) (Ger)

Pastuszko A, Wilson DF, Erecińska M: Net uptake of gamma-aminobutyric acid by a high-affinity system of rat brain synaptosomes. Proc Natl Acad Sci USA 1981 Feb;78(2):1242-4

Patel IH, Wedlund P, Levy RH: Induction effect of phenobarbital on the carbamazepine to carbamazepine-10, 11-epoxide pathway in rhesus monkeys. J Pharmacol Exp Ther 1981 Jun;217(3):555-8

Patey G, De La Baume S, Schwartz JC, et al: Selective protection of methionine enkephalin released from brain slices by enkephalinase inhibition. Science 1981 Jun 5;212(4499):1153-5

Patrick RL: Phenylethylamine effects on dopamine synthesis. Structure-activity relationships. Biochem Pharmacol 1981 Jan 15; 30(2):141-6

Patrick RL, Berkowitz AL, Regenstein AC: Effects of in vivo amphetamine administration on dopamine synthesis regulation in rat brain striatal synaptosomes. J Pharmacol Exp Ther 1981 Jun;217(3):686-91

Patterson T, Venables PH: Bilateral skin conductance and the pupillary light-dark reflex: manipulation by chlorpromazine, haloperidol, scopolamine, and placebo. Psychopharmacology (Berlin) 1981; 73(1):63-9

Paul SM, Marangos PJ, Skolnick P: The benzodiazepine—GABA—chloride ionophore receptor complex: common site of minor tranquilizer action. Biol Psychiatry 1981 Mar; 16(3):213-29

Pavlova VI, Malyshev VV, Meerson FZ: Aktivatsiia GAMK-érgicheskoĭ tormoznoĭ sistemy golovnogo mozga pri stresse. Patol Fiziol Eksp Ter 1981 Jan-Feb;(1):26-30 (Eng. Abstr.) (Rus)

Pawelczak K, Rzeszotarska B: Struktura tyreoglobuliny i jej funkcja w tarczycy. Postepy Biochem 1980;26(4):559-83 (132 ref.) (Pol)

Pawlikowski M, Karasek E, Kunert-Radek J, et al: Effects of dopamine on cyclic AMP concentration in the anterior pituitary gland in vitro. J Neural Transm 1981;50(2-4):179-84

Paykel ES, Sireling L: Manic-depressive disorder. Practitioner 1981 Jan; 225(1351):75-7, 79-81

Paykel ES, Rowan PR, Parker RR: Effects of phenelzine and amitriptyline on depression [proceedings] Psychopharmacol Bull 1981 Jan;17(1):104-6

Pazo JH, Tumilasci OR, Medina JH: Studies on the mechanisms of L-dopa-induced salivary secretion. Eur J Pharmacol 1981 Jan 29; 69(3):255-61

Pearce BR, Currie DN, Dutton GR, et al: A simple perfusion chamber for studying neurotransmitter release from cells maintained in monolayer culture. J Neurosci Methods 1981 Feb;3(3):255-9

Pearce BR, Currie DN, Beale R, et al: Potassium-stimulated, calcium-dependent release of [3H]GABA from neuron- and glia-enriched cultures of cells dissociated from rat cerebellum. Brain Res 1981 Feb 16;206(2):485-9

Pečevski J, Savkovic D, Radivojevic D, et al: Effect of oil of nutmeg on the fertility and induction of meiotic chromosome rearrangements in mice and their first generation. Toxicol Lett 1981 Jan;7(3):239-43

Pedersoli WM, Ganjam VK, Nachreiner RF: Serum digoxin concentrations in dogs before, during, and after concomsitant treatment with phenobarbital. Am J Vet Res 1980 Oct;41(10):1639-42

Peet M, Yates RA, Carroll JA, et al: The interaction of tyramine with a single dose of tranylcypromine in healthy volunteers. Br J Clin Pharmacol 1981 Feb;11(2):212-4

Peeters TL, Depraetere Y, Vantrappen GR: Simple extraction method and radioimmunoassay for somatostatin in human plasma. Clin Chem 1981 Jun;27(6):888-91

Peitsch W, Takeuchi K, Johnson LR: Mucosal gastrin receptor. VI. Induction by corticosterone in newborn rats. Am J Physiol 1981 Jun; 240(6):G442-9

AUTHOR SECTION

Pekary AE, Rosen JI, Geola F, et al: Thyrotropin-releasing hormone and a homologous peptide in the reproductive system of the female rat and pig. Biochem Biophys Res Commun 1981 Mar 16;99(1):73-80

Pellegrino de Iraldi A, Corazza JP: Two pools of amines in synaptic vesicles of rat pineal nerves. Rev Can Biol 1981 Mar;40(1):101-9

Pelletier JL, Moyer BR: Thyrotropin-releasing hormone labeled with 99mTc: a potential agent for neuroendocrinological studies. Int J Nucl Med Biol 1981;8(1):122-7

Pelton EW 2d, Kimelberg HK, Shipherd SV, et al: Dopamine and norepinephrine uptake and metabolism by astroglial cells in culture. Life Sci 1981 Apr 6;28(14):1655-63

Perales L, Tallada M, Romero Maroto J, et al: El empleo de drogas para favorecer el vaciamiento en las neo-vejigas. Actas Urol Esp 1981 Jan-Feb;5(1):59-62 (Eng. Abstr.) **(Spa)**

Perchalski RJ, Wilder BJ: GLC analysis of carbamazepine [letter] Ther Drug Monit 1980;2(3):289

Pérez de la Mora M, Possani LD, Tapia R, et al: Demonstration of central gamma-aminobutyrate-containing nerve terminals by means of antibodies against glutamate decarboxylase. Neuroscience 1981; 6(5):875-95

Pérez-López FR, Gómez Agudo G, Abós MD: Serum prolactin and thyrotrophin responses to thyrotrophin-releasing hormone at different times of the day in normal women. Acta Endocrinol (Copenh) 1981 May;97(1):7-11

Peroutka SJ, Lebovitz RM, Snyder SH: Two distinct central serotonin receptors with different physiological functions. Science 1981 May 15; 212(4496):827-9

Perr IN: Effect of the Rennie decision on private hospitalization in New Jersey: two case reports. Am J Psychiatry 1981 Jun;138(6):774-8

Persson B: GABAergic mechanisms in blood pressure control. A pharmacological analysis in the rat. Acta Physiol Scand [Suppl] 1980; 491:1-54

Peselow ED, Dunner DL, Fieve RR, et al: Prophylactic effect of lithium against depression in cyclothymic patients: a life-table analysis. Compr Psychiatry 1981 May-Jun;22(3):257-64

Petrie WM, McEvoy JP, Wilson WH, et al: Viloxazine in the treatment of depressive neurosis: a placebo and standard (imipramine) controlled clinical study. Int Pharmacopsychiatry 1980;15(3):193-6

Pettersson C, Schill G: Separation of enantiomeric amines by ion-pair chromatography. J Chromatogr 1981 Jan 16;204:179-83

Pettijohn TF: Conditioned social aversion in the male Mongolian gerbil (Meriones unguiculatus). J Comp Physiol Psychol 1981 Apr; 95(2):228-39

Petursson H, Lader MH: Withdrawal reaction from clobazam. Br Med J [Clin Res] 1981 Jun 13;282(6280):1931-2

Pevzner L: Effects of hypoxic and hormonal factors on ribonucleic acid content in spinal cord cells: comparison of the metabolic responses in neurons, perineuronal neuroglia and ependyma cells. Neuroscience 1981; 6(5):963-8

Pfeiffer CJ, Cho CH: Inhibition by zinc of hepatic lysosomal release of beta-glucuronidase induced by phorbol-12-myristate-13-acetate (PMA). Cancer Lett 1980 Jul;10(1):51-6

Pfeifle B, Pfeifle R, Faulhaber JD, et al: Thyroid hormone effects on beta-adrenergic receptors in isolated fat cells in rats. Horm Metab Res 1981 Apr;13(4):218-21

Pfeifle CE, Adler DS, Gannaway WL: Phenytoin sodium solubility in three intravenous solutions. Am J Hosp Pharm 1981 Mar;38(3):358-62

Philippe E, Grenon G, Tremblay JP: Baclofen modifies via the release of monoamines the synaptic depression, frequency facilitation, and posttetanic potentiation observed at an identified cholinergic synapse of Aplysia californica. Can J Physiol Pharmacol 1981 Mar;59(3):244-52

Phillips AG, McDonald AC, Wilkie DM: Disruption of autoshaped responding to a single of brain-stimulation reward by neuroleptic drugs. Pharmacol Biochem Behav 1981 Apr;14(4):543-8

Pickel VM, Beckley SC, Sumal KK, et al: Light and electron microscopic localization of enkephalin and tyrosine hydroxylase in neostriatum of fetal and adult rat brain. Acta Histochem [Suppl] (Jena) 1981;24:97-105

Pickett CB, Lu AY: Effect of phenobarbital on the level of translatable rat liver epoxide hydrolase mRNA. Proc Natl Acad Sci USA 1981 Feb;78(2):893-7

Pickett CB, Wells W, Lu AY, et al: Induction of translationally active rat liver glutathione S-transferase B messenger RNA by phenobarbital. Biochem Biophys Res Commun 1981 Apr 15;99(3):1002-10

Picotti GB, Carruba MO, Ravazzani C, et al: Plasma catecholamines in rats exposed to cold: effects of ganglionic and adrenoreceptor blockade. Eur J Pharmacol 1981 Jan 29;69(3):321-9

Piercey MF, Dobry PJ, Schroeder LA, et al: Behavioral evidence that substance P may be a spinal cord sensory neurotransmitter. Brain Res 1981 Apr 6;210(1-2):407-12

Pietzcker A, Poppenberg A, Schley J, et al: Outcome and risks of ultra-long-term treatment with an oral neuroleptic drug. Relationship between perazine serum levels and clinical variables in schizophrenic outpatients. Arch Psychiatr Nervenkr 1981;229(4):315-29

Pigini M, Brasili L: Molecular requirements of the active sites of the cholinergic receptors. XVI - Synthesis and cholinergic activity of 2- or 5-alkyl or 5-phenyl-4-methyl-3-oxo-1-dimethylaminomethylcyclopentane methiodide. Farmaco [Sci] 1981 Feb;36(2):152-8

Pilotte NS, Porter JC: Dopamine in hypophysial portal plasma and prolactin in systemic plasma of rats treated with 5-hydroxytryptamine. Endocrinology 1981 Jun;108(6):2137-41

Pincus JH, Insler NF: Barbiturates and transmitter release at the frog neuromuscular junction. Brain Res 1981 May 25;213(1):127-37

Pindok MT, Sukowski E, Glaviano VV: Cardiac cyclic nucleotides and norepinephrine during neural sympathetic stimulation. Am J Physiol 1981 Apr;240(4):H630-5

Pinto J, Huang YP, Rivlin RS: Inhibition of riboflavin metabolism in rat tissues by chlorpromazine, imipramine, and amitriptyline. J Clin Invest 1981 May;67(5):1500-6

Pipili E, Poyser NL: Effects of nerve stimulation and of administration of noradrenaline or potassium chloride upon the release of prostaglandins, I2, E2, and F2 alpha from te perfused mesenteric arterial bed of the rabbit. Br J Pharmacol 1981 Jan;72(1):89-93

Pirola CJ: Acetilcolina-bradicinina: una nueva interacción péptido-amina transmisora. Medicina (B Aires) 1980 Nov-Dec;40(6 Pt 2):893-5 **(Spa)**

Pisani FD, Di Perri RG: Intravenous valproate: effects on plasma and saliva phenytoin levels. Neurology (NY) 1981 Apr;31(4):467-70

Pis'ko GT, Tolstopiatova GV, Belianina TV, et al: Obosnovanie predel'no dopustimoi kontsentratsii 5,5-dimetilgidantoina v vode vodoemov. Gig Sanit 1981 May;(5):69-70 **(Rus)**

Platt JE, Campbell M, Cohen IL: Effects of lithium carbonate and haloperidol on cognition in aggressive, hospitalized school age children [proceedings] Psychopharmacol Bull 1981 Jan;17(1):123-5

Platt T: Termination of transcription and its regulation in the tryptophan operon of E. coli. Cell 1981 Apr;24(1):10-23

Pletscher A: Liberation of catecholamines from blood platelets. Br J Pharmacol 1981 Feb;72(2):349-54

Pobedinskii NM, Orlova VG, Pakhomova IA, et al: Androgennaia funktsiia kory nadpochechnikov u zhenshchin, stradaiushchikh besplodiem i giperprolaktinemiei. Akush Ginekol (Mosk) 1981 Feb;(2):10-2 (Eng. Abstr.) **(Rus)**

Pockberger H, Petsche H, Rappelsberger P: Die Wirkung von Clonazepam auf das visuell evozierte Potential des Kaninchens. EEG EMG 1981 Mar;12(1):14-20 (Eng. Abstr.) **(Ger)**

Poitras P, Steinbach JH, Van Deventer G, et al: Effect of somatostatin on blood levels of motilin and the interdigestive myoelectric complex in dogs. Endocrinol Jpn 1980 Dec;27 Suppl 1:163-6

Poklis A, Gantner GE: Drug deaths in St. Louis City and County: a brief survey, 1977-1979. Clin Toxicol 1981 Feb;18(2):141-7

Pöldinger W, Reinhardt B: Neurotropic drugs as co-medication to psychotropics. Combined administration of a neurotropic drug and a tetracyclic antidepressant. Int Pharmacopsychiatry 1980;15(3):137-42

Polish LB, Branch RA, Fitzgerald GA: Digitoxin-quinidine interaction: potentiation during administration of cimetidine. South Med J 1981 May; 74(5):633-4

Pollard HB, Pazoles CJ, Creutz CE, et al: Role of intracellular proteins in the regulation of calcium action and transmitter release during exocytosis. Monogr Neural Sci 1980;7:106-16

Pontiroli AE, De Castro e Silva E, Mazzoleni F, et al: The effect of histamine and H1 and H2 receptors on prolactin and luteinizing hormone release in humans: sex differences and the role of stress. J Clin Endocrinol Metab 1981 May;52(5):924-8

Popiel I, Erasmus DA: Schistosoma mansoni: changes in the rate of tyrosine uptake by unisexual females after stimulation by males and male extracts. J Helminthol 1981 Mar;55(1):33-7

Popkin MK, Mackenzie TB, Callies AL, et al: An interdisciplinary comparison of consultation outcomes. Psychiatry vs cardiology. Arch Gen Psychiatry 1981 Jul;38(7):821-5

Poshivalov VP: Pharmaco-ethological analysis of social behaviour of isolated mice. Pharmacol Biochem Behav 1981;14 Suppl 1:53-9

Post RM, Lockfeld A, Squillace KM, et al: Drug-environment interaction: context dependency of cocaine-induced behavioral sensitization. Life Sci 1981 Feb 16;28(7):755-60

Post RM, Ballenger JC, Rey AC, et al: Slow and rapid onset of manic episodes: implications for underlying biology. Psychiatry Res 1981 Apr; 4(2):229-37

Potter JD, Piascik MT, Wisler PL, et al: Calcium dependent regulation of brain and cardiac muscle adenylate cyclase. Ann NY Acad Sci 1980; 356:220-31

Potter WZ, Calil HM, Extein I, et al: Specific norepinephrine and serotonin uptake inhibitors in man: a crossover study with pharmacokinetic, biochemical, neuroendocrine and behavioral parameters. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):152-65

Potter WZ, Calil HM, Extein I, et al: Crossover study of zimelidine and desipramine in depression: evidence for amine specificity [proceedings] Psychopharmacol Bull 1981 Jan;17(1):26-9

Powell DA, Nahata MC, Durrell DC, et al: Interactions among chloramphenicol, phenytoin, and phenobarbital in a pediatric patient. J Pediatr 1981 Jun;98(6):1001-3

Prakash R, Sethi N, Agrawal SS, et al: A case report of megaloblastic anemia secondary to lithium. Am J Psychiatry 1981 Jun;138(6):849

Prasad AS, Abbasi AA, Rabbani P, et al: Effect of zinc supplementation on serum testosterone level in adult male sickle cell anemia subjects. Am J Hematol 1981;10(2):119–27

Prato A, Clementi G, Nicoletti F, et al: Possible role of prolactin in the modification of medial basal hypothalamic glutamic acid decarboxylase activity. Eur J Pharmacol 1981 Apr 24;71(1):169–72

Predescu V, Alexandrescu L, Ciurea T: Dimensiuni actuale ale terapiei biologice in afectiunile psihice. Nota a II–a. Rev Med Interna [Neurol Psihiatr] 1980 Oct–Dec;25(4):241–51 (205 ref.) (Rum)

Preskorn SH, Irwin GH, Simpson S, et al: Medical therapies for mood disorders alter the blood–brain barrier. Science 1981 Jul 24; 213(4506):469–71

Presl J: Inhibin — nový ovariální hormon. Cesk Gynekol 1981 Mar; 46(2):132–3 (Cze)

Priola DV, O'Brien WJ, Dail WG, et al: Cardiac catecholamine stores after cardiac sympathectomy, 6–OHDA, and cardiac denervation. Am J Physiol 1981 Jun;240(6):H889–95

Prokopczuk A, Pytkowski B, Lewartowski B: Effect of acetylcholine on calcium efflux from atrial myocardium. Eur J Pharmacol 1981 Mar 5; 70(1):1–6

Proshina LIa: Issledovanie gistamina i serotonina v odnoi probe krovi. Lab Delo 1981;(2):90–3 (Eng. Abstr.) (Rus)

Prough RA, Freeman PC, Hines RN: The oxidation of hydrazine derivatives catalyzed by the purified liver microsomal FAD–containing monooxygenase. J Biol Chem 1981 May 10;256(9):4178–84

Prozialeck WC, Cimino M, Weiss B: Photoaffinity labeling of calmodulin byphenothiazine antipsychotics. Mol Pharmacol 1981 Mar;19(2):264–9

Puglisi–Allegra S, Simler S, Kempf E, et al: Involvement of the GABAergic system on shock–induced aggressive behavior in two strains of mice. Pharmacol Biochem Behav 1981;14 Suppl 1:13–8

Pugsley TA, Lippmann W: Affinity of butriptyline and other tricyclic antidepressants for alpha–adrenoceptor binding sites in rat brain. J Pharm Pharmacol 1981 Feb;33(2):113–5

Puşcaş I, Búzás G, Surányi P, et al: Inhibition of carbonic anhydrase by pirenzepine. Int J Clin Pharmacol Ther Toxicol 1981 Feb;19(2):75–7

Pużyński S, Rode A, Załuska M: Aktywność beta–hydroksylazy dopaminy w osoczu chorych z endogennymi zespołami dekpresyjnymi. Psychiatr Pol 1980 Nov–Dec;14(6):581–6 (Eng. Abstr.) (Pol)

Pyke J, Page J: Schizophrenia. Can Nurse 1981 May;77(5):39–43

Q

Qayum A, Yusuf SM: Effect of progesterone therapy on the responses of the isolated rat stomach fundus strip preparations to 5–hydroxytryptamine and acetylcholine. JPMA 1981 Apr;31(4):84–8

Quaglio MP, Bellini AM: A gas chromatographic method for the determination of fluanisone, moperone, aceperone and pipamperone in human plasma. Farmaco [Prat] 1981 Apr;36(4):204–14

Quatrini U, Benigno A: Effetti della somministrazione di sodium pentobarbital sulla tolleranza alla ipossia acuta nel ratto albino. Boll Soc Ital Biol Sper 1981 Feb 15;57(3):333–9 (Ita)

Queisnerová M, Dlabač A, Roubal Z: Srovnání krevních a žlučových hladin oxyprothepinu a dokloxythepinu u krys. Cesk Farm 1981 Feb; 30(1):14–5 (Eng. Abstr.) (Cze)

Quirce CM, Maickel RP: Alterations of biochemical parameters by acute and repetitive stress situations in mice. Psychoneuroendocrinology 1981; 6(1):91–7

Quitkin FM, Kane JM, Rifkin A, et al: Lithium and imipramine in the prophylaxis of unipolar and bipolar II depression: a prospective, placebo–controlled comparison [proceedings] Psychopharmacol Bull 1981 Jan;17(1):142–4

R

Raab A, Haedenkamp G: Impact of social conflict between mice on testosterone binding in the central nervous system. Neuroendocrinology 1981 May;32(5):272–7

Radelet ML: Health beliefs, social networks, and tranquilizer use. J Health Soc Behav 1981 Jun;22(2):165–73

Radulovacki M, Wojcik WJ, Walovitch R, et al: Phenoxybenzamine and bromocriptine attenuate need for REM sleep in rats. Pharmacol Biochem Behav 1981 Mar;14(3):371–5

Radulovacki M, Brodie M, Walovitch R, et al: Bromocriptine, dihydroergotoxine and sleep in rats: effects of repeated administration. Gerontology 1981;27(3):152–7

Rafaelsen OJ, Clemmesen L, Lund H, et al: Comparison of peripheral anticholinergic effects of antidepressants: dry mouth. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):364–9

Raft D, Davidson J, Wasik J, et al: Relationship between response to phenelzine and MAO inhibition in a clinical trial of phenelzine, amitriptyline and placebo. Neuropsychobiology 1981;7(3):122–6

Raghunathan Y, Amsel L, Hinsvark O, et al: Sustained–release drug delivery system I: Coated ion–exchange resin system for phenylpropanolamine and other drugs. J Pharm Sci 1981 Apr; 70(4):379–84

Rahamimoff R, Lev–Tov A, Meiri H, et al: Regulation of acetylcholine liberation from presynaptic nerve terminals. Monogr Neural Sci 1980; 7:3–18

Rahman MK, Nagatsu T, Kato T: New and highly sensitive assay for L–5–hydroxytryptophan decarboxylase activity by high–performance liquid chromatography–voltammetry. J Chromatogr 1980 Dec 12; 221(2):265–70

Raininko R: Histamine release and endothelial leakage from an intravascular contrast medium. ROEFO 1981 Apr;134(4):445–9

Rajkumar K, Sharma PL: Effect of ovulation on the response of the rabbit oviduct to acetylcholine in vitro. Int J Fertil 1981;26(1):57–60

Raleigh MJ, Yuwiler A, Brammer GL, et al: Peripheral correlates of serotonergically–influenced behaviors in vervet monkeys (Cercopithecus aethiops sabaeus). Psychopharmacology (Berlin) 1981; 72(3):241–6

Ralston IM, Dunford HB: Horseradish peroxidase. XLII. Oxidations of L–tyrosine and 3,5–diiodo–L–tyrosine by compound II. Can J Biochem 1980 Nov;58(11):1270–6

Ramos JG: Cortical effects of the electrical stimulation of the N. raphe dorsalis in the cat. Acta Physiol Lat Am 1978;28(2–3):83–95

Rampello L, Nicoletti F, Patti F, et al: Valutazione del behavior motorio in condizioni di iperrolattinemia. Acta Neurol (Napoli) 1981 Feb; 36(1):297–301 (Eng. Abstr.) (Ita)

Rance N, Wise PM, Selmanoff MK, et al: Catecholamine turnover rates in discrete hypothalamic areas and associated changes in median eminence luteinizing hormone–releasing hormone and serum gonadotropins on proestrus and diestrous day 1. Endocrinology 1981 May;108(5):1795–802

Rance N, Wise PM, Barraclough CA: Negative feedback effects of progesterone correlated with changes in hypothalamic norepinephrine and dopamine turnover rates, median eminence luteinizing hormone–releasing hormone, and peripheral plasma gonadotropins. Endocrinology 1981 Jun;108(6):2194–9

Randall PL: An alternative mechanism of actions for neuroleptic and antidepressant drugs. Med Hypotheses 1981 Feb;7(2):251–60

Ranise A, Benassi E, Besio G: Rapid gas chromatography method for the determination of carbamazepine and unrearranged carbamazepine–10,11–epoxide in human plasma. J Chromatogr 1981 Jan 2;222(1):120–4

Rao AG, Cann JR: A comparative study of the interaction of chlorpromazine, trifluoperazine, and promethazine with mouse brain tubulin. Mol Pharmacol 1981 Mar;19(2):295–301

Rao GS: MOde of entry of steroid and thyroid hormones into cells. Mol Cell Endocrinol 1981 Feb;21(2):97–108 (68 ref.)

Rao MV, Atreyi M, Rajeswari MR: Fluorescence spectra of lysozyme excited at 305 NM in presence of urea. Int J Pept Protein Res 1981 Feb;17(2):205–10

Rao SP, Dunn BM: Conformation of pepsin and pepsinogen: some aspects of the role of tyrosine residues and the 1–44 segment of pepsinogen on conformational stability. Arch Biochem Biophys 1981 Mar; 207(1):135–40

Rao VA, Bailey J, Bishop M, et al: A clinical and pharmacodynamic evaluation of sulpiride. Psychopharmacology (Berlin) 1981;73(1):77–80

Rappay G, Komolov IS, Fazekas I, et al: Rate of thymidine incorporation and incidence of parenchymal cell division in adult rat hypophyseal cell cultures. Effect of thyroliberin and somatostatin. Acta Biol Acad Sci Hung 1980;31(1–3):249–55

Ratna L: Addiction to temazepam. Br Med J [Clin Res] 1981 Jun 6; 282(6279):1837–8

Ratnasooriya WD, Gilmore DP, Wadsworth RM: Effect of norephedrine locally applied to the vas deferens on semen quality of rabbits. Indian J Exp Biol 1981 Jan;19(1):20–5

Rattner BA, Eastin WC Jr: Plasma corticosterone and thyroxine concentrations during chronic ingestion of crude oil in mallard ducks (Anas platyrhynchos). Comp Biochem Physiol [C] 1981;68C(2):103–7

Raum WJ, Swerdloff RS: The role of hypothalamic adrenergic receptors in preventing testosterone–induced androgenization in the female rat brain. Endocrinology 1981 Jul;109(1):273–8

Raynaud JP, Moguilewsky M: Corticosteroid–binding globulin and corticosterone interaction with progesterone receptors [letter] Nature 1981 May 14;291(5811):171–2

Rea MA, McBride WJ, Rohde BH: Levels of glutamate, aspartate, GABA, and taurine in different regions of the cerebellum after x–irradiation–induced neuronal loss. Neurochem Res 1981 Jan;6(1):33–9

Reatig N: Department of Health and Human Services regulations affecting psychopharmacology research. Psychopharmacol Bull 1981 Apr; 17(2):56–65

Reavill C, Jenner P, Leigh N, et al: The role of nigral projections to the thalamus in drug–induced circling behaviour in the rat. Life Sci 1981 Mar 30;28(13):1457–66

Rebec GV, Alloway KD, Curtis SD: Apparent serotonergic modulation of the dose–dependent biphasic response of neostriatal neurons produced by D–amphetamine. Brain Res 1981 Apr 6;210(1–2):277–89

Rechberger T, Turski L, Turski W, et al: Wpływ atropiny na

antyamfetaminowe działanie flufenazyny.
Ann Univ Mariae Curie Sklodowska [Med] 1979;34:333–9 (Eng. Abstr.) **(Pol)**

Reddy MM, Bures J: Unit activity changes elicited in amygdala and neocortex of anaesthetized rats by intraperitoneal injection of lithium chloride. Neurosci Lett 1981 Mar 10;22(2):169–72

Reddy PV, Menon KM: Existence of multiple molecular forms of luteinizing hormone in rat: differences in immunological and biological activities between stored and circulating forms.
Acta Endocrinol (Copenh) 1981 May;97(1):33–41

Reed KW, Murray WJ, Roche EB, et al: Conformational analysis of the reverse ester of acetylcholine, cholinergic potency, and cholinergic models. Gen Pharmacol 1981;12(3):177–85

Rees JA: Clinical interpretation of pharmacokinetic data on dothiepin hydrochloride (Dosulepin, Prothiaden). J Int Med Res 1981;9(2):98–102

Rehavi M, Skolnick P, Hulihan B, et al: 'High affinity' binding of [3H]desipramine to rat cerebral cortex: relationship to tricyclic antidepressant-induced inhibition of norepinephrine uptake.
Eur J Pharmacol 1981 Apr 9;70(4):597–9

Rehavi M, Ittah Y, Rice KC, et al: 2-nitroimipramine: a selective irreversible inhibitor of [3H] serotonin uptake and [3H] imipramine binding in platelets. Biochem Biophys Res Commun 1981 Apr 15; 99(3):954–9

Reifler BV, Ward N, Davis CM, et al: Thiothixene plasma levels and clinical response in acute schizophrenia. J Clin Psychiatry 1981 May; 42(5):207–11

Rein G, Glover V, Sandler M: Sulphate conjugation of biologically active monoamines and their metabolites by human platelet phenolsulphotransferase. Clin Chim Acta 1981 Apr 9;111(2–3):247–56

Reinhart W, Stäubli M, Straub PW: The effect of a single dose of propranolol on human erythrocytes in vivo. Eur J Clin Invest 1981 Feb;11(1):65–8

Renaud R, Macler J: Le traitement des bouffées de chaleur de la ménopause. Etude comparative de deux médicaments.
Sem Hop Paris 1981 Feb 18–25;57(7–8):353–5 (Eng. Abstr.) **(Fre)**

Renauld A, Sverdlik RC, Garrido D: Blood sugar, serum insulin and serum free fatty acid responses to slow graded glucose in thyroxine-treated dogs. Acta Diabetol Lat 1980 Jul–Dec;17(3–4):189–97

Rendu F, Nurden AT, Lebret M, et al: Further investigations on Bernard-Soulier platelet abnormalities. J Lab Clin Med 1981 May; 97(5):689–99

Rettig K, Duckett GE, Sweetland M, et al: Urinary excretion of immunoreactive luteinizing hormone-releasing hormone-like material in children correlation with pubertal development.
J Clin Endocrinol Metab 1981 Jun;52(6):1150–5

Rettori V, Seilicovich A, Goljman S, et al: Effect of inhibitors of catecholamine synthesis on the pituitary response to LH-RH.
Arch Androl 1981 Mar;6(2):151–4

Reus VI, Lake CR, Post RM: Effect of piribedil (ET-495) on plasma norepinephrine: relationship to antidepressant response.
Commun Psychopharmacol 1980;4(3):207–13

Reveley MA, Glover V, Sandler M, et al: Increased platelet monoamine oxidase activity in affective disorders. Psychopharmacology (Berlin) 1981;73(3):257–60

Reveley MA, Glover V, Sandler M, et al: Brain monoamine oxidase activity in schizophrenics and controls. Arch Gen Psychiatry 1981 Jun; 38(6):663–5

Reynolds GD, Harding DR, Hancock WS: Use of the chromogenic p-(p-(dimethylamino)phenylazo) benzyl (AZ) ester in the synthesis of leu-enkephalin. Int J Pept Protein Res 1981 Feb;17(2):231–4

Rhee HM, Huang WH, Askari A: Relationship between the positive inotropic effect of ouabain and its inhibitory effects on Na+, K+ -ATPase and active transport of Rb+ in the dog heart.
Eur J Pharmacol 1981 Mar 26;70(3):273–8

Rhoten WB, Hall CE: Four hormones in the pancreas of the lizard, Anolis carolinensis. Anat Rec 1981 Jan;199(1):89–97

Ribeiro AA, Wemmer D, Bray RP, et al: High-resolution nuclear magnetic resonance studies of the Lac repressor. 1. Assignments of tyrosine resonances in the N-terminal headpiece. Biochemistry 1981 Feb 17; 20(4):818–23

Ribes G, Trimble ER, Blayac JP, et al: Effect of a new hypoglycaemic agent (HB 699) on the in vivo secretion of pancreatic hormones in the dog. Diabetologia 1981 Apr;20(4):501–5

Richman CM, Kinnealey A, Hoffman PC: Granulopoietic effects of lithium on human bone marrow in vitro. Exp Hemetol 1981 Apr;9(4):449–55

Richman RA, Weiss JP, Hochberg Z, et al: Regulation of growth hormone release: evidence against negative feedback in rat pituitary cells.
Endocrinology 1981 Jun;108(6):2287–92

Richter H: Suizidverhütung bei Psychosen und kombinierte Pharmakotherapie und Psychotherapie. Agressologie 1980;21(A):41–3 **(Ger)**

Rickels K, Brown AS, Cohen D, et al: Clobazam and diazepam in anxiety. Clin Pharmacol Ther 1981 Jul;30(1):95–100

Rickels K, Case WG, Diamond L: Relapse after short-term drug therapy in neurotic outpatients. Int Pharmacopsychiatry 1980;15(3):186–92

Říčný J, Tuček S: Acetyl coenzyme A and acetylcholine in slices of rat caudate nuclei incubated in the presence of metabolic inhibitors.
J Biol Chem 1981 May 25;256(10):4919–23

Ridley RM, Haystead TA, Baker HF: An analysis of visual object reversal learning in the marmoset after amphetamine and haloperidol.
Pharmacol Biochem Behav 1981 Mar;14(3):345–51

Rigter H, Greven HM, van Nispen JW, et al: Behavioral activity of met-enkephalin and ACTH4-10 and other peptides containing a phenylalanine and methionine residue.
Biochem Biophys Res Commun 1981 Jan 30;98(2):424–30

Riley GJ, Shaw DM: Plasma tryptophan binding to albumin in unipolar depressives. Acta Psychiatr Scand 1981 Feb;63(2):165–72

Rimón R, Averbuch I, Rozick P, et al: Serum and CSF levels of haloperidol by radioimmunoassay and radioreceptor assay during high-dose therapy of resistant schizophrenic patients. Psychopharmacology (Berlin) 1981; 73(2):197–9

Rioux F, Quirion R, St-Pierre S, et al: The hypotensive effect of centrally administered neurotensin in rats. Eur J Pharmacol 1981 Jan 29; 69(3):241–7

Riva R, de Anna M, Albani F, et al: Rapid quantitation of flurazepam and its major metabolite, N-desalkylflurazepam, in human plasma by gas-liquid chromatography with electron-capture detection.
J Chromatogr 1981 Mar 13;222(3):491–5

Rivett AJ, Smith IL, Tipton KF: The enzymes catalysing succinic semialdehyde reduction in rat brain. Biochem Pharmacol 1981 Apr 1; 30(7):741–7

Roberts ML: A comparison of the actions of acetylcholine and bradykinin on the guinea pig ileum. Naunyn Schmiedebergs Arch Pharmacol 1980 Nov;314(3):267–70

Robertson HA: Octopamine—after a decade as a putative neuroregulator. Essays Neurochem Neuropharmacol 1981;5:47–73 (83 ref.)

Robinson GM, Sellers EM, Janecek E: Barbiturate and hypnosedative withdrawal by a multiple oral phenobarbital loading dose technique. Clin Pharmacol Ther 1981 Jul;30(1):71–6

Røed A, Brodal B: Inhibition of sarcolemma ATPases by some membrane-stabilizing drugs. Acta Pharmacol Toxicol (Copenh) 1981 Jan;48(1):65–8

Roesch CL, Borowitz JL: Contrasting effects of diethylstilbestrol and estradiol on contraction of isolated rat aorta. Pharmacology 1981; 22(1):15–23

Rohner-Jeanrenaud F, Jeanrenaud B: Possible involvement of the cholinergic system in hormonal secretion by the perfused pancreas from ventromedial-hypothalamic lesioned rats. Diabetologia 1981 Mar; 20(3):217–22

Ron M, Shapiro A, Caine M: The action of bromocriptine on human detrusor muscle. Urol Res 1980 Dec 19;8(4):207–9

Roquebert J, Demichel P, Malek A: Antinoradrenergic activity of thymoxamine and its metabolites in rats.
Arch Int Pharmacodyn Ther 1981 Jan;249(1):12–25

Rorsman B, Franzén G, Sjöstedt L, et al: Hemodialysis in schizophrenia: psychiatric aspects of treatment failure in a pilot study.
Neuropsychobiology 1981;7(3):127–36

Rosen AJ, Mueser KT, Sussman S, et al: The effects of neuroleptic drugs on the social interactions of hospitalized psychotic patients.
J Nerv Ment Dis 1981 Apr;169(4):240–3

Rosenberg HC, Chiu TH: Tolerance during chronic benzodiazepine treatment associated with decreased receptor binding.
Eur J Pharmacol 1981 Apr 9;70(4):453–60

Rosenberg JM, Kirschenbaum HL: What to watch for with lithium.
RN 1981 Jul;44(7):44–6

Rosenkrantz H, Fleischman RW, Grant RJ: Toxicity of short-term administration of cannabinoids to rhesus monkeys.
Toxicol Appl Pharmacol 1981 Mar 30;58(1):118–31

Rosenshtraukh LV, Zakharov SI, Bogdanov KY: The load clamp analysis of mammalian heart contraction in the presence of noradrenaline.
Can J Physiol Pharmacol 1980 Dec;58(12):1504–8

Rosenthal GA: A mechanism of L-canaline toxicity. Eur J Biochem 1981 Feb;114(2):301–4

Roskoski R Jr, Rauch N, Roskoski LM: Glutamate, aspartate, and gamma-aminobutyrate transport by membrane vesicles prepared from rat brain. Arch Biochem Biophys 1981 Apr 1;207(2):407–15

Ross ME, Reis DJ, Joh TH: Monoclonal antibodies to tyrosine hydroxylase: production and characterization. Brain Res 1981 Mar 16; 208(2):493–8

Ross T: Psychiatry. 4. Drugged to the eyeballs. Nurs Mirror 1981 Apr 16;152(16):16–8

Roth JA, Eddy BJ, Pearce LB, et al: Phenylhydrazine: selective inhibition of human brain type B monoamine oxidase. Biochem Pharmacol 1981 May 1;30(9):945–50

Roth RD: Utilization of epinephrine-containing anesthetic solutions in the toes. J Am Podiatry Assoc 1981 Apr;71(4):189–99

Rothschild AM: Plasma kallikrein-generating activity evoked by rat peritoneal-fluid mast cells following treatment with epinephrine, 8-bromo-cyclic 3',5'-guanosine monophosphate or compound 48/80. Biochem Pharmacol 1981 Mar 1;30(5):481–7

Rothwell NJ, Stock MJ: Influence of noradrenaline on blood flow to brown adipose tissue in rats exhibiting diet-induced thermogenesis.

Pfluegers Arch 1981 Mar;389(3):237–42

Rotiroti D, Naccari F, Nisticò G: Behavioural, ECoG spectrum power and body temperature effects of BW 245C, a prostaglandin analogue after intraventricular microinjection in chicks. Neuropharmacology 1981 May;20(5):517–20

Rotrosen J, Stanley M, Lautin A, et al: Discrimination of functionally heterogeneous receptor subpopulations: antipsychotic and antidopaminergic properties of metoclopramide [proceedings] Psychopharmacol Bull 1981 Jan;17(1):110–3

Roubicek J, Krebs E, Poeldinger W: Classification of endorphins/enkephalins in brain physiology and pathology (based on EEG and clinical study of synthetically-modified methionine-enkephalin). Prog Neuropsychopharmacol 1980; 4(4–5):507–18

Roufogalis BD: Phenothiazine antagonism of calmodulin: a structurally-nonspecific interaction. Biochem Biophys Res Commun 1981 Feb 12;98(3):607–13

Routledge PA, Stargel WW, Kitchell BB, et al: Sex-related differences in the plasma protein binding of lignocaine and diazepam. Br J Clin Pharmacol 1981 Mar;11(3):245–50

Rowell FJ, Hui SM, Kamel SR: 3H and 125I radioimmunoassays of haloperidol compared with fluoroimmunoassay involving antibody coupled to magnetizable solid phase. Clin Chem 1981 Jul;27(7):1249–54

Roy TK: Histochemical studies on Raillietina (Raillietina) johri (Cestoda: Davaineidae). III. Esterases. J Helminthol 1980 Sep;54(3):219–22

Royall DR, Klemm WR: Dopaminergic mediation of reward: evidence gained using a natural reinforcer in a behavioral contrast paradigm. Neurosci Lett 1981 Jan 20;21(2):223–9

Rozengurt E, Gelehrter TD, Legg A, et al: Melittin stimulates Na entry, Na–K pump activity and DNA synthesis in quiescent cultures of mouse cells. Cell 1981 Mar;23(3):781–8

Rudorfer MV, Young RC: Plasma desipramine levels after single dosage and at steady state in outpatients. Commun Psychopharmacol 1980; 4(3):185–8

Ruffieux A, Schultz W: Influence de la dopamine sur les neurones de la pars reticulata de la substance noire. J Physiol (Paris) 1981 Apr; 77(1):63–9 (Eng. Abstr.) **(Fre)**

Rufo GA Jr, Yorek MA, Ray PD: The influences of glucagon, epinephrine and alpha- and beta-adrenergic agents on glycogenolysis in isolated rabbit hepatocytes and perfused livers. Biochim Biophys Acta 1981 May 18;674(3):297–305

Rush ME, Ashiru OA, Lipner H, et al: The actions of porcine follicular fluid and estradiol on periovulatory secretion of gonadotropic hormones in rats. Endocrinology 1981 Jun;108(6):2316–23

Russell JA, Harrison DJ, McNeilly AS: Bromocriptine and alpha-ergocryptine do not inhibit oxytocin secretion in the lactating rat. J Endocrinol 1981 Apr;89(1):91–8

Russell RW, Pechnick R, Jope RS: Effects of lithium on behavioral reactivity: relation to increases in brain cholinergic activity. Psychopharmacology (Berlin) 1981;73(2):120–5

Rüther E, Nedopil N, Strauss A: Verlauf schizophrener Psychosen unter neuroleptischer Therapie. MMW 1981 May 8;123(19):803–4 **(Ger)**

S

Saameli W: Ambulante Langzeittherapie mit Depot-Neuroleptika. Praxis 1981 Feb 3;70(6):206–10 (Eng. Abstr.) **(Ger)**

Saano V, Urtti A, Airaksinen MM: Increase in 3H-flunitrazepam binding in vitro and in vivo to rat brain benzodiazepine receptors by tofizopam, a 3,4-benzo-diazepine. Pharmacol Res Commun 1981 Jan;13(1):75–85

El-Sabbagh HN, Bloom SR, Adrian TE, et al: The effect of pirenzepine on meal-stimulated gastrointestinal hormones. Scand J Gastroenterol [Suppl] 1980;15(66):57–61

el-Sabbagh HN, Prinz RA, Welbourn RB, et al: Influence of intravenous pirenzepine on gastric acid and pepsin in man. Scand J Gastroenterol [Suppl] 1980;15(66):73–7

Saccà L, Cicala M, Corso G, et al: Effect of counterregulatory hormones on kinetic response to ingested glucose in dogs. Am J Physiol 1981 May;240(5):E465–73

Sahgal V, Sahgal S, Subramani V: Morphological and histochemical correlation of recovery after spinal transection in rat. Paraplegia 1981; 19(1):1–6

Sahu SC, Dominic CJ: Evidence for the involvement of serotoninergic system in the male-induced ovo-implantation failure (Bruce effect) in mice. Ann Endocrinol (Paris) 1980 Sep–Oct;41(5):425–9

Sairam MR, Ranganathan MR, Ramasharma K, et al: Isolation and characterization of a bovine seminal plasma protein inhibiting pituitary FSH secretion. Mol Cell Endocrinol 1981 May;22(2):231–50

Saito H: The effects of strychnine and bicuculline on the responses of X- and Y-cells of the isolated eye-cut preparation of the cat. Brain Res 1981 May 11;212(1):243–8

Sakakura M, Yoshioka M, Kobayashi M, et al: The site of inhibitory action of a natural (corticosterone) and synthetic steroid (dexamethasone) in the hypothalamic-pituitary-adrenal axis. Neuroendocrinology 1981 Mar;32(3):174–8

Sakanashi M, Hirata A, Takenaka F: A further study on constrictor responses of dog coronary arterial strips to acetylcholine under potassium-contracture. Jpn Heart J 1981 Mar;22(2):211–7

Sakanashi M, Nishi K: Relaxation of isolated dog coronary artery induced by propranolol. Eur J Pharmacol 1981 Mar 5;70(1):83–5

Sakoda H: [Effect of adrenaline, noradrenaline and acetylcholine on rabbit and human uterine activity in vivo (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1980 Jun;32(6):697–705 (Eng. Abstr.) **(Jpn)**

El-Salhy M, Abou-el-Ela R, Falkmer S, et al: Immunohistochemical evidence of gastro-entero-pancreatic neurohormonal peptides of vertebrate type in the nervous system of the larva of a dipteran insect, the hoverfly, Eristalis aeneus. Regul Pept 1980 Dec;1(3):187–204

Saligaut C, Moore N, Boulu R, et al: hypobaric hypoxia: central catecholamine levels and cortical PO2 and avoidance response in rats treated with apomorphine. Aviat Space Environ Med 1981 Mar; 52(3):166–70

Salisbury JL, Condeelis JS, Satir P: Evidence for the involvement of calmodulin in endocytosis. Ann NY Acad Sci 1980;356:429–32

Salmon DM, Fatih S, Schulster D: Cyclic AMP is not obligatory for adrenal steroidogenesis. Biochem Soc Trans 1981 Feb;9(1):96–7

Salt TE, Hill RG: Excitatory amino acids as transmitter candidates of vibrissae afferent fibres to the rat trigeminal nucleus caudalis. Neurosci Lett 1981 Mar 10;22(2):183–7

Samanin R, Mennini T, Garattini S: Evidence that it is possible to cause anorexia by increasing release and/or directly stimulating postsynaptic serotonin receptors in the brain. Prog Neuropsychopharmacol 1980; 4(4–5):363–9

Samnegård H, Tydén G, Thulin L, et al: Effect of somatostatin on regional splanchnic blood flows in man. Angiographic studies. Acta Chir Scand [Suppl] 1980;Suppl 500:71–3

Samols E, Stagner JI, Weir GC: Autonomic function and control of pancreatic somatostatin. Diabetologia 1981 Mar;20 Suppl:388–92

Samson WK, Snyder G, Fawcett CP, et al: Chromatographic and biologic analysis of ME and OVLT LHRH. Peptides (Fayetteville) 1980 Spring; 1(1):97–102

Sanada H, Miyazaki M: Regulation of tryptophan-niacin metabolism by hormones. J Nutr Sci Vitaminol (Tokyo) 1980;26(6):617–27

Sandberg BE, Lee CM, Hanley MR, et al: Synthesis and biological properties of enzyme-resistant analogues of substance P. Eur J Biochem 1981 Feb;114(2):329–37

Sanders SW: Prediction of phenytoin dosage requirements [letter] J Pediatr 1981 May;98(5):856–7

Sano Y, Inoue H: Effect of monovalent cations on the aggregation of tobacco mosaic virus by chondroitin sulfate. Microbiol Immunol 1981; 25(2):155–61

Sansone M, Ammassari-Teule M, Renzi P, et al: Different effects of apomorphine on locomotor activity in C57BL/6 and DBA/2 mice. Pharmacol Biochem Behav 1981 May;14(5):741–3

Santer RM, Lever JD, Davies TW: The detection by x-ray microanalysis of noradrenaline in sympathetic nerve terminals of the rat vas deferens. Histochemistry 1981;71(1):155–60

Santidrian S, Young VR: Effect of androgens on the rate of muscle protein breakdown in rats treated with glucocorticoids. Reproduccion 1980 Oct–Dec;4(4):331–3

Santolaya RC, Ciocca D: Effects of pimozide on the ultrastructure of the pars intermedia in the rat. Cell Tissue Res 1981;217(2):397–403

Saraswat LD, Holdiness MR, Justice JB, et al: Determination of dopamine, homovanillic acid and 3,4-dihydroxyphenylacetic acid in rat brain striatum by high-performance liquid chromatography with electrochemical detection. J Chromatogr 1981 Mar 13;222(3):353–62

Sarlièvé LL, DeFeudis FV, Ossola L, et al: Development of [3H]muscimol binding to subcellular particles of a culture of mouse brain. Neurochem Res 1980 Dec;5(12):1279–90

Sarto G: Modulazione dell'effetto della morfina da parte di noradrenalina e serotonina sull'intestino isolato di cavia. Boll Soc Ital Biol Sper 1981 Feb 28;57(4):394–400 (Eng. Abstr.) **(Ita)**

Sarukhanian ZhG, Babaian EA, Darbinian GV: Nekotorye dannye ob okislitel'nom dezaminirovanii biogennykh monoaminov v mitokhondrial'noĭ fraktsii golovnogo mozga i pecheni krys. Gig Tr Prof Zabol 1981 Apr;(4):30–3 (Eng. Abstr.) **(Rus)**

Satir BH, Garofalo RS, Gilligan DM, et al: Possible functions of calmodulin in protozoa. Ann NY Acad Sci 1980;356:83–91

Sato T, Ono H: Facilitation of Neuromuscular transmission by calcium antagonists, diltiazem, nifedipine and verapamil, in the dog. Arch Int Pharmacodyn Ther 1981 Feb;249(2):235–46

Satterfield JH, Schell AM, Barb SD: Potential risk of prolonged administration of stimulant medication for hyperactive children. JDPB 1980 Sep;1(3):102–7

Savickij IV, Rozanov VA: Denkbare Wege zur gerichteten Regulierung des zerebralen Gamma-Aminobuttersäure- (GABS-) Umsatzes bei lokaler Bestrahlung des Kopfes. Radiobiol Radiother (Berl) 1980; 21(6):800–8 (Eng. Abstr.) **(Ger)**

Savina LS, Ivanova IV: Vliianie kholinergicheskikh faktorov na sostoianie membrannykh belkov éritrotsitov zhivotnykh. Biull Eksp Biol Med 1981 Feb;91(2):153–5 (Eng. Abstr.) **(Rus)**

AUTHOR SECTION

Savva D: Mutation in Escherichia coli during substrate-accelerated death. Microbios 1980;28(113-114):157-65

Sawada S, Yamamoto C: Postsynaptic inhibitory actions of catecholamines and opioid peptides in the bed nucleus of the stria terminalis. Exp Brain Res 1981;41(3-4):264-70

Sawhney RC, Rastogi GK, Kumar M, et al: Relationship between thyrotropin, thyroid hormones, thyroxine-binding globulin and estradiol-17 beta levels in normal pregnancy. Indian J Med Res 1981 Jan;73:41-52

Schanbacher BD: Importance of the episodic nature of luteinizing hormone secretion for normal development of the bovine testis during puberty: interference with oestradiol-17 beta. J Endocrinol 1981 Mar; 88(3):393-400

Scharbach H: Essai en double aveugle (oxprénolol/diazépam) dans l'anxiété. Encephale 1981;7(1):51-8 (Eng. Abstr.) (Fre)

Schatz RA, Wilens TE, Sellinger OZ: Decreased transmethylation of biogenic amines after in vivo elevation of brain S-adenosyl-l-homocysteine. J Neurochem 1981 May;36(5):1739-48

Schatzman RC, Wise BC, Kuo JF: Phospholipid-sensitive calcium-dependent protein kinase: inhibition by antipsychotic drugs. Biochem Biophys Res Commun 1981 Feb 12;98(3):669-76

Scheiber SC, Cohen I, Yamamura H, et al: Dialysis for schizophrenia: an uncontrolled study of 11 patients. Am J Psychiatry 1981 May; 138(5):662-5

Schelkunov EL, Andreeva OG, Korovin KF, et al: The functional role of the noradrenergic neurons in the thermoregulatory circuits in mice. J Neural Transm 1981;50(2-4):113-37

Schenck-Gustafsson K, Dahlqvist R: Pharmacokinetics of digoxin in patients subjected to the quinidine-digoxin interaction. Br J Clin Pharmacol 1981 Feb;11(2):181-6

Scheuermann DW, Stilman C, Reinhold C, et al: Microspectrofluorometric study of monoamines in the auricle of the heart of Protopterus aethiopicus. Cell Tissue Res 1981;217(2):443-9

Schildkraut JJ, Orsulak PJ, Schatzberg AF, et al: Possible pathophysiological mechanisms in subtypes of unipolar depressive disorders based on differences in urinary MHPG levels [proceedings] Psychopharmacol Bull 1981 Jan;17(1):90-91

Schilt J, Richoux JP, Dubois MP: Demonstration of peptides immunologically related to vertebrate neurohormones in Dugesia lugubris (Turbellaria, Tricladida). Gen Comp Endocrinol 1981 Mar; 43(3):331-5

Schlemmer RF Jr, Davis JM: Evidence for dopamine mediation of submissive gestures in the stumptail macaque monkey. Pharmacol Biochem Behav 1981;14 Suppl 1:95-102

Schlienger JL, Kapfer MT, Singer L, et al: Effets différents d'antidépresseurs tricycliques (clomipramine et amitriptyline) et tétracyclique (maprotiline) sur la réponse de thyrostimuline, de prolactine et d'hormone somatotrope après thyroliberine chez des patients atteints de psychose maniaco-dépressive. Acta Psychiatr Belg 1980 Sep-Oct;80(5):584-99 (Eng. Abstr.) (Fre)

Schmid FX: A native-like intermediate on the ribonuclease A folding pathway. 1. Detection by tyrosine fluorescence changes. Eur J Biochem 1981;114(1):105-9

Schmidt P: Das Verhältnis von Pharmakotherapie, Milieuregulierung und analytisch orientierter Einzeltherapie bei schizophrenen Psychosen unter den Bedingungen einer ambulanten psychiatrischen Sprechstunde. Agressologie 1980;21(A):27-9 (Eng. Abstr.) (Ger)

Schmidt-Gollwitzer M, Hardt W, Schmidt-Gollwitzer K, et al: Influence of the LH-RH analogue buserelin on cyclic ovarian function and on endometrium. A new approach to fertility control? Contraception 1981 Feb;23(2):187-95

Schmucker DL, Wang RK: Effects of aging and phenobarbital on the rat liver microsomal drug-metabolizing system. Mech Ageing Dev 1981 Feb;15(2):189-202

Schoemaker H, Bliss M, Yamamura HI: Specific high-affinity saturable binding of [3H] R05-4864 to benzodiazepine binding sites in the rat cerebral cortex. Eur J Pharmacol 1981 Apr 24;71(1):173-5

Schoemaker J, Simons AH, van Osnabrugge GJ, et al: Pregnancy after prolonged pulsatile administration of luteinizing hormone-releasing hormone in a patient with clomiphene-resistant secondary amenorrhea. J Clin Endocrinol Metab 1981 May;52(5):882-5

Schofield SP, Everitt BJ: The organization of indoleamine neurons in the brain of the rhesus monkey (Macaca mulatta). J Comp Neurol 1981 Apr 10;197(3):369-83

Schöpf J: Ungewöhnliche Entzugssymptome nach Benzodiazepin-Langzeitbehandlungen. Nervenarzt 1981 May; 52(5):288-92 (Ger)

Schot LP, Boer HH, Swaab DF, et al: Immunocytochemical demonstration of peptidergic neurons in the central nervous system of the pond snail Lymnaea stagnalis with antisera raised to biologically active peptides of vertebrates. Cell Tissue Res 1981;216(2):273-91

Schrey MP, Larsen PR: Evidence for a possible role for Ca++ in the 3,5,3'-triiodothyronine inhibition of thyrotropin-releasing hormone-induced secretion of thyrotropin by rat anterior pituitary in vitro. Endocrinology 1981 May;108(5):1690-6

Schuldiner S, Maron R, Kanner BI: Active transport of biogenic amines in chromaffin granule membrane vesicles. Monogr Neural Sci 1980; 7:117-28

Schulz DW, Macdonald RL: Barbiturate enhancement of GABA-mediated inhibition and activation of chloride ion conductance: correlation with anticonvulsant and anesthetic actions. Brain Res 1981 Mar 23; 209(1):177-88

Schuurkes JA, Van Nueten JM: Is dopamine an inhibitory modulator of gastrointestinal motility? Scand J Gastroenterol [Suppl] 1981;67:33-6

Seamon K: NMR studies on tyrosine-138 of calmodulin. Ann NY Acad Sci 1980;356:433-4

Segal DS, Geyer MA, Schuckit MA: Stimulant-induced psychosis: an evaluation of animal methods. Essays Neurochem Neuropharmacol 1981;5:95-129 (123 ref.)

Segawa T, Mizuta T: Effect of imipramine on central 5-hydroxytryptamine turnover and metabolism in rats. Jpn J Pharmacol 1980 Dec;30(6):789-93

Seinsch W, Hasse F, Rümmler A: Ultrastruktur der FSH-Zelle der weiblichen Ratte nach zweimaliger LH-RH-Stimulation. Anat Anz 1980;148(3):207-13 (Eng. Abstr.) (Ger)

Seki T: Chromatographic separation of some biogenic amines on a weakly acidic ion-exchange resin. J Chromatogr 1981 Mar 20;207(2):286-7

Selmanoff M, Wise PM: Decreased dopamine turnover in the median eminence in response to suckling in the lactating rat. Brain Res 1981 May 11;212(1):101-15

Selmanoff M: The lateral and medial median eminence: distribution of dopamine, norepinephrine, and luteinizing hormone-releasing hormone and the effect of prolactin on catecholamine turnover. Endocrinology 1981 May;108(5):1716-22

Semple CG, Thomson JA, Beastall GH, et al: Autonomous prolactin secretion in schizophrenic male on long-term neuroleptic therapy [letter] Lancet 1981 Jul 11;2(8237):103

Senanayake N, Vyravanathan S: Histamine reactions due to ingestion of tuna fish (Thunnus argentivittatus) in patients on anti-tuberculosis therapy. Toxicon 1981;19(1):184-5

Serra G, Argiolas A, Fadda F, et al: Repeated electroconvulsive shock prevents the sedative effect of small doses of apomorphine. Psychopharmacology (Berlin) 1981;73(2):194-6

Sethi N, Prakash R, Sethi BB: Relationship between lithium levels of saliva and serum [letter] Biol Psychiatry 1981 Apr;16(4):413-4

Severson JA, Randall PK, Finch CE: Genotypic influences on striatal dopaminergic regulation in mice. Brain Res 1981 Apr 6;210(1-2):201-15

Seybold V, Elde R, Hökfelt T: Terminals of reserpine-sensitive vasopressin-neurophysin neurons in the external layer of the rat median eminence. Endocrinology 1981 May;108(5):1803-9

Seymour AA, Davis JO, Echtenkamp SF, et al: Adrenergically induced renin release in conscious indomethacin-treated dogs and rats. Am J Physiol 1981 Jun;240(6):F515-21

Shalif I, Lerner Y, Dasberg H: A symptom profile analysis of antipsychotic drug treatment: nonparametric multidimensional technique Psychiatry Res 1981 Feb;4(1):1-12

Shank RP, Aprison MH: Present status and significance of the glutamine cycle in neural tissues. Life Sci 1981 Feb 23;28(8):837-42 (36 ref.)

Shank RP, Campbell GL: Avid Na+-dependent, high-affinity uptake of alpha-ketoglutarate by nerve terminal enriched material from mouse cerebellum. Life Sci 1981 Feb 23;28(8):843-50

Shanks MF, Clement-Jones V, Linsell CJ, et al: A study of 24-hour profiles of plasma met-enkephalin in man. Brain Res 1981 May 18; 212(2):403-9

Shanks RG, Griffiths K, Harron DW: Debendox and congenital malformations in Northern Ireland [letter] Br Med J [Clin Res] 1981 Jun 13;282(6280):1972-3

Shannon HE, Cone EJ, Yousefnejad D: Physiologic effects and plasma kinetics of phenylethanolamine and its N-methyl homolog in the dog. J Pharmacol Exp Ther 1981 May;217(2):379-85

Shannon HE, DeGregorio CM: Effects of N-substituted analogs and metabolites of phencyclidine on avoidance behavior in the rat. J Pharmacol Exp Ther 1981 Jul;218(1):55-62

Sharpe RM, Fraser HM, Cooper I, et al: Sertoli-Leydig cell communication via an LHRH-like factor. Nature 1981 Apr 30; 290(5809):785-7

Shaw NA, Cant BR: The effect of pentobarbital on central somatosensory conduction time in the rat. Electroencephalogr Clin Neurophysiol 1981 Jun;51(6):674-7

Shears SB, Bronk JR: The effects of thyroxine treatment, in vivo and in vitro, on Ca2+ efflux from rat liver mitochondria. FEBS Lett 1981 Apr 6;126(1):9-12

Sheaves RM, Hope DB: Calmodulin and neurosecretion. Ann NY Acad Sci 1980;356:435

Shefner SA, Levy RA: Interaction between amino acid induced and K+-induced depolarization of primary afferents in the bullfrog spinal cord. Can J Physiol Pharmacol 1980 Nov;58(11):1286-94

Shen YC: [A study of renovation rate of dopamine and 5-hydroxytryptamine in brain in chronic schizophrenics (author's transl)] Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1979; 12(3):158-60 (Chi)

Shenkman L, Wadler S, Borkowsky W, et al: Adjuvant effects of lithium chloride on human mononuclear cells in suppressor-enriched and suppressor-depleted systems. Immunopharmacology 1981 Feb;3(1):1-8

Shepherd M: Classification and psychotropic drugs. Prog Neuropsychopharmacol 1980;4(4-5):447-54

Sherman WR, Leavitt AL, Honchar MP, et al: Evidence that lithium alters phosphoinositide metabolism: chronic administration elevates primarily D-myo-inositol-1-phosphate in cerebral cortex of the rat. J Neurochem 1981 Jun;36(6):1947-51

Shibasaki T, Ling N, Guillemin R, et al: The regional distribution of gamma 3-melanotropin-like peptides in bovine brain is correlated with adrenocorticotropin immunoreactivity but not with beta-endorphin. Regul Pept 1981 Apr;2(1):43-52

Shibata K, Motooka K, Murata K, et al: Metabolic control for maintaining NAD in rats fed on tryptophan-limiting amino acid diets. J Nutr Sci Vitaminol (Tokyo) 1980;26(6):571-84

Shibla DB, Gardell MA, Neale JH: The insensitivity of developing benzodiazepine receptors to chronic treatment with diazepam, GABA and muscimol in brain cell cultures. Brain Res 1981 Apr 6;210(1-2):471-4

Shnaps Y, Frand M, Rotem Y, et al: The chemically abused child. Pediatrics 1981 Jul;68(1):119-21

Shopsin B: Second generation antidepressants: a clinical pharmacotherapeutic research strategy [proceedings] Psychopharmacol Bull 1981 Jan;17(1):33-5

Shukla UA, Gokhale RD, Tipnis HP, et al: In vivo and in vitro availability of commercial phenytoin formulations containing phenobarbitone. Indian J Med Res 1980 Dec;72:910-5

Siddall JW, Keogh NJ: Psychotherapeutic drug recommendations based on the Mini-Mult. Psychol Rep 1980 Dec;47(3 Pt 2):1283-8

Sierakowski S, Hryszko S, Bernacka K: Wpływ chlorku litowego na przemianę blastyczną limfocytów. Pol Tyg Lek 1981 Jan 12;36(2):63-4 (Eng. Abstr.) (Pol)

Siever LJ, Cohen RM, Murphy DL: Antidepressants and alpha 2-adrenergic autoreceptor desensitization. Am J Psychiatry 1981 May; 138(5):681-2

Sievers J, Lolova I: Effects of pre- and postnatal treatment with 6-hydroxydopamine on the development of the rat locus coeruleus. Bibl Anat 1981;(19):258-63

Sievers J, Lolova I, Jenner S, et al: Morphological and biochemical studies on the ontogenesis of the nucleus locus coeruleus. Bibl Anat 1981; (19):52-130

Sievers J, Baumgarten HG, Klemm HP, et al: Distribution of the radioactivity in the central nervous system of the developing rat following intracisternal or subcutaneous administration of 14C-5,7-dihydroxytryptamine. Bibl Anat 1981;(19):302-7

Sillén U: Central neurotransmitter mechanisms involved in the control of urinary bladder function. An experimental study in the rat. Scand J Urol Nephrol [Suppl] 1980;58:1-45

Sillito AM, Kemp JA, Blakemore C: The role of GABAergic inhibition in the cortical effects of monocular deprivation. Nature 1981 May 28; 291(5813):318-20

Silverman AJ, Hoffman D, Gadde CA, et al: Adrenal steroid inhibition of the vasopressin-neurophysin neurosecretory system to the median eminence of the rat. Differential effects of corticosterone and deoxycorticosterone administration after adrenalectomy. Neuroendocrinology 1981 Mar;32(3):129-33

Silverstone T: Psychopharmacology of anorectic drugs in man. Prog Neuropsychopharmacol 1980;4(4-5):371-4

Simansky KJ, Harvey JA: Altered sensitivity to footshock after selective serotonin depletion: comparison of electrolytic lesions and neurotoxin injections in the medial forebrain bundle of the rat. J Comp Physiol Psychol 1981 Apr;95(2):341-50

Simon H: Neurones dopaminergiques A10 et système frontal. J Physiol (Paris) 1981 Apr;77(1):81-95 (Eng. Abstr.) (Fre)

Simon P: Reflexions sur la classification des antidepresseurs. Prog Neuropsychopharmacol 1980;4(4-5):503-5 (Eng. Abstr.) (Fre)

Simpson NE, Elliott CR: Cholinesterase Newfoundland: a new succinylcholine-sensitive variant of cholinesterase at locus 1. Am J Hum Genet 1981 May;33(3):366-74

Sinden RR, Pettijohn DE: Chromosomes in living Escherichia coli cells are segregated into domains of supercoiling. Proc Natl Acad Sci USA 1981 Jan;78(1):224-8

Singer I: Lithium and the kidney. Kidney Int 1981 Feb;19(2):374-87

Singh IJ, Klein RM, Herskovits M: Autoradiographic assessment of 3H-proline uptake by osteoblasts following guanethidine-induced sympathectomy in the rat. Cell Tissue Res 1981;216(1):215-20

Singh RC, Saxena KK, Gupta B, et al: Modification of glybenclamide hypoglycaemia by phenytoin in rabbits. Indian J Exp Biol 1981 Jan; 19(1):54-6

Singhal RL: Testicular cyclic nucleotide and adrenal catecholamine metabolism following chronic exposure to cadmium. Environ Health Perspect 1981 Apr;38:111-7

Sioufi A, Richard A: Gas chromatographic determination of maprotiline and its N-desmethyl metabolite in human blood using nitrogen detection. J Chromatogr 1980 Dec 12;221(2):393-8

Sippell WG: Unconjugated cortisol and corticosterone levels in amniotic fluid [letter] Am J Obstet Gynecol 1981 Jun 1;140(3):353-4

Skarin G, Nillius SJ, Wide L: Chronic effects of the stimulatory luteinizing hormone-releasing hormone analogue D-Ser (TBU) 6-EA 10-LRH on the gonadotrophin and gonadal steroid secretion in women with amenorrhoea. Ups J Med Sci 1980;85(2):103-12

Skaug N, Detar R: Contractility of vascular smooth muscle: maximum ability to contract in response to a stimulus. Am J Physiol 1981 Jun; 240(6):H971-9

Skrabanek P, Balfe A, McDonald D, et al: Substance P in human cord blood and its degradation by placenta in vitro. Eur J Obstet Gynaecol Reprod Biol 1980 Dec;11(3):157-61

Slater P: Effect of morphine on circling behaviour in rats with 6-hydroxydopamine striatal lesions and electrolesions of the raphe nucleus. Pharmacol Biochem Behav 1981 May;14(5):625-30

Small G, Mandel MR: The medically ill elderly, tricyclic response, and ECT [letter] Am J Psychiatry 1981 May;138(5):703-4

Small JG, Milstein V, Kellams JJ, et al: Auditory brain stem evoked responses in hospitalized patients undergoing drug treatment or ECT. Biol Psychiatry 1981 Mar;16(3):287-90

Smith BL: Excessive premedication of diazepam [letter] Gastrointest Endosc 1981 May;27(2):110

Smith CB, Garcia-Sevilla JA, Hollingsworth PJ: alpha 2-Adrenoreceptors in rat brain are decreased after long-term tricyclic antidepressant drug treatment. Brain Res 1981 Apr 6;210(1-2):413-8

Smith DF: Role of monoamines in behavior of reserpinized rats given tranylcypromine stereoisomers. J Neural Transm 1981;50(2-4):193-200

Smith DJ: The separation and determination of chlorpromazine and some of its related compounds by reversed-phase high performance liquid chromatography. J Chromatogr Sci 1981 Feb;19(2):65-71

Smith FP: Detection of amphetamine in bloodstains, semen, seminal stains, saliva, and saliva stains. Forensic Sci Int 1981 May-Jun;17(3):225-8

Smith JR: The effects of thyrotropin-releasing hormone on cyclic AMP accumulation in rabbit cerebral cortical tissue in the presence and absence of CNS depressants. Life Sci 1981 May 4;28(18):2065-9

Smith RS Jr, Ayd FJ Jr: A critical appraisal of amoxapine. J Clin Psychiatry 1981 Jun;42(6):238-42

Smock T, Fields HL: ACTH1-24 blocks opiate - induced analgesia in the rat. Brain Res 1981 May 11;212(1):202-6

Smotherman WP, Levine S: ACTH4—10 affects behavior but not plasma corticosterone levels in a conditioned taste aversion situation. Peptides (Fayetteville) 1980 Fall;1(3):207-10

Smotherman WP, Kolp LA, Coyle S, et al: Hippocampal lesion effects on conditioned taste aversion and pituitary-adrenal activity in rats. Behav Brain Res 1981 Jan;2(1):33-48

Snyder S: The interaction of psychopharmacology and psychoanalysis in the borderline patient. Psychiatr Q 1980 Winter;52(4):240-50 (51 ref.)

Sobolev ES, Zaitsev SG: Effektivnost' lecheniia rano nachavsheisia zlokachestvennoĭ shizofrenii razlichnymi psikhotropnymi sredstvami i ikh sochetaniiami. Zh Nevropatol Psikhiatr 1981;81(1):114-21 (Eng. Abstr.) (Rus)

Soboll S, Bünger R: Compartmentation of adenine nucleotides in the isolated working guinea pig heart stimulated by noradrenaline. Hoppe Seylers Z Physiol Chem 1981 Feb;362(2):125-32

Soine WH: Analytical determination of purity of 1-piperidinocyclohexanecarbonitrile and its hydrobromide salt. J Pharm Sci 1981 Jan;70(1):106-8

Soliman KF, Kolta MG: In vitro response of the regenerating adrenal gland to epinephrine. Res Commun Chem Pathol Pharmacol 1981 May; 32(2):373-6

Sollenne NP, Wu HL, Means GE: Disruption of the tryptophan binding site in the human serum albumin dimer. Arch Biochem Biophys 1981 Apr 1;207(2):264-9

Solntseva EI, Bezrukova LV: Izmenenie otvetov neĭronov na serotonin pri ego mnogokratnom pred'iavlenii. Dokl Akad Nauk SSSR 1981; 256(6):1499-503 (Rus)

Solov'ev GM, Ivannikov MN: Taktika primeneniia adrenomimeticheskikh preparatov v kardiokhirurgii. Kardiologiia 1981 Feb;21(2):26-31 (Eng. Abstr.) (Rus)

Solyom C, Solyom L, LaPierre Y, et al: Phenelzine and exposure in the treatment of phobias. Biol Psychiatry 1981 Mar;16(3):239-47

Somogyi A, Thielscher S, Gugler R: Influence of phenobarbital treatment on cimetidine kinetics. Eur J Clin Pharmacol 1981;19(5):343-7

Sonnenberg A, Koelz HR, Herz R, et al: Limited usefulness of the breath test in evaluation of drug metabolism: a study in human oral contraceptive users treated with dimethylaminoantipyrine and diazepam. Hepatogastroenterology 1980 Apr;27(2):104-8

Soon-Shiong P, Bock LA, Debas HT: Non-vasoactive intestinal polypeptide, nonsomatostatin fundic inhibitoy mechanism. J Surg Res 1981 May;30(5):473-77

Sørensen PG: Some properties of the Na+ + K+-linked Mg2+-dependent adenosine triphosphatase from the erythrocyte plasma membrane of the flounder (Platichthys flesus L.). Comp Biochem Physiol [C] 1981;69C(1):45-52

Sorimachi M, Nishimura S, Yamagami K: Possible occurrence of Na+-dependent Ca2+ influx mechanism in isolated bovine chromaffin cells. Brain Res 1981 Mar 16;208(2):442-6

Sotaniemi EA, Anttila M, Rautio A, et al: Propranolol and sotalol metabolism after a drinking party. Clin Pharmacol Ther 1981 Jun;

AUTHOR SECTION

29(6):705-10

Soueif M, El-Sayed AM, Honnovrah MA, et al: The non-medical use of psychoactive substances among secondary school male students in Egypt: an epidemiological study (a brief report).
Egypt J Psychiatry 1979 Oct;2(2):198-204

Sovner RD: The clinical characteristics and treatment of atypical depression. J Clin Psychiatry 1981 Jul;42(7):285-9

Spannhake EW, Levin JL, Hyman AL, et al: 6-keto-PGE1 exhibits more potent bronchodilatory activity in the cat than its precursor, PGI2.
Prostaglandins 1981 Feb;21(2):267-75

Sparrow MP, Mrwa U, Hofmann F, et al: Calmodulin is essential for smooth muscle contraction. FEBS Lett 1981 Mar 23;125(2):141-5

Speight A, Fink G: Changes in responsiveness of dispersed pituitary cells to luteinizing hormone releasing hormone at different times of the oestrous cycle of the rat. J Endocrinol 1981 Apr;89(1):129-34

Spertini F, Brunner HR, Waeber B, et al: The opposing effects of chronic angiotensin-converting enzyme blockade by captopril on the responses to exogenous angiotensin II and vasopressin vs. norepinephrine in rats.
Circ Res 1981 May;48(5):612-8

Spiker DG: The pharmacological treatment of schizoaffective disorder-depressed: a review of the literature [proceedings]
Psychopharmacol Bull 1981 Jan;17(1):75-8

Spindel E, Pettibone D, Fisher L, et al: Characterization of neuropeptides by reversed-phase, ion-pair liquid chromatography with post-column detection by radioimmunoassay. Application to thyrotropin-releasing hormone, substance P, and vasopressin. J Chromatogr 1981 Mar 13; 222(3):381-7

Spinweber CL: Daytime effects of L-tryptophan [proceedings]
Psychopharmacol Bull 1981 Jan;17(1):81-2

Spirduso WW, Abraham LD, Wolf MD: Effects of chlorpromazine on escape and avoidance responses: a closer look.
Pharmacol Biochem Behav 1981 Apr;14(4):433-8

Spyraki C, Fibiger HC: Intravenous self-administration of nomifensine in rats: implications for abuse potential in humans. Science 1981 Jun 5;212(4499):1167-8

Squire LR, Davis HP: The pharmacology of memory: a neurobiological perspective. Annu Rev Pharmacol Toxicol 1981;21:323-56 (203 ref.)

Srinivasa BR, Ramachandran LK: Deacylation of polymyxin B by hydrazine & solvolysis. Indian J Biochem Biophys 1980 Aug; 17(4):298-302

Srivastava RP, Shukla GD: Preoperative anxiety and its management in orostomatology. Uttar Pradesh State Dent J 1980 Oct;11(4):167-71

Srivastava VK, Satsangi RK, Kumar P, et al: Monoamine oxidase inhibitory activity of
2-aryl-3-(5'-chlorobenzophenon-2'-yl)-quinazolin-4-(3H)-ones
[letter] Indian J Physiol Pharmacol 1980 Oct-Dec;24(4):361-3

Stambaugh JE Jr, Wainer IW: Drug interaction: meperidine and chlorpromazine, a toxic combination. J Clin Pharmacol 1981 Apr; 21(4):140-6

Starr MS, Kilpatrick IC: Nigral-derived muscimol circling—ipsiversive, contraversive or controversial? [letter] Nature 1981 Apr 16; 290(5807):610

Staunton DA, Wolfe BB, Groves PM, et al: Dopamine receptor changes following destruction of the nigrostriatal pathway: lack of a relationship to rotational behavior. Brain Res 1981 May 4;211(2):315-27

Stefoni S, Coli L, Mosconi G, et al: Ibopamine (SB 7505) in normal subjects and in chronic renal failure: a preliminary report.
Br J Clin Pharmacol 1981 Jan;11(1):69-72

Steger RW, Silverman AY, Johns A, et al: Interactions of cocaine and delta 9-tetrahydrocannabinol with the hypothalamic-hypophysial axis of the female rat. Fertil Steril 1981 May;35(5):567-72

Stegink LD, Filer LJ Jr, Baker GL: Plasma and erythrocyte concentrations of free amino acids in adult humans administered abuse doses of aspartame. J Toxicol Environ Health 1981 Feb;7(2):291-305

Stein RS, Howard CA: Clinical assessment of cimetidine myelotoxicity. South Med J 1981 Mar;74(3):293-4

Steinberg H, Das DK: Competition between platelets and lung for 5-hydroxytryptamine uptake. Exp Lung Res 1980 Jun;1(2):121-30

Steinberg V, Rowe V, Watanabe I, et al: Effects of norepinephrine and dibutyryl adenosine 3',5'-cyclic monophosphate on the ultrastructure of pineal cells in monolayer culture. Cell Tissue Res 1981;216(1):181-91

Steinbusch HW, Verhofstad AA, Penke B, et al: Immunohistochemical characterization of monoamine-containing neurons in the central nervous system by antibodies to serotonin and noradrenalin. A study in the rat and the lamprey (Lampetra fluviatilis).
Acta Histochem [Suppl] (Jena) 1981;24:107-22

Steinbusch HW: Distribution of serotonin-immunoreactivity in the central nervous system of the rat-cell bodies and terminals. Neuroscience 1981; 6(4):557-618

Steiner S: Beeinflussung schizophrener Erkrankungen durch eine neuroleptische Intensivbehandlung und der weitere Verlauf nach Absetzen jeder neuroleptischen Medikation. Psychiatr Clin (Basel) 1980; 13(3-4):165-78 (Eng. Abstr.) (Ger)

Stejskal P: Vliv krátkodobé submaximální práce na množství noradrenalinu v plazmě. Cas Lek Cesk 1981 Feb 26;120(8):218-23 (Eng. Abstr.) (Cze)

Stengaard-Pedersen K, Fredens K, Larsson LI: Enkephalin and zinc in the hippocampal mossy fiber System. Brain Res 1981 May 11; 212(1):230-3

Stephens JK, Masserano JM, Vulliet PR, et al: Immunocytochemical localization of tyrosine hydroxylase in rat adrenal medulla by the peroxidase labeled antibody method: effects of enzyme activation on ultrastructural distribution of the enzyme. Brain Res 1981 Mar 30; 209(2):339-54

Stern AS, Jones BN, Shively JE, et al: Two adrenal opioid polypeptides: proposed intermediates in the processing of proenkephalin.
Proc Natl Acad Sci USA 1981 Mar;78(3):1962-6

Stern JE, Conn PM: Perifusion of rat pituitaries: requirements for optimal GnRH-stimulated LH release. Am J Physiol 1981 May;240(5):E504-9

Stern R: Psychotropic drugs and behaviour therapy. Practitioner 1981 Jan;225(1351):21-5

Stevenson JS, Cox NM, Britt JH: Role of the ovary in controlling luteinizing hormone, follicle stimulating hormone, and prolactin secretion during and after lactation in pigs. Biol Reprod 1981 Mar; 24(2):341-52

Stewart DJ, Sen AK: Role of cyclic GMP in cholinergic activation of Na-K pump in duck salt gland. Am J Physiol 1981 May;240(5):C207-14

Stewart JJ, Jobe PC: Effects of reserpine on monoamines and intestinal transit in the rat. J Pharmacol Exp Ther 1981 May;217(2):357-62

Stewart JW, Quitkin F, Liebowitz MR, et al: Efficacy of desipramine in mildly depressed patients: a double-blind, placebo-controlled trial [proceedings] Psychopharmacol Bull 1981 Jan;17(1):136-8

Stokes PE, Frazer A, Casper R: Unexpected neuroendocrine-transmitter relationships [proceedings] Psychopharmacol Bull 1981 Jan;17(1):72-5

Stolerman IP, D'Mello GD: Role of training conditions in discrimination of central nervous system stimulants by rats.
Psychopharmacology (Berlin) 1981;73(3):295-303

Stone EA: Mechanism of stress-induced subsensitivity to norepinephrine. Pharmacol Biochem Behav 1981 May;14(5):719-23

Storm H, van Hardeveld C, Kassenaar AA: Thyroid
hormone-catecholamine interrelationships during exposure to cold.
Acta Endocrinol (Copenh) 1981 May;97(1):91-7

Strandhoy JW, Steg BD, Buckalew VM Jr: Antagonism of the hydrosmotic effect of vasopressin by the antihypertensive, guanabenz. Life Sci 1980 Dec 22-29;27(25-26):2513-8

Straumanis JJ Jr, Shagass C, Roemer RA, et al: Cerebral evoked potential changes produced by treatment with lithium carbonate.
Biol Psychiatry 1981 Feb;16(2):113-29

Streit F: Recommendations for demand reduction of amphetamines.
Chem Depend 1980;4(1-2):135-43

Stroebel H: Die Rehabilitation psychisch Kranker und Behinderter in Ubergangs-einrichtungen und ihre Einordnung in das System der sozialen Sicherheit. Rehabilitation (Stuttg) 1981 Feb;20(1):42-4 (Eng. Abstr.) (Ger)

Strollo F, Harlin J, Hernandez-Montes H, et al: Qualitative and quantitative differences in the isoelectrofocusing profile of biologically active lutropin in the blood of normally menstruating and post-menopausal women. Acta Endocrinol (Copenh) 1981 Jun; 97(2):166-75

Strosser MT, Cohen L, Koch B, et al: La somatostatine : une hormone pancréatique qui pourrait être importante.
Journ Annu Diabetol Hotel Dieu 1981;:197-210 (51 ref.) (Fre)

Strugala G, Overhoff H, Forth W: Absorption of 14C-clanobutin-Na isolated perfused intestinal segments in vitro of rats.
Arzneimittelforsch 1981;31(3):429-33

Sugrue MF: Effects of acutely and chronically administered antidepressants on the clonidine-induced decrease in rat brain 3-methoxy-4-hydroxyphenylethylene-glycol sulphate content.
Life Sci 1981 Jan 26;28(4):377-84

Sullivan DT, Bell LA, Paton DR, et al: Genetic and functional analysis of tryptophan transport in Malpighian tubules of Drosophila.
Biochem Genet 1980 Dec;18(11-12):1109-30

Sullivan S, Akil H, Blacker D, et al: Enkephalinase: selective inhibitors and partial characterization. Peptides (Fayetteville) 1980 Spring; 1(1):31-5

Sullivan SN, Lamki L, Corcoran P: Inhibition of gastric emptying by enkephalin analogue [letter] Lancet 1981 Jul 11;2(8237):86-7

Sumi T, Umeda Y: Epinephrine-independent production of hyperuricemia by means of hypothalamic stimulation in the conscious rat. Life Sci 1981 Mar 9;28(10):1183-8

Summers MC, Hayes RJ: The interaction of N alpha-alkylenkephalins with opiate receptors. Tissue-dependent shifts in the opiate activity of methionine-enkephalin following N alpha-alkylation. J Biol Chem 1981 May 25;256(10):4951-6

Sumners C, De Vries JB, Dijkstra D, et al: Involvement of both dopaminergic and alpha-adrenergic receptors in the hypomotility induced by dibenzoyl-6,7-ADTN. Eur J Pharmacol 1981 Apr 9; 70(4):541-50

Sundaram K, Cao YQ, Wang NG, et al: Inhibition of the action of sex steroids by gonadotropin-releasing hormone (GnRH) agonists: a new biological effect. Life Sci 1981 Jan 5;28(1):83-8

Sur RN, Shanker G, Rathore RK, et al: Pharmacological studies on

AUTHOR SECTION

1–(p–aminophenoxy)–3–[N1–(O–methoxyphenyl)–N4–piperazinyl] propane dihydrochloride (74–637). Indian J Exp Biol 1980 Oct; 18(10):1190–1

Surewicz KW, Fijalkowska I, Leyko W: The effect of propranolol on the osmotic fragility of red cells and liposomes and the influence of the drug on glycerol transport across the membrane of red cells. Biochem Pharmacol 1981 Apr;30(8):839–42

Surewicz WK, Leyko W: Interaction of propranolol with model phospholipid membranes. Monolayer, spin label and fluorescent spectroscopy studies. Biochim Biophys Acta 1981 May 6;643(2):387–97

Suzuki T, Isozaki S, Ohkuma T, et al: Influence of the route of administration on the mean hepatic extraction ratio of propranolol in the rat. J Pharmacobiodyn 1980 Nov;3(11):603–11

Svensson TH, Dahlöf C, Engberg G, et al: Central pre– and postsynaptic monoamine receptors in antidepressant therapy. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):67–78

Svinarchuk FP, Berdnikov VA: Razdelenie dansilirovannykh aminokislot metodom élektroforeza v poliakrilamidnom gele. Prikl Biokhim Mikrobiol 1981 Jan–Feb;17(1):144–50 (Eng. Abstr.) (Rus)

Svoboda P, Mosinger B: Catecholamines and the brain microsomal Na, K–adenosinetriphosphatase--I. Protection against lipoperoxidative damage. Biochem Pharmacol 1981 Mar 1;30(5):427–32

Svoboda P, Mosinger B: Catecholamines and the brain microsomal Na, K–adenosinetriphosphatase--II. The mechanism of action. Biochem Pharmacol 1981 Mar 1;30(5):433–9

Swann AC, Heninger GR, Roth RH, et al: Differential effects of short and long term lithium on tryptophan uptake and serotonergic function in cat brain. Life Sci 1981 Jan 26;28(4):347–54

Swanson LW, Sawchenko PE, Bérod A, et al: An immunohistochemical study of the organization of catecholaminergic cells and terminal fields in the paraventricular and supraoptic nuclei of the hypothalamus. J Comp Neurol 1981 Feb 20;196(2):271–85

Swanson MA, Custer TR, Suey CM: Free thyroxine and free thyroxine index in women taking oral contraceptives. Clin Nucl Med 1981 Apr; 6(4):168–71

Swenson RP Jr, Armstrong CM: K+ channels close more slowly in the presence of external K+ and Rb+. Nature 1981 Jun 4;291(5814):427–9

Swift CG, Haythorne JM, Clarke P, et al: Cardiovascular, sedative and anticholinergic effects of amitriptyline and zimelidine in young and elderly volunteers. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):425–32

Szabolcs I, Weber M, Kovács Z, et al: Exhaustibility of pituitary thyrotropin pool in old age by repeated administration of thyrotropin releasing hormone. ZFA (Dresden) 1981;36(1):23–8

Szkilnik R, Brus R, Herman ZS: The concentration of gamma–aminobutyric acid (GABA) in discrete areas of rat brain after chemical sympathectomy or serotoninectomy. Acta Physiol Pol 1980; 31(5):513–5

T

Taban CH: Neuropeptides et psychiatrie. (texte du rapport présenté à la réunion Franco–Suisse de Psychiatrie, à Bel–Air, Genève, le 4 mai 1980). Schweiz Arch Neurol Neurochir Psychiatr 1981;128(1):85–103 (Eng. Abstr.) (Fre)

Taborsky GJ Jr, Halter JB, Porte D Jr: Morphine: dual effects on plasma catecholamines. Endocrinology 1981 Jul;109(1):319–21

Tabsh K, Nuwayhid B, Erkkola R, et al: Hemodynamic responses of the pelvic vascular bed to vasoactive stimuli in pregnant sheep. Biol Neonate 1981;39(1–2):52–60

Takabayashi Y, Kataoka K, Matsuki S: Role of adrenergic mechanism in ketogenesis. Keio J Med 1980 Apr;29(1):1–8

Takada K, Shibata H, Yamamoto M: [A cytochemical study of T, active T, non active T and B lymphocytes in respect to acid phosphatase and beta–glucuronidase activity (author's transl)] Rinsho Byori 1981 Feb; 29(2):183–6 (Jpn)

Takahashi K, Wada Y, Haneda A, et al: [Influences of hypothalamus prolactin inhibiting factor and releasing factors and pineal gland on pituitary prolactin secreting functions (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1980 Sep;32(9):1249–56 (Jpn)

Takatsuki K, Shiosaka S, Sakanaka M, et al: Somatostatin in the auditory system of the rat. Brain Res 1981 May 25;213(1):211–6

Takeo S, Taam GM, Beamish RE, et al: Effect of adrenochrome on calcium accumulation by heart mitochondria. Biochem Pharmacol 1981 Jan 15; 30(2):157–63

Takeshige K, Minakami S: Involvement of calmodulin in phagocytotic respiratory burst of leukocytes. Biochem Biophys Res Commun 1981 Mar 31;99(2):484–90

Taketani Y: [Effects of hypothalamic deafferentation and estrogen on the distribution and content of hypothalamic LHRH (author's transl)] Acta Obstet Gynaecol Jpn 1981 May;33(5):625–34 (Eng. Abstr.) (Jpn)

Takeyasu K, Hata F, Uchida S, et al: Action of colchicine on cholinergic and adrenergic mechanisms in guinea pig vas deferens. Life Sci 1981 Feb 23;28(8):851–60

Tamburus EL, Rothschild AM: Reversible swelling evoked by epinephrine, 8–bromo–cyclic 3',5'–guanosine monophosphate and feeding in the mast cells of the rat. Biochem Pharmacol 1981 Mar 1;30(5):469–79

Tamura S, Matsumoto Y: Comparative studies on postnatal development of liver beta–glucuronidase activity between Gunn rats and Wistar rats. J Toxicol Sci 1980 Nov;5(4):331–8

Tan L, Yu PH: De novo biosynthesis of enkephalins and their homologues in the human placenta. Biochem Biophys Res Commun 1981 Feb 12; 98(3):752–60

Tang LK, Tang FY: LH responses to LHRH, DBcAMP, and 17 beta–estradiol in cultures derived from aged rats. Am J Physiol 1981 May;240(5):E510–8

Tang SW, Stancer HC, Takahashi S, et al: Controlled exercise elevates plasma but not urinary MHPG and VMA. Psychiatry Res 1981 Feb; 4(1):13–20

Tang SW, Seeman P, Kwan S: Differential effect of chronic desipramine and amitriptyline treatment on rat brain adrenergic and serotonergic receptors. Psychiatry Res 1981 Apr;4(2):129–38

Tanigawa K, Kuzuya H, Sakurai H, et al: Effects of antisomatostatin and antiglucagon sera on insulin release from isolated Langerhans' islets of rats. Horm Metab Res 1981 Feb;13(2):78–80

Taniguchi H, Murakami K, Tsutou A, et al: Role of glucagon and somatostatin in insulin release. Endocrinol Jpn 1980 Dec;27 Suppl 1:103–7

Tarr GE: Rapid separation of amino acid phenylthiohydantoins by isocratic high–performance liquid chromatography. Anal Biochem 1981 Feb;111(1):27–32

Tawakkol MS, Mohamed ME, Ibrahim MA: Alkalimetric determination of glafenine. Pharmazie 1981;36(2):163

Taya K, Sasamoto S: Pituitary function during pseudopregnancy and lactation in the rat. J Reprod Fertil 1981 May;62(1):93–8

Taylor DC, Grundy R, Loveday B: Chronic dog intestinal loop model for studying drug absorption as exemplified by beta–adrenoreceptor blocking agents, atenolol and propranolol. J Pharm Sci 1981 May; 70(5):516–21

Taylor DP, Allen LE, Ashworth EM, et al: Treatment with trazodone plus phenoxybenzamine accelerates development of decreased type 2 serotonin binding in rat cortex. Neuropharmacology 1981 May; 20(5):513–6

Taylor RL, Burt DR: Preparation of 3H–[3–M3–His2]TRH as an improved ligand for TRH receptors. Neuroendocrinology 1981 May;32(5):310–6

Tayyaba B, Qayum A, Yusuf SM: Effect of 5–hydroxytryptamine on isolated aortic strip preparations obtained from untreated and reserpine treated rabbits. Planta Med 1981 Mar;41(3):295–7

Teicher MH, Shaywitz BA, Kootz HL, et al: Differential effects of maternal and sibling presence of hyperactivity of 6–hydroxydopamine–treated developing rats. J Comp Physiol Psychol 1981 Feb;95(1):134–45

Tennant FS Jr, Rawson RA, McCann M: Withdrawal from chronic phencyclidine (PCP) dependence with desipramine. Am J Psychiatry 1981 Jun;138(6):845–7

Tenovuo J, Mielityinen H, Larjava H, et al: Release of lysosomal hydrolases from bone explants affected by dental plaque. Acta Odontol Scand 1980;38(6):355–61

Thalmann RH, Peck EJ, Ayala GF: Biphasic response of hippocampal pyramidal neurons to GABA. Neurosci Lett 1981 Feb 6;21(3):319–24

Theodorou A, Gommeren W, Clow A, et al: Chronic neuroleptic treatment specifically alters the number of dopamine receptors in rat brain. Life Sci 1981 Apr 6;28(14):1621–7

Thomas WE: The kinetics of somatostatin inhibition of gastric acid secretion. Regul Pept 1980 Dec;1(3):245–51

Thomas WE, Townsel JG: The identification of an invertebrate acetylcholine receptor. Life Sci 1981 Mar 2;28(9):965–71 (42 ref.)

Thorel JB, Daragon A, Manchon N, et al: Thrombopénie aiguë au cortrimoxazole. Rôle facilitant du phénobarbital. Sem Hop Paris 1981 May 8–15;57(17–18):914–5 (Eng. Abstr.) (Fre)

Thorén P, Oberg B: Studies on the endoanesthetic effects of lidocaine and benzonatate on non–medullated nerve endings in the left ventricle. Acta Physiol Scand 1981 Jan;111(1):51–8

Threatte RM, Fregly MJ, Connor TM, et al: L–5–Hydroxytryptophan–induced drinking in rats: possible mechanisms for induction. Pharmacol Biochem Behav 1981 Mar;14(3):385–91

Threatte RM, Fregly MJ, Field FP: Use of lactoperoxidase–catalyzed iodination of L–tyrosine to assess antithyroid activity of a factor present in certain tissues of mammals. Pharmacology 1981;22(1):31–40

Tilley L, Summers RJ, Redgrave TG, et al: Inhibition of phenylephrine–stimulated gluconeogenesis by chlorpromazine is mediated by alpha–adrenergic receptors. FEBS Lett 1981 Apr 20; 126(2):313–7

Timchenko OI, Antipenko EN: Ob usloviiakh primeneniia tiroksina kak antimutagena posle obshchego rentgenovskogo oblucheniia. Radiobiologiia 1981 Mar–Apr;21(2):204–10 (Eng. Abstr.) (Rus)

Titeler M, Van Loon GR, Seeman P, et al: D2– but not D3–dopamine receptors detected in the anterior pituitary. Eur J Pharmacol 1981 Apr 24;71(1):143–6

Toh YC: Combined effects of neonatal thyroxine treatment and neonatal

AUTHOR SECTION

castration on sebum production in adult male rats. J Endocrinol 1981 May;89(2):225–8

Tokimasa T: The effect of 5-hydroxytryptamine on the slow inward current of bullfrog atrium. Jpn Heart J 1981 Mar;22(2):227–37

Tombaugh TN: Effects of pimozide on nordiscriminated and discriminated performance in the pigeon. Psychopharmacology (Berlin) 1981; 73(2):137–41

Tomkins CP, Soldin SJ, MacLeod SM, et al: Analysis of pemoline in serum by high performance liquid chromatography: clinical application to optimize treatment of hyperactive children. Ther Drug Monit 1980; 2(3):255–60

Tomomatsu E, Nishi K: Increased activity of carotid sinus baroreceptors by sympathetic stimulation and norepinephrine. Am J Physiol 1981 Apr; 240(4):H650–8

Tonew M: Mechanism of action of antiviral hetarylhydrazones in vitro. Acta Virol (Praha) 1981 Mar;25(2):108–14

Topiar A: Die Wirkung von Thioridazin auf sexuelle Reaktivität des Mannes (Phalloplethysmographische Studie). Agressologie 1980; 21(A):49–51 (Eng. Abstr.) (Ger)

Tordet C, Bertin R, Cardey C, et al: Lung catecholamines and cyclic nucleotides during perinatal development in the rat. Possible relationships with biochemical and morphological differentiation. Pediatr Res 1981 May;15(5):787–93

Torrellas A, Guaza C, Borrell J, et al: Adrenal hormones and brain catecholamines responses to morning and afternoon immobilization stress in rats. Physiol Behav 1981 Jan;26(1):129–33

Tosteson DC: Cation countertransport and cotransport in human red cells. Fed Proc 1981 Apr;40(5):1429–33

Tosteson DC: Lithium and mania. Sci Am 1981 Apr;244(4):164–6, 168, 171–2 et passim

Towart R: The selective inhibition of serotonin-induced contractions of rabbit cerebral vascular smooth muscle by calcium-antagonistic dihydropyridines. An investigation of the mechanism of action of nimodipine. Circ Res 1981 May;48(5):650–7

Towell JF, Erwin VG: Characterization of the isolated perfused mouse brain as a system for neurochemical studies. Brain Res 1981 Mar 30; 209(2):476–81

Towell ME, Lysak I, Layne EC, et al: The effect of epinephrine on blood and tissue PO2 in the rabbit. Circ Shock 1981;8(2):123–30

Toyama M, Satake M: Increased concentration and accelerated synaptosomal uptake of noradrenaline in the central nervous tissues of neonatally hemispherectomized adult rats. Brain Res 1981 Mar 16; 208(2):447–50

Tramposch A, Sangdee C, Franz DN, et al: Cannabinoid-induced enhancement and depression of cat monosynaptic reflexes. Neuropharmacology 1981 Jun;20(6):617–21

Tran VT, Lebovitz R, Toll L, et al: [3H]doxepin interactions with histamine H1-receptors and other sites in guinea pig and rat brain homogenates. Eur J Pharmacol 1981 Apr 9;70(4):501–9

Träskman L, Asberg M, Bertilsson L, et al: Monoamine metabolites in CSF and suicidal behavior. Arch Gen Psychiatry 1981 Jun;38(6):631–6

Träskman-Bendz L, Asberg M, Bertilsson L: Serotonin and noradrenaline uptake inhibitors in the treatment of depression—relationship to 5-HIAA in spinal fluid. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):209–18

Trent DF, Weir GC: Heterogeneity of somatostatin-like peptides in rat brain, pancreas, and gastrointestinal tract. Endocrinology 1981 Jun; 108(6):2033–8

Trigo GG, Martínez M, Gálvez E: PMR and 13C-NMR spectroscopy of tropane and N-substituted nortropane spirohydantoins. J Pharm Sci 1981 Jan;70(1):87–9

Trocklé G, Catau G, Barberi C, et al: Investigations of new structures with pharmacological activity. II: Anticonvulsant properties of benzocyclobutenols and benzocylenones. Life Sci 1981 Jan 5;28(1):23–9

Tsang D, Ng SC: Development of radioimmunoassayable beta-endorphin and methionine-enkephalin binding sites in regions of rat brain. Can J Physiol Pharmacol 1980 Aug;58(8):947–50

Tse FL, Sanders TM, Reo JP: Bioavailability of propranolol in the dog. Arch Int Pharmacodyn Ther 1980 Dec;248(2):180–9

Tsudzuki T: Studies on the uptake of [3H]dopamine by synaptic vesicle fraction isolated from bovine brain. J Biochem (Tokyo) 1981 Jan; 89(1):61–9

Tsujimoto A, Tanaka S: Stimulatory effect of somatostatin on norepinephrine release from rat brain cortex slices. Life Sci 1981 Feb 23;28(8):903–10

Tufik S: Changes of response to dopaminergic drugs in rats submitted to REM-sleep deprivation. Psychopharmacology (Berlin) 1981; 72(3):257–60

Turbott J, Norman TR, Burrows GD, et al: Pharmacokinetics of nortriptyline in elderly volunteers. Commun Psychopharmacol 1980; 4(3):225–31

Turley WA Jr, Floody OR: Delta-9-Tetrahydrocannabinol stimulates receptive and proceptive sexual behaviors in female hamsters. Pharmacol Biochem Behav 1981 May;14(5):745–7

Turner BB, Wilens TE, Schroeder KA, et al: Comparison of brainstem and adrenal circadian patterns of epinephrine synthesis. Neuroendocrinology 1981 May;32(5):257–61

Turner CE, Ma CY, Elsohly MA: Constituents of Erythroxylon coca. II. Gas-chromatographic analysis of cocaine and other alkaloids in coca leaves. J Ethnopharmacol 1981 Mar–May;3(2–3):293–8

Twum-Barima Y, Carruthers SG: Quinidine-rifampin interaction. N Engl J Med 1981 Jun 11;304(24):1466–9

Tynan RF, Fisher MM, Ibels LS: Self-poisoning with propranolol. Med J Aust 1981 Jan 24;1(2):82–3

Tyrer P, Rutherford D, Huggett T: Benzodiazepine withdrawal symptoms and propranolol. Lancet 1981 Mar 7;1(8219):520–2

Tyrer P: Dependence on benzodiazepines. Br J Psychiatry 1980 Dec; 137:576–7

Tyrer SP, Grof P, Kalvar M, et al: Estimation of lithium dose requirement by lithium clearance, serum lithium and saliva lithium following a loading dose of lithium carbonate. Neuropsychobiology 1981;7(3):152–8

U

Uebelhack R, Franke L, Kitzrow W, et al: Phenylalaninbelastung bei endogenen Psychosen. Psychiatr Neurol Med Psychol (Leipz) 1980 Oct; 32(10):631–3 (Ger)

Ukikusa M, Ozawa K, Shimahara Y, et al: Changes in blood ketone body ratio: their significance after major hepatic resection. Arch Surg 1981 Jun;116(6):781–5

Uldall PR, Awad AG, McCormick WO, et al: Renal function in patients receiving long-term lithium therapy. Can Med Assoc J 1981 Jun 1; 124(11):1471–4

Unger T, Rascher W, Schuster C, et al: Central blood pressure effects of substance P and angiotensin II: role of the sympathetic nervous system and vasopressin. Eur J Pharmacol 1981 Apr 24;71(1):33–42

Unnithan RR, Dembla M: Effects of neonatal administration of gonadotropins-releasing hormone (Gn-RH) on the testis of mice. Indian J Exp Biol 1981 Jan;19(1):12–5

Uran B, Tulunay FC, Ayhan IH, et al: Correlation between the dose and development of acute tolerance to the hypothermic effect of THC. Pharmacology 1980;21(6):391–5

Uvnäs-Wallensten K, Efendic S, Johansson C, et al: Effect of intraluminal pH on the release of somatostatin and gastrin into antral, bulbar and ileal pouches of conscious dogs. Acta Physiol Scand 1980 Dec; 110(4):391–400

Uyeda M, Peisach J: Ultraviolet difference spectroscopy of myoglobin: assignment of pK values of tyrosyl phenolic groups and the stability of the ferryl derivatives. Biochemistry 1981 Mar 31;20(7):2028–35

Uzan A, Phan T, Le Fur G: Selective labelling of murine B lymphocytes by [3H]spiroperidol. J Pharm Pharmacol 1981 Feb;33(2):102–3

Uzbekov MG, Bernshtein KhG: Vzaimodeistvie indolaminov s serotoninergicheskimi retseptorami sinaptosom mozga. Biokhimiia 1980 Jan;45(1):109–12 (Eng. Abstr.) (Rus)

V

Vaccheri A, Gandolfi O, Dall'Olio R, et al: Azione difasica della apomorfina sulla motilita' del ratto: II) Andamento temporale dell'effetto di una singola dose. Boll Soc Ital Biol Sper 1981 Feb 28;57(4):381–6 (Eng. Abstr.) (Ita)

Vaccheri A, Dall'Olio R, Gandolfi O, et al: Azione difasica della apomorfina sulla motilita' del ratto: I) Relazione dose-effetto sulla motilita' esplorativa e basale. Boll Soc Ital Biol Sper 1981 Feb 28; 57(4):374–80 (Eng. Abstr.) (Ita)

Vachon L, Roberge AG: Involvement of serotonin and catecholamine metabolism in cats trained to perform a delayed response task. Neuroscience 1981;6(2):189–94

Vaeusorn N, Viranuvatti J, Singchoovong L: Post-biopsy haematuria successfully treated by selective transcatheter epinephrine injection. Br J Radiol 1981 May;54(641):425–6

Valzelli L, Bernasconi S, Sala A: Piracetam activity may differ according to the age of the recipient mouse. Int Pharmacopsychiatry 1980; 15(3):150–6

Vanage GR, Sheth AR, Kadam MS: In vivo effect of inhibin on FSH uptake by rat testis. Experientia 1981 Apr 15;37(4):433–4

Vandel B, Vandel S, Allers G, et al: Clinical pharmacology of viloxazine hydrochloride. Pharmacopsychiatria 1981 Mar;14(2):66–70

Vandel B, Vandel S, Allers G, et al: Evolution comparée des concentrations plasmatiques de prolactine au cours des traitements antidépresseurs. Therapie 1981 Jan–Feb;36(1):87–94 (Eng. Abstr.) (Fre)

van der Kooy D, Coscina DV, Hattori T: Is there a non-dopaminergic nigrostriatal pathway? Neuroscience 1981;6(3):345–57

Van der Velde EA, Driessen O: Prediction of phenytoin dosage in relation to the variability of phenytoin plasma concentration. Br J Clin Pharmacol 1981 Jan;11(1):41–52

van Eys GJ, van den Oetelaar P: Cytological localization of alpha-MSH, ACTH and beta-endorphin in the pars intermedia of the cichlid teleost Sarotherodon mossambicus. Cell Tissue Res 1981;215(3):625–33

Van Iren F, Boers-Van der Sluijs P: Further studies on the precipitative

AUTHOR SECTION

freeze dissolution technique for the localization of inorganic ions. Histochemistry 1981;71(2):195–201

van Leeuwen FW: An introduction to the immunocytochemical localization of neuropeptides and neurotransmitters. Acta Histochem [Suppl] (Jena) 1981;24:49–77 (162 ref.)

Van Loon GR, Shum A, De Souza EB: Brain serotonin turnover correlates inversely with plasma adrenocorticotropin during the triphasic response to adrenalectomy in rats. Endocrinology 1981 Jun;108(6):2269–76

van Niekerk JP, Teggin AF: Understanding stress. S Afr Med J 1981 May 16;59(21):749–50

van Praag HM: Management of depression with serotonin precursors. Biol Psychiatry 1981 Mar;16(3):291–310

van Putten T, May PR, Jenden DJ: Plasma levels of chlorpromazine and clinical response [proceedings] Psychopharmacol Bull 1981 Jan; 17(1):113–5

Vanstratt W: The poisoned pen. A case report. Forensic Sci Int 1981 Mar–Apr;17(2):153–6

Van Vugt DA, Sylvester PW, Aylsworth CF, et al: Comparison of acute effects of dynorphin and beta-endorphin on prolactin release in the rat. Endocrinology 1981 May;108(5):2017–8

Vardi J, Flechter S, Oberman Z, et al: Plasma dopamine beta hydroxylase activity in chronic schizophrenic patients tested with single dose of 2-bromo-alpha ergocriptine (Parlodel). Encephale 1981;7(1):95–103

Vaticón MD, Aguilar E, Fernández-Galaz C, et al: LH and prolactin in estrogenized female rats: response to LHRH. Rev Esp Fisiol 1980 Dec; 36(4):371–6

Vaughn JE, Famiglietti EV Jr, Barber RP, et al: GABAergic amacrine cells in rat retina: immunocytochemical identification and synaptic connectivity. J Comp Neurol 1981 Mar 20;197(1):113–27

Vavilova NI, Kassil' VG: Formirovanie i sokhranenie uslovnoreflektornoi vkusovoi aversii u sobak. Zh Vyssh Nerv Deiat 1981 Jan–Feb; 31(1):171–2 **(Rus)**

Vawter MP, Green KF: Effects of desglycinamide-lysine vasopressin on a conditioned taste aversion in rats. Physiol Behav 1980 Dec;25(6):851–4

Vaysse N, Pradayrol L, Chayvialle JA, et al: Effects of somatostatin-14 and somatostatin-28 on bombesin-stimulated release of gastrin, insulin, and glucagon in the dog. Endocrinology 1981 May;108(5):1843–7

Verbiese-Genard N, van Damme M, Hanocq M, et al: Toxicological analysis of phenylethylamines by high performance reversed-phase ion-pair partition thin-layer and liquid chromatographies. Clin Toxicol 1981;18(4):391–400

Vergnes H, Sevin J, Peralta M: Plasma cholinesterase variants in population samples from south-west France. Ann Hum Biol 1981 Jan–Feb;8(1):59–63

Vergnes M, Kempf E: Tryptophan deprivation: effects on mouse-killing and reactivity in the rat. Pharmacol Biochem Behav 1981;14 Suppl 1:19–23

Verhofstad AA, Steinbusch HW, Penke B, et al: Serotonin-immunoreactive cells in the superior cervical ganglion of the rat. Evidence for the existence of separate serotonin- and catecholamine-containing small ganglionic cells. Brain Res 1981 May 11;212(1):39–49

Vermes I, Mulder GH, Berkenbosch F, et al: Release of beta-lipotropin and beta-endorphin from rat hypothalami in vitro. Brain Res 1981 Apr 27;211(1):248–54

Verpooten GA, De Broe ME, Moerman EJ: The effect of charcoal hemoperfusion on the catecholamine levels in severely intoxicated patients. Clin Toxicol 1981 Feb;18(2):127–31

Viinikka L, Kivinen S, Rönnberg L, et al: Experimental hyperprolactinemia and hypoprolactinemia and human chorionic gonadotropin during early pregnancy. Obstet Gynecol 1981 Apr;57(4):441–3

Villanueva GB, Danishefsky I: Differential effect of high affinity heparin and low affinity heparin on methylene blue titration. Thromb Res 1981 Jan 1–15;21(1–2):191–9

Vinar O: Treatment with psychotropic drugs and age of patients. Agressologie 1980;21(A):53–5

Vincenzi FF, Hinds TR, Raess BU: Calmodulin and the plasma membrane calcium pump. Ann NY Acad Sci 1980;356:232–44

Vinson GP, Whitehouse BJ, Dell A, et al: Specific stimulation of steroidogenesis in rat adrenal zona glomerulosa cells by pituitary peptides. Biochem Biophys Res Commun 1981 Mar 16;99(1):65–72

Virtanen R: Excretion of nortriptyline into saliva. Int J Clin Pharmacol Ther Toxicol 1981 Feb;19(2):78–81

Viscio DB, Prestegard JH: NMR studies of 5-hydroxytryptamine transport through large unilamellar vesicle membranes. Proc Natl Acad Sci USA 1981 Mar;78(3):1638–42

Visser TJ, Klootwijk W: Approaches to a markedly increased sensitivity of the radioimmunoassay for thyrotropin-releasing hormone by derivatization. Biochim Biophys Acta 1981 Apr 3;673(4):454–66

Vitaliano PP, Prinz P, Vitiello MV, et al: On the use of repeated measures designs in psychopharmacology. Psychopharmacology (Berlin) 1981; 72(3):247–9

Vizi ES, Hársing LG Jr, Zsilla G: Evidence of the modulatory role of serotonin in acetylcholine release from striatal interneurons. Brain Res 1981 May 11;212(1):89–99

Voigt J, Sekeris CE: Induction of tryptophan oxygenase and tyrosine aminotransferase by metabolites of hydrocortisone. Biochim Biophys Acta 1980 Dec 15;633(3):422–35

Volkova OV, Kharchevnikova GV, Milovidova NS: Morphological picture of hormone synthesis in the thyroid and its dependence on neurohumoral regulatory mechanisms. Folia Morphol (Praha) 1981;29(1):46–8

Volpe M, Rengo F, Chiariello M, et al: Studio preliminare sulla somministrazione associata di furosemide e propranololo. Valutazione della propranololemia. Boll Soc Ital Cardiol 1978;23(6):1001–5 **(Ita)**

Volpi M, Sha'afi RI, Epstein PM, et al: Local anesthetics, mepacrine, and propranolol are antagonists of calmodulin. Proc Natl Acad Sci USA 1981 Feb;78(2):795–9

Volpi M, Sha'afi RI, Epstein PM, et al: Antagonism of calmodulin by local anesthetics, mepacrine, and propranolol. Ann NY Acad Sci 1980; 356:441–2

von Essen C, Kistler JP, Lees RS, et al: Cerebral blood flow and intracranial pressure in the dog during intravenous infusion of nitroglycerin alone and in combination with dopamine. Stroke 1981 May–Jun;12(3):331–8

Voogt JL, Carr LA: Inhibition of LH and prolactin release in the cycling rat following inhibition of dopamine-beta-hydroxylase. Brain Res 1981 Mar 30;209(2):411–9

Voronin LL, Dereviagin VI, Logunov DB: Parametry modeli raskhody peredatchika v sinapsakh identifitsirovannykh neironov ulitki. Neirofiziologiia 1981;13(1):88–97 (Eng. Abstr.) **(Rus)**

Voronina AS, Bogatyreva SA: Ravnovesnoi tsentrifugirovanie v gradientakh plotnosti metavol'framata litiia i fosforno-vol'framata tris-(oksimetil)aminometana. Mol Biol (Mosk) 1980;14(1):190–9 (Eng. Abstr.) **(Rus)**

W

Wada Y: [Prolactin secretion during normal pregnancy and puerperium, particularly with regard to nursing (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1980 Jul;32(7):891–8 (Eng. Abstr.) **(Jpn)**

Waddington JL, Gamble SJ: Prolonged dopamine receptor blockade in rats after termination of long-term depot fluphenazine [letter] Lancet 1981 Jun 20;1(8234):1375–6

Waite JH, Tanzer ML: Specific colorimetric detection of o-diphenols and 3,4-dihydroxyphenylalanine-containing peptides. Anal Biochem 1981 Feb;111(1):131–6

Wakayama Y, Takagi M, Yano K: Photosensitized inactivation of E. coli cells in toluidine blue-light system. Photochem Photobiol 1980 Nov; 32(5):601–5

Walden EL, Thompson SA: A review of some alternative approaches to drug management of hyperactivity in children. J Learn Disabil 1981 Apr;14(4):213–7, 238 (36 ref.)

Waldmeier PC: Noradrenergic transmission in depression: under- or overfunction? Pharmacopsychiatria 1981 Jan;14(1 Suppl):3–9

Wålinder J, Carlsson A, Persson R: 5-HT reuptake inhibitors plus tryptophan in endogenous depression. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):179–90

Walker LC, Gerall AA, Kostrzewa RM: Rostral midbrain lesions and copulatory behavior in male rats. Physiol Behav 1981 Mar;26(3):349–53

Walker P, Weil ML, Weichsel ME Jr, et al: Effect of thyroxine on nerve growth factor concentration in neonatal mouse brain. Life Sci 1981 Apr 13–20;28(15–16):1777–87

Wallace JE, Shimek EL Jr, Harris SC: Determination of tricyclic antidepressants by high-performance liquid chromatography. J Anal Toxicol 1981 Jan–Feb;5(1):20–3

Wallach DP, Brown VR: A novel preparation of human platelet lipoxygenase. Characteristics and inhibition by a variety of phenyl hydrazones and comparisons with other lipoxygenases. Biochim Biophys Acta 1981 Feb 23;663(2):361–72

Wallach MB, Alps BJ, Roszkowski AP, et al: The neuro- and cardiovascular pharmacology of RS-51324, a potential antidepressant. Prog Neuropsychopharmacol 1980;4(6):569–84

Wallis D, Nash H: Relative activities of substances related to 5-hydroxytryptamine as depolarizing agents of superior cervical ganglion cells. Eur J Pharmacol 1981 Mar 26;70(3):381–92

Wallnau LB, Bordash GD, Corso P Jr: Tonic immobility in domestic fowl: possible interaction of serotonergic and dopaminergic mechanisms. Pharmacol Biochem Behav 1981 Apr;14(4):469–73

Wallnau LB, Bordash GD, Corso P Jr: The effects of tryptophan and manipulations of serotonergic receptors on tonic immobility in chickens. Pharmacol Biochem Behav 1981 Apr;14(4):463–8

Walsh TJ, Palfai T: Reversal of guanethidine- and diethyldithiocarbamate-induced amnesia by peripherally-administered catecholamines. Pharmacol Biochem Behav 1981 May;14(5):713–8

Walum E, Westermark B, Pontén J: Growth dependent induction of high affinity gamma-amino-butyric acid transport in cultures of a normal human brain cell line. Brain Res 1981 May 11;212(1):215–8

Warchol JB, Karaś Z: The effect of dopamine on prolactin cells in vivo. Acta Med Pol 1980;21(4):403–4

Wardlaw SL, Stark RI, Daniel S, et al: Effects of hypoxia on beta-endorphin and beta-lipotropin release in fetal, newborn, and

AUTHOR SECTION

maternal sheep. Endocrinology 1981 May;108(5):1710-5

Waroux MJ, Métivier H: Effet de l'âge et du sexe sur la dissolution non dénaturante du collagène pulmonaire de Rat. C R Acad Sci [D] (Paris) 1981 Feb 2;292(5):395-8 (Eng. Abstr.) (Fre)

Wasilewska E, Swięcka E, Bargiel Z: Urinary catecholamine excretion and plasma dopamine-beta-hydroxylase activity during mental work performed in some periods of menstrual cycle in women. Acta Physiol Pol 1980;31(6):647-51

Watanabe H, Nakano S, Ogawa N: Pharmacokinetic study of apomorphine-induced stereotypy in food deprived rats. Pharmacol Biochem Behav 1981 Apr;14(4):493-6

Waterfall NB, Williams G: Effects of phenoxybenzamine on bladder neck opening. J R Soc Med 1980 May;73(5):345-7

Watkins JC, Evans RH: Excitatory amino acid transmitters. Annu Rev Pharmacol Toxicol 1981;21:165-204 (294 ref.)

Watkins WB: Differential immunostaining of adenohypophysial cells with antisera to ACTH and beta-endorphin. Regul Pept 1981 Mar; 1(6):375-85

Watkins WB, Yen SS, Moore RY: Presence of beta-endorphin-like immunoreactivity in the anterior pituitary gland of rat and man and evidence for the differential localization with ACTH. Cell Tissue Res 1981;215(3):577-89

Watson JM, Tiplady B: Zimelidine: comparison of different dosage regimes in general practice. Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):464-70

Watson JM, Barber JH: Depressive illness in general practice: a pilot study. Health Bull (Edinb) 1981 Mar;39(2):112-6

Watson SJ, Richard CW 3d, Ciaranello RD, et al: Interaction of opiate peptide and noradrenalin systems: light microscopic studies. Peptides (Fayetteville) 1980 Spring;1(1):23-30

Watson SJ, Akil H, Ghazarossian VE, et al: Dynorphin immunocytochemical localization in brain and peripheral nervous system: preliminary studies. Proc Natl Acad Sci USA 1981 Feb; 78(2):1260-3

Wdowinski JM, Schwedes U, Faulstich H, et al: Beneficial effect of somatostatin in phalloidin-intoxicated rats. Influence on survival rate, biochemical and morphological data, and 3H-demethylphalloin absorption rate by the liver. Res Exp Med (Berl) 1981;178(2):155-63

Weber A, Fussler C, O'Hanlon JF, et al: Psychophysiological effects of repetitive tasks. Ergonomics 1980 Nov;23(11):1033-46

Weber E, Truscott RJ, Evans C, et al: Alpha-N-acetyl beta-endorphins in the pituitary: immunohistochemical localization using antibodies raised against dynorphin(1-13). J Neurochem 1981 Jun;36(6):1977-85

Weick RF: A reevaluation of the refractory period following the estrogen-induced luteinizing hormone surge in the rhesus monkey. Can J Physiol Pharmacol 1980 Aug;58(8):995-8

Weidenfeld J, Siegel RA, Conforti N, et al: Site and mode of action of indomethacin on the hypothalamo-hypophyseal-adrenal axis: a temporal study in intact, hypothalamic-deafferentated, and hypothalamic-lesioned male rats. Endocrinology 1981 Jul;109(1):205-9

Weil-Fugazza J, Godefroy F, Coudert D, et al: Morphine analgesia and newly synthesized 5-hydroxytryptamine in the dorsal and the ventral halves of the spinal cord of the rat. Brain Res 1981 Jun 15;214(2):440-4

Weiler MH, Gundersen CB, Jenden DJ: Choline uptake and acetylcholine synthesis in synaptosomes: investigations using two different labeled variants of choline. J Neurochem 1981 May;36(5):1802-12

Weinberg J, Brett LP, Levine S, et al: Long-term effects of early iron deficiency on consummatory behavior in the rat. Pharmacol Biochem Behav 1981 Apr;14(4):447-53

Weindl A, Sofroniew MV: Funktionelle Anatomie neuroendokriner Systeme. Verh Dtsch Ges Inn Med 1980;86:12-25 (36 ref.) (Ger)

Weiner N: The participation of cyclic nucleotides and protein kinase in the regulation of norepinephrine synthesis and release during nerve stimulation. Monogr Neural Sci 1980;7:146-60

Weinstein D, Schenker JG, Gloger I, et al: The mode of action of bromocriptine. FEBS Lett 1981 Apr 6;126(1):29-32

Weinstein I, Wasfi I, Heimberg M: Lack of effect of somatostatin on the glucagon-induced alterations of hepatic metabolism of [1-14C]oleate. Biochim Biophys Acta 1981 Apr 23;664(1):124-32

Weiss B, Prozialeck W, Cimino M, et al: Pharmacological regulation of calmodulin. Ann NY Acad Sci 1980;356:319-45 (137 ref.)

Wellman PJ, Peters RH: Effects of amphetamine and phenylpropanolamine on food intake in rats with ventromedial hypothalamic or dorsolateral tegmental damage. Physiol Behav 1980 Dec;25(6):819-27

Wellman PJ, McIntosh P, Guidi E: Effects of dorsolateral tegmental lesions on amphetamine- and lithium-induced taste aversions. Physiol Behav 1981 Feb;26(2):341-4

Welsch F: Human fetal membranes: investigations on membrane potentials and membrane 24Na permeability in vitro and the possible involvement of acetylcholine. Gynecol Obstet Invest 1981;12(3):113-22

Welzl H, Huston JP: Sensitization of the perioral biting reflex by intranigral GABA agonist after detelencephalization. Neurosci Lett 1981 Feb 6;21(3):351-4

Wessendorf MW, Proudfit HK, Anderson EG: The identification of serotonergic neurons in the nucleus raphe magnus by conduction velocity. Brain Res 1981 Jun 9;214(1):168-73

Wester HA, Siegers CP: Cardiovascular effects of mianserin and amitriptyline in healthy volunteers. Int J Clin Pharmacol Ther Toxicol 1980 Dec;18(12):513-7

Wharton J, Polak JM, Probert L, et al: Peptide containing nerves in the ureter of the guinea-pig and cat. Neuroscience 1981;6(5):969-82

Whicher SJ, Uniyal S, Brash JL: Platelet-foreign surface interactions: the release reaction from singly adherent platelets and adherent platelet aggregates. Trans Am Soc Artif Intern Organs 1980;26:268-73

White BA, Lebovic GS, Nicoll CS: Prolactin inhibits the induction of its own renal receptors in Rana catesbeiana tadpoles. Gen Comp Endocrinol 1981 Jan;43(1):30-8

White DC, Sutherland DE, Najarian JS: Systemic thyroxin levels in sheep with a bioartificial thyroid using xenogeneic canine tissue. Trans Am Soc Artif Intern Organs 1980;26:423-7

White DK, Barrett RJ: The effects of electroconvulsive shock on the discriminative stimulus properties of d-amphetamine and apomorphine: evidence for dopamine receptor alteration subsequent ECS. Psychopharmacology (Berlin) 1981;73(3):211-4

White FJ, Holohean AM, Appel JB: Lack of specificity of an animal behavior model for hallucinogenic drug action. Pharmacol Biochem Behav 1981 Mar;14(3):339-43

Whitney CC, Weinstein SH, Gaylord JC: High-performance liquid chromatographic determination of ethmozin in plasma. J Pharm Sci 1981 Apr;70(4):462-3

Whitsett JA, Manton MA, Darovec-Beckerman C, et al: II. Beta-adrenergic receptors and catecholamine sensitive adenylate cyclase in the developing rat lung. Life Sci 1981 Jan 26;28(4):339-45

Whittaker M, Britten JJ, Wicks RJ: Inhibition of the plasma cholinesterase variants by propranolol. Br J Anaesth 1981 May;53(5):511-6

Wightman RM, Bright CE, Caviness JN: Direct measurement of the effect of potassium, calcium, veratridine, and amphetamine on the rate of release of dopamine from superfused brain tissue. Life Sci 1981 Mar 16;28(11):1279-86

Wildbolz A: Die medikamentöse Therapie psychiatrischer Notfälle in der Allgemeinpraxis. Praxis 1981 Feb 3;70(6):211-4 (Eng. Abstr.) (Ger)

Wildt L, Hausler A, Hutchison JS, et al: Estradiol as a gonadotropin releasing hormone in the rhesus monkey. Endocrinology 1981 May; 108(5):2011-3

Wilkinson M, Grovestine D: A simple, inexpensive filtration device suitable for neurotransmitter receptor binding studies in brain tissue. Can J Physiol Pharmacol 1981 May;59(5):504-6

Williams EF, Rice KC, Mattson M, et al: In vivo effects of two novel alkylating benzodiazepines, irazepine and kenazepine. Pharmacol Biochem Behav 1981 Apr;14(4):487-91

Williams IH, Sugden PH, Morgan HE: Use of aromatic amino acids as monitors of protein turnover. Am J Physiol 1981 Jun;240(6):E677-81

Williams JF Jr, Mathew B: Effect of quinidine on positive inotropic action of digoxin. Am J Cardiol 1981 May;47(5):1052-5

Williams RS, Bishop T: Selectivity of dobutamine for adrenergic receptor subtypes: in vitro analysis by radioligand binding. J Clin Invest 1981 Jun;67(6):1703-11

Willis LR, Lappe RW, Henry DP, et al: Urinary excretion of radiolabelled norepinephrine after release from renal sympathetic nerves. Life Sci 1980 Dec 22-29;27(25-26):2541-6

Willner P, Theodorou A, Montgomery A: Subchronic treatment with the tricyclic antidepressant DMI increases isolation-induced fighting in rats. Pharmacol Biochem Behav 1981 Apr;14(4):475-9

Willow M, Johnston GA: Pentobarbitone slows the dissociation of GABA from rat brain synaptosomal binding sites. Neurosci Lett 1981 Apr 9; 23(1):71-4

Wilson CL, Sherman JE, Holman EW: Aversion to the reinforcer differentially affects conditioned reinforcement and instrumental responding. J Exp Psychol [Anim Behav] 1981 Apr;7(2):165-74

Wilson SP, Abou-Donia MM, Chang KJ, et al: Reserpine increases opiate-like peptide content and tyrosine hydroxylase activity in adrenal medullary chromaffin cells in culture. Neuroscience 1981;6(1):71-9

Wilting J, Hart BJ, De Gier JJ: The role of albumin conformation in the binding of diazepam to human serum albumin. Biochim Biophys Acta 1980 Dec 16;626(2):291-8

Winberg M, Holmgren S, Nilsson S: Effects of denervation and 6-hydroxydopamine on the activity of choline acetyltransferase in the spleen of the cod, Gadus morhua. Comp Biochem Physiol [C] 1981; 69C(1):141-3

Winek CL, Collom WD, Bricker JD: A death due to 4-bromo-2,5-dimethoxyamphetamine. Clin Toxicol 1981;18(3):267-71

Winkel CA, Casey ML, Simpson ER, et al: Deoxycorticosterone biosynthesis from progesterone in kidney tissue of the human fetus. J Clin Endocrinol Metab 1981 Jul;53(1):10-5

Winkel CA, Simpson ER, Milewich L, et al: Deoxycorticosterone biosynthesis in human kidney: potential for formation of a potent mineralocorticosteroid in its site of action. Proc Natl Acad Sci USA 1980 Dec;77(12):7069-73

Wise PM, Rance N, Barraclough CA: Effects of estradiol and progesterone on catecholamine turnover rates in discrete hypothalamic regions in

AUTHOR SECTION

ovariectomized rats. Endocrinology 1981 Jun;108(6):2186-93

Wise PM, Rance N, Selmanoff M, et al: Changes in radioimmunoassayable luteinizing hormone-releasing hormone in discrete brain areas of the rat at various times on proestrus, diestrous day 1, and after phenobarbital administration. Endocrinology 1981 Jun;108(6):2179-85

Wise RA: Action of drugs of abuse on brain reward systems. Pharmacol Biochem Behav 1980;13 Suppl 1:213-23 (117 ref.)

Wise RA: Intracranial self-stimulation: mapping against the lateral boundaries of the dopaminergic cells of the substantia nigra. Brain Res 1981 May 25;213(1):190-4

Wistedt B, Wiles D, Kolakowska T: Slow decline of plasma drug and prolactin levels after discontinuation of chronic treatment with depot neuroleptics [letter] Lancet 1981 May 23;1(8230):1163

Wode-Helgodt B, Alfredsson G: Concentrations of chlorpromazine and two of its active metabolites in plasma and cerebrospinal fluid of psychotic patients treated with fixed drug doses. Psychopharmacology (Berlin) 1981;73(1):55-62

Woggon B: Veränderungen der psychopathologischen Symptomatik während 20tägiger antidepressiver oder neuroleptischer Behandlung. Psychiatr Clin (Basel) 1980;13(3-4):150-64 (Eng. Abstr.) **(Ger)**

Wolcott DL: Effect of potassium and lithium ions on protein synthesis in the sea urchin embryo. Exp Cell Res 1981 Apr;132(2):464-7

Wolf WA, Kuhn DM, Lovenberg W: Blood pressure responses to local application of serotonergic agents in the nucleus tractus solitarii. Eur J Pharmacol 1981 Jan 29;69(3):291-9

Wölfle D, Hartmann H, Jungermann K: Induction of phosphoenolpyruvate carboxykinase by sympathetic agents in primary cultures of adult rat hepatocytes. Biochem Biophys Res Commun 1981 Feb 27;98(4):1084-90

Wong EH, Loten EG, Exton JH, et al: The effect of phenoxybenzamine on the relationship between glycerol release and cyclic AMP levels in the presence of insulin in epinephrine-stimulated rat adipocytes. FEBS Lett 1981 May 18;127(2):217-20

Wong TY, Dreyfus H, Massarelli R: Transport and metabolism of choline in synaptosomes: ionic requirement. Biochem Soc Trans 1981 Feb;9(1):84-5

Woodruff GN, Freedman SB: Binding of [3H]sulpiride to purified rat striatal synaptic membranes. Neuroscience 1981;6(3):407-10

Woolf PD: Resumption of prolactin secretion after dopaminergic inhibition: differential effects of dopamine and its agonists. Am J Physiol 1981 Jun;240(6):E700-4

Woolverton WL, Balster RL: Effects of combinations of phencyclidine and pentobarbital on fixed-interval performance in rhesus monkeys. J Pharmacol Exp Ther 1981 Jun;217(3):611-8

Wright KC, Hedge GA: Pharmacological studies of the involvement of hypothalamic prostaglandins in the regulation of thyrotropin secretion. Environ Health Perspect 1981 Apr;38:83-8

Wright ML, Sicbaldi EM, Loveridge KM, et al: Cell population kinetics in tadpole limb epidermis during thyroxine-induced, spontaneous, and prolactin-inhibited metamorphosis. Gen Comp Endocrinol 1981 Apr;43(4):451-61

Wu CS, Lee NM, Ling N, et al: Conformation of beta-endorphin analogues in cerebroside sulfate solution. Mol Pharmacol 1981 Mar;19(2):302-6

Wu CS, Ikeda K, Yang JT: Ordered conformation of polypeptides and proteins in acidic dodecyl sulfate solution. Biochemistry 1981 Feb 3;20(3):566-70

Wu PH, Phillis JW, Bender AS: Do benzodiazepines bind at adenosine uptake sites in CNS? Life Sci 1981 Mar 2;28(9):1023-31

Wu WC, Raftery MA: Reconstitution of acetylcholine receptor function using purified receptor protein. Biochemistry 1981 Feb 17;20(4):694-701

Wunderlich V, Sydow G: Lytic action of neurotropic drugs on retroviruses in vitro. Eur J Cancer 1980 Sep;16(9):1127-32

Wurtman RJ, Magil SG, Reinstein DK: Piracetam diminishes hippocampal acetylcholine levels in rats. Life Sci 1981 Mar 9;28(10):1091-3

Wurzburger RJ, Miller RL, Marcum EA, et al: A new radioimmunoassay for haloperidol: direct measurement of serum and striatal concentrations. J Pharmacol Exp Ther 1981 Jun;217(3):757-63

Y

Yagisawa S: Studies on protein semisynthesis. I. Formation of esters, hydrazides, and substituted hydrazides of peptides by the reverse reaction of trypsin. J Biochem (Tokyo) 1981 Feb;89(2):491-501

Yamada K, Furukawa T: The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats. Naunyn Schmiedebergs Arch Pharmacol 1981 Apr;316(2):155-60

Yamaguchi M: Effects of calcitonin and epinephrine on serum glucose concentration in rats. Chem Pharm Bull (Tokyo) 1980 Dec;28(12):3693-5

Yamaguchi N, Garceau D: Correlations between hemodynamic parameters of the liver and norepinephrine release upon hepatic nerve stimulation in the dog. Can J Physiol Pharmacol 1980 Nov;58(11):1347-55

Yamauchi T, Nakata H, Fujisawa H: A new activator protein that activates tryptophan 5-monooxygenase and tyrosine 3-monooxygenase in the presence of Ca2+-, calmodulin-dependent protein kinase. Purification and characterization. J Biol Chem 1981 Jun 10;256(11):5404-9

Yamazaki I, Okada H: A radioimmunoassay for a highly active luteinizing hormone-releasing hormone analogue and relation between the serum level of the analogue and that of gonadotropin. Endocrinol Jpn 1980 Oct;27(5):593-605

Yanaihara N: [Gut-brain peptides-structures and functions (author's transl)] Horumon To Rinsho 1980 Oct;28(10):1153-60 (34 ref.) **(Jpn)**

Yazulla S, Brecha N: Localized binding of [3H]muscimol to synapses in chicken retina. Proc Natl Acad Sci USA 1981 Jan;78(1):643-7

Yeager EP, Goebelsmann U, Soares JR, et al: delta 9-Tetrahydrocannabinol by GLC-MS validated radioimmunoassays of hemolyzed blood or serum. J Anal Toxicol 1981 Mar-Apr;5(2):81-4

Yeary RA: Serum concentrations of primidone and its metabolites, phenylethylmalonamide and phenobarbital, in the dog. Am J Vet Res 1980 Oct;41(10):1643-5

Yeh HH, Moises HC, Waterhouse BD, et al: Modulatory interactions between norepinephrine and taurine, beta-alanine, gamma-aminobutyric acid and muscimol, applied iontophoretically to cerebellar Purkinje cells. Neuropharmacology 1981 Jun;20(6):549-60

Yehuda S, Ben-Uriah Y, Carasso RL: A comparison of the hypothermic effects of methylphenidate and d-amphetamine. Int J Neurosci 1981;13(2-3):117-20

Yehuda S, Kastin AJ: Interaction of MIF-I or alpha-MSH with D-amphetamine or chlorpromazine on thermoregulation and motor activity of rats maintained at different ambient temperatures. Peptides (Fayetteville) 1980 Fall;1(3):243-8

Yeung HW, Yamashiro D, Tseng LF, et al: Human beta-endorphin: synthesis and biological activity of analogs with substitutions in positions 2, 9, 18, 27 and 31. Int J Pept Protein Res 1981 Feb;17(2):235-8

Yokoi I, Rose SE, Yanagihara T: Benzodiazepine receptor: heterogeneity in rabbit brain. Life Sci 1981 Apr 6;28(14):1591-5

Yorkston NJ, Zaki SA, Weller MP, et al: DL-propranolol and chlorpromazine following admission for schizophrenia. A controlled comparison. Acta Psychiatr Scand 1981 Jan;63(1):13-27

Yoshinaga K: Induction of delayed implantation in rats by LH-RH. J Reprod Fertil [Suppl] 1981;29:131-3

Youdim MB, Oppenheim B: The effect of tryptolines (1, 2, 3, 4-tetrahydro-beta-carbolines) on monoamine metabolism and the platelet aggregation response in human platelets. Neuroscience 1981;6(4):801-10

Young AM, Herling S, Winger GD, et al: Comparison of discriminative and reinforcing effects of ketamine and related compounds in the rhesus monkey. Natl Inst Drug Abuse Res Monogr Ser 1980;(34):173-9

Young RC, Allen R, Meissner G: Permeability of reconstituted sarcoplasmic reticulum vesicles. Reconstitution of the K+, Na+ channel. Biomembranes 1981 Jan 22;640(2):409-18

Young SN, Gauthier S: Effect of tryptophan administration on tryptophan, 5-hydroxyindoleacetic acid and indoleacetic acid in human lumbar and cisternal cerebrospinal fluid. J Neurol Neurosurg Psychiatry 1981 Apr;44(4):323-7

Young WS 3d, Kuhar MJ: Neurotensin receptor localization by light microscopic autoradiography in rat brain. Brain Res 1981 Feb 16;206(2):273-85

Yu HS, Pang SF, Tang PL, et al: Persistence of circadian rhythms of melatonin and N-acetylserotonin in the serum of rats after pinealectomy. Neuroendocrinology 1981 May;32(5):262-5

Yu PH: Studies on the pargyline-binding site of different types of monoamine oxidase. Can J Biochem 1981 Jan;59(1):30-7

Yui Y, Kawai C: Comparison of the sensitivity of various post-column methods for catecholamine analysis by high-performance liquid chromatography. J Chromatogr 1981 Feb 27;206(3):586-8

Yui Y, Wakabayashi A, Kawai C: [Recent advances in high-performance liquid chromatographic method for the determination of picogram amounts of catecholamines and its clinical application (author's transl)] Kokyu To Junkan 1980 Oct;28(10):1125-7 **(Jpn)**

Yukimura T, Fuxe K, Ganten D, et al: Acute sino-aortic denervation in rats produces a selective increase of adrenaline turnover in the dorsal midline area of the caudal medulla oblongata and a reduction of adrenaline levels in the anterior and posterior hypothalamus. Eur J Pharmacol 1981 Jan 29;69(3):361-5

Yuwiler A, Brammer GL, Morley JE, et al: Short-term and repetitive administration of oral tryptophan in normal men. Effects on blood tryptophan, serotonin, and kynurenine concentrations. Arch Gen Psychiatry 1981 Jun;38(6):619-26

Z

Zaldívar R: 'Gradients geográficas en concentraciones de litio en aguassuperficiales y de consumo y en plasma sanguineo de sujetos expuestos'. Rev Med Chil 1980 Sep;108(9):822-4 (Eng. Abstr.) **(Spa)**

Zapletálek M, Preiningerová O, Hanus H: Verursacht Clozapin eine Abhängigkeit? Agressologie 1980;21(A):19-21 (Eng. Abstr.) **(Ger)**

Zatz M, Herkenham MA: Intraventricular carbachol mimics the phase-shifting effect of light on the circadian rhythm of wheel-running activity. Brain Res 1981 May 11;212(1):234-8

AUTHOR SECTION

Zeiger E, Guthrie J: Cyclic hydrazides are mutagenic for Salmonella typhimurium. Mutat Res 1981 May;91(3):199-205

Zemon V, Kaplan E, Ratliff F: Bicuculline enhances a negative component and diminishes a positive component of the visual evoked cortical potential in the cat. Proc Natl Acad Sci USA 1980 Dec;77(12):7476-8

Zigmond MJ, Heffner TG, Stricker EM: The effect of altered dopaminergic activity on food intake in the rat: evidence for an optimal level of dopaminergic activity for behavior.
Prog Neuropsychopharmacol 1980;4(4-5):351-62

Zigun JR, Bannon MJ, Roth RH: Comparison of two alpha-noradrenergic agonists (clonidine and guanfacine) on norepinephrine turnover in the cortex of rats during morphine abstinence. Eur J Pharmacol 1981 Apr 9;70(4):565-70

Zimmer R, Teelken AW, Meier KD, et al: Preliminary studies on CSF gamma-aminobutyric acid levels in psychiatric patients before and during treatment with different psychotropic drugs.
Prog Neuropsychopharmacol 1980;4(6):613-20

Zolman JC, Valenta LJ: Effect of calcium and potassium on basal and gonadotrophin-releasing hormone (GnRH) stimulated release of luteinizing hormone (LH). Acta Endocrinol (Copenh) 1981 May; 97(1):26-32

Zou G, Tu ZH, Lu RF, et al: [Neuropharmacological actions of some N-phenyl piperazine derivatives (author's transl)]
Yao Hsueh Hsueh Pao 1981 May;16(5):321-7 (Eng. Abstr.) **(Chi)**

Zsigmond EK, Flynn KB, Kothary SP: Improved method for the identification of the fluoride-resistant plasmacholinesterase genotypes. Biochem Genet 1980 Oct;18(9-10):861-7

Zuardi AW, Finkelfarb E, Bueno OF, et al: Characteristics of the stimulus produced by the mixture of cannabidiol with delta 9-tetrahydrocannabinol. Arch Int Pharmacodyn Ther 1981 Jan; 249(1):137-46

Zühlke H, Ziegler B, Ratzmann KP: Somatostatin. Teil I: Struktur, Bildung, Wirkung. Z Gesamte Inn Med 1981 Jan 15;36(2):51-5 (Eng. Abstr.) **(Ger)**

Zung WW, Daniel JT Jr, King RE, et al: A comparison of prazepam, diazepam, lorazepam and placebo in anxious outpatients in non-psychiatric private practices. J Clin Psychiatry 1981 Jul;42(7):280-4

Zwagemakers JM, Claassen V: Secoverine selectively antagonizes muscarinic effects in various in vivo preparations. Eur J Pharmacol 1981 Apr 24;71(1):165-8

Zweymüller E: Endokrinologie und Erkrankungen der Hoden im Kindesalter. Wien Med Wochenschr 1981 Feb 15;131(3):68-72 **(Ger)**

ANONYMOUS

Acta Psychiatr Scand [Suppl]

Recent advances in the treatment of depression. Proceedings of an international symposium, Corfu, Greece, April 16--18, 1980.
Acta Psychiatr Scand [Suppl] 1981;63(Suppl 290):1-477

Long-term neuroleptic treatment. Benefits and risks. Proceedings from a workshop, Copenhagen, 6th-7th September, 1979.
Acta Psychiatr Scand [Suppl] 1981;63(291):1-159

Agressologie

IInd Czechoslovakian Symposium of Psychopharmacology Smolenice, 28th-30th September 1977. Agressologie 1980;21(A):1-69 **(Ger)**

Br Med J [Clin Res]

The psychiatrically violent patient [letter] Br Med J [Clin Res] 1981 Mar 7;282(6266):821

Chlormethiazole and temazepam [letter] Br Med J [Clin Res] 1981 Mar 7;282(6266):825

Can Med Assoc J

Therapeutic monograph on anxiolytic-sedative drugs.
Can Med Assoc J 1981 Jun 1;124(11):1439-46

Drug Ther Bull

Trazodone (Molipaxin): another antidepressive drug. Drug Ther Bull 1981 May 8;19(10):39-40

Lithium updated. Drug Ther Bull 1981 Mar 13;19(6):21-4

FDA Drug Bull

New standards for phenytoin products. FDA Drug Bull 1981 Mar;11(1):4

Hosp Pract

EENT cocaine shortage leaves mystery in its wake. Hosp Pract 1981 Jun;16(6):164-5

J Ethnopharmacol

Coca and cocaine 1981. J Ethnopharmacol 1981 Mar-May;3(2-3):110-379

Med J Aust

Mianserin: a possible cause of neutropenia and agranulocytosis. Adverse Drug Reactions Advisory Committee. Med J Aust 1980 Dec 13; 2(12):673-4

Med Lett Drugs Ther

Maprotiline (Ludiomil)--another antidepressant. Med Lett Drugs Ther 1981 Jun 26;23(13):58-9

Pharmacol Biochem Behav

The psychopharmacology of aggression and social behavior. Symposium of the International Society for Research on Aggression. July 12, 1980, Groningen, The Netherlands. Pharmacol Biochem Behav 1981;14 Suppl 1:1-124

S Afr Med J

Digitalis-quinidine interaction [editorial] S Afr Med J 1981 May 9; 59(20):695

Scand J Gastroenterol [Suppl]

Advances in basic and clinical pharmacology of pirenzepine. Proceedings of the Second International Symposium on Pirenzepine. Hamburg, FRG, 8 June 1980. Scand J Gastroenterol [Suppl] 1980;15(66):1-114

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-341-180/101

The *Psychopharmacology Bulletin* is prepared by the Pharmacologic and Somatic Treatments Research Branch of the National Institute of Mental Health. Its purpose is to facilitate the dissemination and exchange of information among the national and international scientific community. The emphasis is on rapid, informal reporting of work which has not appeared in the more formal literature. We invite contributions such as review articles, letters to the Editor, news items, books for review, and announcements appropriate for the *Bulletin*.

All material published in the *Psychopharmacology Bulletin* is in the public domain unless otherwise noted.

Individuals interested in submitting material to the *Psychopharmacology Bulletin* should contact:

Allen Raskin, Ph.D.
Editor-in-Chief
Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

We respectfully ask you to adhere to the following guidelines when preparing a paper for the *Psychopharmacology Bulletin:*

1. Manuscript Format: Manuscripts should be typed double-spaced with ample margins, and submitted in triplicate. Do not split paragraphs from one page to another, even if this makes page lengths uneven. Also, do not hyphenate words at the end of a line, even if this makes uneven lines.

Title page should include each author's name, degree, and full address.

Papers should be written in *third* person, e.g., the investigators found, **Not:** I found, we found. Contents should be *substantive*, not indicative, e.g., the investigator used the gas chromatography method to determine the three molecular structures, **Not:** The author described the method for determining the structure of the drug.

2. Figures: Figures, charts, or graphs should be submitted as glossies (photographs printed on smooth shiny paper) or should be professionally prepared using black ink on white paper. Only one copy is needed. Indicate in the text where these figures and their legends should be placed.

3. References: References mentioned in the text should appear as full citations in the **References** following the article. We are now using the author-date method of citation, that is, the surname of the author and the year of publication are to be used in the text, i.e.: Smith (1970) compared reaction times . . . or, In a recent study of reaction times (Smith 1970) . . . This method gives readers useful information in the text and enables them to locate the citation easily in the alphabetical reference list at the end of the article.

If a work has two authors, always cite both names every time the reference occurs in the text. If more than two authors, cite all authors the first time the reference occurs; include only the surname of the first author followed by "et al." (not italicized) and the year in subsequent citations of the same reference, i.e.:

Williams, Jones, and Smith (1963) found their data . . . (1st occurrence)

Williams et al. (1963) found their data . . . (2nd occurrence)

4. Abbreviations: Abbreviations should appear in parentheses after the first time they are mentioned in the paper, i.e., Brief Psychiatric Rating Scale (BPRS).

Use generic names in referring to drugs; trade names may be given in parenthesis the first time a drug is mentioned only.

Journal titles should be abbreviated in the *References* according to the National Library of Medicine's Index Medicus.

DEPARTMENT OF
HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20857

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U. S. DEPARTMENT OF H.H.S.
HHS 396

THIRD CLASS
BULK RATE

U.S.MAIL

DHHS Publication No. (ADM) 82 - 173
Printed 1982

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20857

18/2

National Institute of Mental Health

NEWARK PUBLIC LIBRARY

JUN 2 2 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

Psychopharmacology Bulletin

Vol. 18, No. 2
April 1982

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

HE 20.8109

Contributions and inquiries should be sent to:

Allen Raskin, Ph.D.
Editor-in-Chief

Lillian Altman
Managing Editor

Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

The *Psychopharmacology Bulletin* is available on subscription from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402. Subscription price $11.00 per year for the United States. All other countries add $2.75 for postage. Please make check or money order payable to the Superintendent of Documents. An annual subscription for four quarterly issues begins with the next issue following receipt of the order. Single copies and back issues may also be ordered from the Superintendent of Documents. The expiration date is printed on the top line of the address label. Change of address and complaints about non-receipt of issues should be sent to the Superintendent of Documents, and should include the old address, preferably a mailing label, as well as the new address.

ORDER FORM Mail To: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Enclosed is $_______ ☐ check,
(U.S. Currency Only)
☐ money order, or charge to my
Deposit Account No.
☐☐☐☐☐☐☐–☐

Order No.____________

VISA

master charge

Credit Card Orders Only

Total charges $_______ Fill in the boxes below.

Credit Card No. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Expiration Date Month/Year ☐☐☐☐

Please enter my subscription to: **PSYCHOPHARMACOLOGY BULLETIN** [*PSBU*]
@ $11.00 domestic, @ $13.75 foreign.

Name—First, Last

Street address

Company name or additional address line

City **State** **ZIP Code**

(or Country)

PLEASE PRINT OR TYPE

For Office Use Only.

	Quantity	Charges
Enclosed		
To be mailed		
Subscriptions		
Postage		
Foreign handling		
MMOB		
OPNR		
UPNS		
Discount		
Refund		

Psychopharmacology Bulletin

CONTENTS

Vol. 18, No.2 **April 1982**

Page

Book Review 1

Books Received 1

Letter to the Editor and Reply 2

Report from a WHO Collaborative Reference Center for the Study of Psychotropic Drugs— ... 3

Psychopharmacological Research in India 3

Adverse Drug Reactions—When Is an Adverse Drug Reaction Not an Adverse Drug Reaction? —*Paul Leber* 6

Brief Reports and Reviews—

The Brief Psychiatric Rating Scale for Children—*John E. Overall and Betty Pfefferbaum* 11

On the Clinical Response/Serum Level Relationship for Antidepressants II: Lofepramine and Imipramine—*John E. Dutt* 17

Models of Cognitive Impairment: Cognitive Changes in Depression—*Herbert Weingartner and Edward Silberman* 27

Electroconvulsive Therapy: Research Goals—

The Importance of Diagnostic Criteria for Depression in the Study of ECT—*Michael Alan Taylor* 44

Clinical Prediction of ECT Response in Depressed Patients—*Richard Abrams* 48

Predictors of Outcome in Convulsive Therapy—*Max Fink* 50

Relevance of Neuroendocrine Strategies for Electroconvulsive Therapy Research—*Roger F. Haskett and A. Ariav Albala* 57

Hemispheric Asymmetry in Affective Disorders—*Henry A. Nasrallah* 62

The Relative Efficacy of Unilateral Nondominant and Bilateral Stimulation—*Charles A. Welch* 68

The Role of Stimulus Waveform In Therapeutic and Adverse Effects of ECT—*Richard D. Weiner* 71

ECT and Tricyclic Antidepressants in the Treatment of Endogenous Depression—*Richard Abrams* 73

Factors Affecting Outcome After Successful Electroconvulsive Therapy—*Roger F. Haskett* 75

Electroencephalographic Correlates of ECT—*Richard D. Weiner* 78

Short- and Long-Term Cognitive Effects of ECT: Part I—Effects on Memory—*Trevor R.P. Price* 81

Short- and Long-Term Cognitive Effects of ECT: Part II— Effects on Nonmemory-Associated Cognitive Functions—*Trevor R.P. Price* 91

Nonmemory Higher Cognitive Function and Electroconvulsive Treatment—*Sheri A. Berenbaum and Michael Alan Taylor* 101

Convulsive Therapy: A Risk-Benefit Analysis—*Max Fink* 110

Psychopharmacology—A Recurring Bibliography

Subject Section S-1

Author Section A-63

Book Review

•Psychotropic Drug Handbook—Third Edition, is a small book, 6½ x 4½ inches and 198 pages, containing a wealth of information for the physician who prescribes psychoactive medication. For each of the major classes of psychoactive drugs, antipsychotics, antidepressants, hypnotics, etc., there is a general statement describing the symptoms, behaviors, and diagnostic groups for whom the class of drugs is intended, a brief description of the mechanism of action of these drugs, dosage recommendations based on factors such as severity of illness, a section on pharmacokinetics, and a lengthy and complete description of adverse drug effects and how these should be managed.

In addition, the authors, two pharmacologists and a psychiatrist, provide the generic and trade names for marketed drugs in each drug class and the direct cost from the manufacturers for the medication. Other features of the book which I would commend are an initial section on general principles of drug use which discusses issues such as the dangers of polypharmacy, the advantages and disadvantages of divided doses, and the concerns with drug-drug interactions. The back of the book contains sample patient instruction forms which may be given to patients to instruct them in how the medication should be taken and to alert them to possible adverse effects. These are very complete and written in language that would be understandable to most patients.

In sum, I would highly recommend this book to any physician who prescribes psychotropic medication, particularly those in nonpsychiatric fields who would be less likely to be current with research and experience with these drugs than their psychiatric brethren. One note of caution: the book does represent the views of the authors, and others in the field may not always agree with their recommendations for drug use. I was also a little disappointed with the references cited at the back of the book which I felt were skimpy and could be expanded.

The book may be purchased from the publisher, Harvey Whitney Books, 4906 Cooper Road, P.O. Box 42442, Cincinnati, OH 45242. Price: U.S.$9.50, Softbound; 198 pp.

Allen Raskin, Ph.D.
National Institute of Mental Health,
Rockville, MD

Books Received

- **Halluzinogene:** Psychische Grenzzustande in Forschung und Psychotherapie (Hanscarl Leuner, editor) has recently been published by Verlag Hans Huber Publishers, Berne, Switzerland. It is a 458-page, soft-cover book with extensive references. It is in the German language.

• • • •

- **PCP (Phencyclidine): Current and Historical Perspectives.** Ed Domino (ed.), Ann Arbor, MI: NPP Books, P.O. Box 1491, Ann Arbor, MI 48106. Price: $40.00; 527 pp.

• • • •

- **Nutrition and Behavior.** Sanford A. Miller (ed.), Philadelphia, PA: The Franklin Institute Press, Box 2266, Philadelphia, PA 19103. Price: $24.50; 320 pp.

• • • •

- **Serotonin: Current Aspects of Neurochemistry and Function.** (Series: *Advances in Experimental Medicine and Biology*, Vol. 133). Haber, B., Gabay, S., Issidorides, M.R., and Alivisatos, S.G.A. (eds.). New York: Plenum Publishing Corp., 223 Spring Street, New York, NY 10013. Price: $75.00; 798 pp.

• • • •

- **Psychopharmacology of Sleep.** David Wheatley (ed.). New York: Raven Press, 1140 Avenue of the Americas, New York, NY 10036. Price: $29.00; 256 pp.

• • • •

Letter to the Editor:

Sudden Death and Neuroleptics

It has recently come to our attention that the otherwise very excellent column by Dr. Paul Leber in the July 1981 *Psychopharmacology Bulletin* (1) regarding sudden death as a risk of neuroleptic treatment contains an erroneous reference to a recent publication of ours (2). The column indicated us as suggesting that hospitalized chronic schizophrenics may be at *decreased* (emphasis in the column) risk for death compared to the age- and sex-matched general population. The analyses of the article in question were limited to age- and sex-specific mortality rates at two points in time (1970 and 1977) for *hospitalized psychiatric patients only* and indicated a reduction in mortality risk over time in this population. In a subsequent report (3), we compared mortality rates among hospitalized psychiatric patients with general population rates after age adjustment and found consistently elevated mortality among psychiatric patients as compared to the general population. In neither study did we report mortality rates by diagnosis.

We have examined mortality rates (unpublished data) by diagnosis in a large inpatient psychiatric population in comparison to general population rates and have consistently found increased mortality among patients in all age-, sex-, and diagnosis-specific categories. Thus, while it is true that the mortality risk for chronic schizophrenics is the lowest of all diagnostic groups we studied, it is still substantially increased over the risk expected in an age- and sex-matched general population sample.

In a word, chronic schizophrenics in our studies were at *increased* risk for death compared to the age- and sex-matched general population.

We hesitated to make this rather minor point, since the major thrust of the column is excellent and points to important directions for further investigation of rarely occurring potential adverse drug reactions. However, we simultaneously felt that your readership should not be misled by the above misattribution.

Thomas J. Craig, M.D., M.P.H., and
Shang P. Lin, Ph.D.
Information Sciences Division
Rockland Research Institute
Orangeburg, NY 10962

References

1. Leber, P. Sudden death as a risk of neuroleptic treatment: (A Continuing Controversy). *Psychopharmacol. Bull.*, 17:6-9, 1981.
2. Craig, T.J., and Lin, S.P. Death and deinstitutionalization. *Am. J. Psychiatry*, 138:224-227, 1981.
3. Craig, T.J., and Lin, S.P. Mortality among psychiatric inpatients: Age-adjusted comparison of populations before and after psychotropic drug era. *Arch. Gen. Psychiatry*, 38:935-938, 1981.

Reply to Drs. Craig and Lin

I thank Drs. Craig and Lin for the gracious way in which they draw attention to my mis-interpretation of their findings (1). I assumed, incorrectly, that their calculations of expected 1977 patient deaths employed population based mortality rates for 1970. Their paper clearly states that hospital based rates were used, and I apologize for the confusion created by my incorrect citation of their work.

The actual findings of Drs. Craig and Lin support the generally held view that populations of chronic psychiatric patients (i.e., subjects likely to have received neuroleptics) have a mortality risk exceeding that of the general population. Thus, their findings do not militate against arguments supporting an etiologic role for neuroleptics in sudden death (the implication I intended in citing their work in my paper).

Paul Leber, M.D.
Food and Drug Administration,
Rockville, MD.
December 7, 1981

1. Craig, T.J., and Lin, S.P. Death and deinstitutionalization. *Am. J. Psychiatry*, 138:224-227, 1981.

Errata

In the January 1982 issue (Vol. 18, No. 1) of the *Bulletin*, pages 95/96 and 97/98 were transposed.

On pages 110 and 111 of Dr. Campbell's article in the January issue (Vol. 18, No. 1) the footnotes should read: *ND= < .50 ng/ml.

Report from a WHO Collaborative Reference Center for the Study of Psychotropic Drugs

Psychopharmacological Research in India

The following is a short resumé of work done in the field of psychopharmacology in India in 1980. The Report was provided by Drs. V.N. Bagadia, V.K. Mundra, and K.M. Dhawale of the Department of Psychiatry, KEM Hospital, Parel, Bombay, India. Their material was obtained from the *Indian Journal of Psychiatry*, and the papers read at the 33d Annual Conference of the Indian Psychiatric Society (IPS) at Ahmedabad and the 11th Annual Conference of the Indian Psychiatric Society—West Zone (IPS—WZ), Mahableshwar, India.

Antidepressant Drugs

A comparative evaluation of dothiepin (Prothiaden) and imipramine in the treatment of severe depression demonstrated no significant differences in efficacy and tolerability between the two drugs (Chaturvedi et al., 1980).

Gurmeet Singh (1980) found a single bedtime dose of Sintamil superior to divided doses in depression. With the single dose there were fewer side effects and greater patient compliance than with the divided doses.

Sharma and Hegde (1980) compared doxepin in a similar fashion and concluded there were no significant differences in effectiveness and incidence of side effects between the two regimes. They caution, however, against using single-dose therapy in a geriatric population.

Sethi and Bhiman (1980) failed to find any significant differences in efficacy of doxepin vs. that of imipramine and amitriptyline. The correlations between serum levels and therapeutic response for each of the three drugs was also poor.

Quadri et al. (1980) found response to d-amphetamine to be an accurate predictor of antidepressant response to the tricyclics imipramine and amitriptyline.

Sethi et al. (1980) have reported four cases of unipolar depressed patients who developed manic features while on antidepressant medication. They consider the age of the patient, metabolic products of the tricyclic antidepressant, and the central monoamine systems as important in the genesis of this effect.

Antipsychotic Drugs

Deo et al. (1980) found fluphenazine decanoate to be an effective treatment in chronic schizophrenics at a dose of 12.5 mg/week.

DeSouza and DeSouza (1980c) compared a weekly vs. biweekly schedule of fluphenazine decanoate. They found that with the weekly schedule, the compliance was superior with fewer side effects and greater therapeutic efficacy.

V.D. Shah et al. (1980) carried out an open clinical trial with penfluridol in chronic schizophrenics and found a good response to this drug in the dosage range of 20-80 mg/week over a period of 3-6 months.

Sharma and Nandkumar (1980) reported results of a double-blind clinical trial of trifluoperazine against trifluoperazine combined with trihexyphenidyl hydrochloride.

Lithium

Venkoba Rao et al. (1980) studied the effects of lithium on the kidney by means of renal function tests and renal biopsy. They failed to find any correlation between renal function and the intensity and duration of lithium therapy. Khandelwal et al. (1980) studied renal function after 1 year of lithium therapy and also found no significant renal dysfunction.

Sampath et al. (1980a) studied the red blood cell-plasma lithium ratios in manic patients treated with lithium. They found that lithium responders had indeed higher ratios than nonresponders but could not establish a cutoff value to differentiate the two groups. Nataraj and Bhat (1980) did not find any correlation between the saliva serum lithium ratio and clinical response.

Lakdawalla et al. (1980) reported on their experience in treating aggressive behavior and hyperkinetic syndrome with lithium. They have also attempted to draw a correlation between clinical response, dose, and serum lithium levels.

Venkoba Rao and Hariharasubramanian (1980) have reported significant electrocardiographic changes in long-term lithium therapy with serum lithium levels in their patients well within accepted therapeutic range and with no obvious electrolyte disturbance in evidence. They suggested occasional electrocardiogram (ECG) monitoring to forestall impairment of cardiac function.

Hariprasad et al. (1980) have not found lithium to be hepatotoxic, and Sampath et al. (1980c) have failed to note a significant correlation between the patient's insight into his illness and lithium compliance.

Sampath et al. (1980b) presented a single case report of the occurrence of severe neurotoxicity in a young manic patient who had a lithium serum level within the therapeutic range.

Miscellaneous

DeSouza and DeSouza (1980a) reported on the treatment of 1,000 alcoholics with disulfiram. Seventy-six percent of these patients showed a satisfactory response at the end of 6 months. In another paper (1980b), these workers discussed the toxicity of this drug and concluded that it is a safe drug in a dosage of 250 mg/day.

Dhawale et al. (1980) tried disulfiram on 57 patients after giving them an initial challenge with this drug. Using an extensive evaluation scale, they reported a 50% improvement at the end of 6 months.

Khorana (1980) found a fair degree of improvement at the end of the 3d or 4th week in emotionally disturbed children treated with nitrazepam.

Bagadia et al. (1980) tried piracetam vs. placebo in a double-blind fashion in cases of cognitive deficiency resulting from electroconvulsive therapy (ECT). They did not find any statistical difference in the improvement recorded by the two groups.

Kulkarni and Mulay (1980) investigated the value of propanidid vs. thiopentone as an inducing agent in ECT and concluded that propanidid was a better agent because of its faster induction, earlier recovery, and shorter half-life. This would be particularly helpful in rendering better service at public hospitals.

Gada (1980) has reported on three cases of prolonged apnea with succinylcholine during ECT.

Vyavahare and Deo (1980) presented a case report of the value of carbamazepine in brain trauma.

Gautam et al. (1980) tried out an ayurvedic compound (Unmad Bhanjan Ras) in acute psychotic excitement (Vatanmada) in a double-blind fashion. They reported an 85% response recovery rate with the active drug vs. 15% with placebo.

Shah et al. (1980) have carried out a drug surveillance program in psychiatry, the first of its kind in India. They have examined the side effects of drugs, correlation of drug response with socio-demographic factors, clinical characteristics and pharmacological profile of the drug, mechanisms of side effects, and level of patient acceptance. In general, they reported a low incidence and intensity of side effects with the psychoactive drugs. Acceptance was good, and no correlations were found between side effects, socio-demographic factors, and clinical response.

Chakraborty et al. (1980) expressed concern about psychotropic drug use and called on psychiatrists to use minimally effective doses to avoid the danger of turning patients into drug addicts.

References

Bagadia, V.N., Gada, M.T., Mundra, V.K., et al. A double-blind trial of piracetam (VCB-6215) and placebo in cases of post-ECT cognitive deficiency. *J. Postgrad. Med.*, 26:116, 1980.

Chakraborty, A., Dutta, P., and Sandel, B. Psychoactive drugs—How much and how long? A guideline for OPD treatment. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Chaturvedi, M.K., Agrawal, P.K., Pareek, N.K., and Vyas, B.K. A comparative evaluation of dothiepin (Prothiaden) and imipramine. *Indian J. Psychiatry*, 22:124, 1980.

Deo, V.K., Kutkoti, M.J., and Nerlikar, P.N. Long-acting phenothiazines in chronic schizophrenics. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

DeSouza, A., and DeSouza, D.A. Disulfiram therapy in alcoholics. Paper read at the 11th Annual Conference of the Indian Psychiatric Society, West Zone, Mahableshwar, India, 1980a.

DeSouza, A., and DeSouza, D.A. Disulfiram toxicity. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980b.

DeSouza, A., and DeSouza, D.A. Weekly dose scheduling of injectable fluphenazine decanoate in chronic schizophrenics. Paper read at the 11th Annual Conference of the Indian Psychiatric Society, West Zone, Mahableshwar, India, 1980c.

Dhawale, K.M., Pradhan, P.V., Shah, L.P., and Bagadia, V.N. Evaluation of disulfiram in the treatment of alcoholism. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Gada, M.T. Prolonged apnoea with succinylcholine during electroconvulsive therapy. Paper read at the 11th Annual Conference of the Indian Psychiatric Society, West Zone, Mahableshwar, India, 1980.

Gautam, S., Sahu, A.K., and Swami, R.P. A double-blind trial of Unmad Bhanjan Ras in Vatomada. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Gurmeet Singh. Sintamil in the treatment of depression: A comparison of single vs. divided dose administration. *Indian J. Psychiatry*, 22:195, 1980.

Hariprasad, C.H., Nanda, P.K., and Das P.K. Is lithium hepatotoxic? Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Khandelwal, S.K., Khare, S.B., Chugh, K.S., and Srinivasmurthy, R. Renal functions following long-term lithium therapy. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Khorana, A.B. Nitrazepam in emotional disorders in children. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Kulkarni, M.R., and Mulay, V.P. Value of propanidid in electroconvulsive therapy (comparison with thiopentone). *Indian J. Psychiatry*, 22:371, 1980.

Lakdawala, P.D., Mundra, V.K., Desai, N.K., et al. Early experiences of Lithium Clinic. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Nataraj, G.S., and Bhat, V.K. A study of saliva: Serum lithium ratio in lithium-treated patients. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Quadri, A.A., Shalini, K., and Channabasavanna, S.M. d-Amphetamine as a predictor for response to imipramine and amitriptyline. *Indian J. Psychiatry*, 22:182, 1980.

Sampath, G., John, C.J., and Channabasavanna, S.M. Insight and lithium compliance. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Sampath, G., Sridhara Rama Rao, B.S., Channabasavanna, S.M., and Subash, M. Lithium neurotoxocity at "therapeutic" levels: A case report. *Indian J. Psychiatry*, 22:176, 1980.

Sampath, G., Vikram Kumar, Y., Narayanan, H.S., and Sridhara Rama Rao, B.S. Lithium neurotoxicity at "therapeutic" levels: A case report. *Indian J. Psychiatry*, 22:304, 1980.

Sethi, B.B., and Bhiman, A. Doxepin vs. imipramine and amitriptyline: Clinical efficacy and plasma level correlates. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Shah, L.P., Ayyar, K.S., Agarwal, B.R., Pradhan, P.V., Bagadia, V.N., Paul, T., Santhanam, M., and Sheth, U.K. Drug surveillance program in psychiatry in India. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Shah, V.D., Jain, L.K., Mehta, P.N., and Desai, S.P. An open clinical trial of penfluridol (R-16341), a long-acting neuroleptic in schizophrenia. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Sharma, S., and Hegde, R. Therapeutic efficacy of doxepin in divided and single-dose regime. *Indian J. Psychiatry*, 2:283, 1980.

Sharma, S., and Nandkumar, V.K. Double-blind clinical trial of trifluoperazine against trifluoperazine with trihexyphenidyl hydrochloride. Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Venkoba Rao, A., and Hariharasubramaniam, N. Electrocardiographic changes during lithium treatment. *Indian J. Psychiatry*, 22:135, 1980.

Venkoba Rao, A., Sugumar, A., Hariharasubramaniam, N., et al. Lithium and kidney (a study of renal biopsy in lithium patients). Paper read at the 33d Annual Conference of the Indian Psychiatric Society, Ahmedabad, India, 1980.

Vyavahare, P.N., and Deo, P.K. Brain trauma and carbamazepine (case report). Paper read at the 11th Annual Conference of the Indian Psychiatric Society, West Zone, Mahableshwar, India, 1980.

Adverse Drug Reactions—When Is an Adverse Drug Reaction Not an Adverse Drug Reaction?

Paul Leber, M.D.[1]

When is an adverse drug reaction (ADR) not an ADR? Why, when it's not due to drug, of course! When is it not due to drug? When it's due to something else! A child's riddle? Perhaps, but the questions asked are not uncommon ones in both clinical drug research and clinical practice.

The solution to the riddle may or may not be straightforward. When a treatment-emergent event is "characteristic," uncommon in the absence of drug, and occurs in the appropriate temporal relationship to drug administration (i.e., acute dystonia occurring in a young male shortly after beginning on haloperidol), the causal role of the drug seems reasonably established. Moreover, in some circumstances, dechallenge and rechallenge of the patient (if safe and ethical) may provide additional reasons to accept the link between drug administration and the untoward event as causal.

In many circumstances, however, it is not possible to distinguish between events caused by the drug and those contemporaneously associated with drug administration by chance alone. This is especially so when the event in question is a complaint by the patient about an internal subjective state (i.e., mood, feeling, sensation) neither objectively assessable nor readily understood as a predictable pharmacological consequence of the drug's action. Dizziness, headache, light-headedness, nausea, and dysphoric affects are all examples of this sort of alleged ADR. Moreover, when the untoward event may be a sign or symptom of the patient's underlying disorder or condition, the likelihood of making an accurate assessment of the etiology of the event is even more problematic.

It is common, however, to behave as though an event has a known specific cause. The assignment of an etiology to a specific event is often justified on the basis of "clinical judgment." Why clinical judgment should be accepted as a method to certify causality and how it differs from any other "post hoc, ergo propter hoc" argument is unclear. Reflection on the matter will reveal that for all its mystique, clinical judgment is little more than a hunch, an idiosyncratic sentiment. Admittedly, the sentiment (at least in the minds of "good clinicians") is probably close to an intuitively established, experientially based, conditional probability. In the setting of clinical practice, the hunch (read conditional probability estimate) takes the form of the argument that given event "A" there is a likelihood, P(D/A) that the event is caused by drug. What might be used to estimate this likelihood?

Logic alone allows one to argue that nondrug causes of untoward clinical events fall into two conceptually distinct catagories: 1) the pathogenic (i.e., those related to the condition or disease), and 2) the pathoplastic (i.e., those related to each patient's intrinsic characteristics).

If this hypothesis is true, the incidence of clinically observed adverse events will be a function not only of drug, but of both subject- and disease-related factors.

It is, of course, impossible to estimate the relative contributions drug, disease, and population characteristics make to the incidence of untoward clinical events in naturalistic clincial practice settings. Furthermore, criterion variance, observer variance (variability attributable to differences in observer sensitivity to phenomena near their clinical threshold, technique of elicitation of clinical data, etc.), occasion variance, and duration of observation interval all contribute to uncertainty about the overall event rate, let alone estimation of specific event rates.

---

[1] Food and Drug Administration, Rockville, MD 20857.

NOTE: The opinions expressed here are those of the author, and do not necessarily reflect the views or the policy of the Food and Drug Administration.

Placebo-controlled, double-blind clinical drug trials of parallel design with randomized assignment of subjects to treatment, therefore, offer an unusually valuable opportunity to estimate the drug and nondrug contributions to the incidence of untoward events. Further, when placebo-controlled trials are conducted using the same drug in different diseases or syndromes, comparison of incidence of events between clinical trials may offer some insight into the relative contributions of disease and subject characteristics to the overall event rate (i.e., a distinction between events of pathogenic and pathoplastic origin). As we shall see, however, such inferences must be highly qualified.

One problem in the estimation of adverse event incidence is the variation in event detection and enumeration which arises because of the lack of standardized criteria for the identification of the events themselves (i.e., criterion variance). While one observer's "acute dystonia" is likely to be another's, less concurrence may be expected if "agitation" is the event in question. To some degree, criterion variance can be reduced by employing operational definitions and training raters to the criterion. Clearly, in contrast to clinical practice, this can be done in controlled multicenter clinical trials and, therefore, makes such trials a relatively reliable source of untoward event incidence data. Nevertheless, standardized criteria are only useful for relatively common and previously recognized phenomena. If new or novel untoward events emerge for the first time during trials with a new drug, prospective measures to reduce criterion variance are not possible. Post hoc adjustments of terminology, in cooperation with participating investigators, can be made, however, and may prove helpful. For example, combining several like phenomena under a single heading will reduce the number of distinct adverse events and contribute to the systematic organization and display of the drug's adverse event profile.

Events must also be described in terms of their severity. Again, the excessive criterion and observer variances, characteristic of spontaneous reports from naturalistic sources, may be reduced in large multicenter studies through the use of carefully written protocols and co-training of investigators.

Accurate estimation of adverse event incidence also requires standardized calculation. Defining incidence as the number of individuals experiencing the event divided by the number of individuals exposed seems most consistent with usual statistical practice.

Another problem is the need to account for event duration in event incidence tabulations. To some extent, severity ratings can reflect duration. For example, two headaches of identical intensity but lasting for 1 hour and 3 days, respectively, can be given differential severity gradings. This approach, however, seems somewhat unsatisfactory for it confounds duration and intensity.

While not yet in general use, life table or survivor function methodologies could be applied to this problem. For example, for a given adverse event, it is possible to construct a function which describes the likelihood of experiencing the event (adjusted for dose level or cumulative exposure) as a function of duration of exposure. For the moment, however, it would seem most critical to avoid combining adverse event incidence data obtained from studies of differing duration. While not explicitly stated, incidence figures always imply incidence during a period of specified duration. This point is often overlooked. Indeed, the author has seen instances in which unadjusted incidence figures from clinical trials of different duration have been unwittingly combined.

This brings the author to a major point. The rules for combining adverse event data obtained in clinical trials are essentially those same rules for combining efficacy data. Pooling of data should only be attempted for trials of the same design and duration into which patient samples drawn from the same population have been entered. If event incidence is a function of the disease under treatment (and the author believes that it often is), then it may be misleading to pool data obtained from clinical studies using the same drug in different diseases. Parenthetically, this point is subject to experimental verification.

Again, standard statistical applications of these principles to adverse data analysis are not widely disseminated, but it is theoretically possible to test the appropriateness of pooling adverse event data (i.e., estimate incidence vs. investigator interactions, etc.).

If these points are adhered to, it is possible to arrive at incidence figures for a spectrum of relatively common adverse events reported by or observed in patients participating in placebo-controlled trials. The proportion of subjects experiencing the event on drug and placebo can then be compared. Placebo incidence figures can be used to estimate the spontaneous rate of the event in the population.

This approach was attempted recently in the drafting of the professional product label for a new benzodiazepine anxiolytic drug product, alprazolam (Xanax©, Upjohn, 1981). Both the Food and Drug Administration (FDA) and Upjohn Pharmaceuticals were interested in reporting, in the most accurate manner possible, the "real" incidence of adverse events observed with the drug. Everyone involved in the joint effort recognized that the absolute rate of adverse events is often meaningless. Even when using identical protocols, two "trained" investigators may still detect adverse events at quite dissimilar rates. Our intent was, therefore, not to generate incidence figures for comparison with other drug products, but simply to present the incidence data in the most meaningful way possible.

Consideration was given to the possibility of presenting corrected incidence figures arrived at by either 1) subtracting the placebo incidence rate from the drug incidence rate, or 2) calculating the ratio of the drug incidence to placebo incidence. Both possibilities were rejected because they discarded valuable information. Clearly, it is more meaningful to know that an event was observed 30% of the time among drug recipients and 25% of the time among placebo recipients than it is to learn that the "corrected" incidence is 5% or the "relative incidence" ratio is 1.2.

The final tabulation of adverse events in the alprazolam (Xanax©) label was restricted to those which occurred at a frequency of greater than 1%. The choice of this cutoff point was arbitrary, but it did take into consideration the generally accepted view that typical new drug clinical trials enrolling 500 to 1,000 subjects are unlikely to be reliable at detecting events which occur with a frequency below 5% or so. For example, it is estimated that, in order to be 95% certain of detecting at least one example of a class of events which occur at a true frequency of 1% in the population, at least 300 subjects must be enrolled (Sackett, Haynes, Gent, & Taylor, 1980). It is thus very difficult to get enough events to observe statistically significant differences between drug and placebo rates when absolute rates are low.

As discussed earlier, it is exceedingly difficult to compare adverse reaction severity assessments among investigators. The Xanax© labeling attempts to give some basis for comparative judgment by presenting the incidence of intervention required because of adverse events among drug recipients. (A similar tabulation for placebo was not presented, mainly to avoid further complexity in the labeling.)

It is of interest that the alprazolam vs. placebo incidence figures reveal that it is possible to begin to identify when an ADR is not an ADR.

Whereas drowsiness (a pharmacologically predictable event) among alprazolam recipients was observed at a rate approximately double that of placebo recipients, other observed "traditional" ADRs are subject to different interpretations. For example, light-headedness, confusion, dry mouth, constipation, diarrhea, blurred vision, and weight gain were observed at essentially similar rates in both treatment groups. Depression, headache, insomnia, nervousness, and palpitations occurred at lower frequency among alprazolam-treated subjects. Thus, not only do the ADR incidence figures illustrate the epiphenomena of anxiety, but the comparative incidence figures support the anxiolytic efficacy of alprazolam.

It will be of considerable interest to examine the ADR rates for alprazolam and placebo when and if its efficacy is evaluated in conditions other than anxiety. This may permit some distinction between events commonly reported by subjects in any drug study (pathoplastic phenomena) and those which are more rationally explained as epiphenomena of the condition under treatment (pathogenic phenomena).

Before closing, however, it is critical to emphasize that, at best, untoward event incidence figures are imprecise estimators of true ADR rates. This should be borne in mind when one must assess the claims of commercial sponsors about the relative incidence of ADRs observed with their product and its competitors. Even among studies involving only a single active drug and placebo, it is virtually impossible to decipher the meaning of rates reported from clinical studies conducted by different investigators, in different patient samples, receiving different amounts of drug in different environmental settings in different historical epochs. Comparisons among two active drug products are even more complicated because, in order to be useful, they must compare patient samples receiving therapeutically equivalent dosages of drug. In short, comparisons of ADR incidence, even if based on data obtained from "poolable" clinical studies of similar design and execution, require cautious interpretation.

References

Sackett, D.L., Haynes, R.B., Gent, M., and Taylor, D.W. Compliance. Chapter 35. In: Inman, W.H.W. (ed.), *Monitoring for drug Safety*. Lancester, England: MTP Press Ltd., 1980.

Xanax® Package Insert, The Upjohn Company, Kalamazoo, Michigan, August 1981.

Brief Reports and Reviews—

The Brief Psychiatric Rating Scale for Children[1]

John E. Overall, Ph.D.,[2] and Betty Pfefferbaum, M.D.[2]

Introduction

The Brief Psychiatric Rating Scale for Children (BPRS-C) has been developed to provide a parsimonious description of childhood emotional and behavioral disorders. Beginning with an extended description of the symptom and behavior characteristics associated with some 18 Diagnostic and Statistical Manual-III (DSM-III) categories, the methodology of factor analysis was used to identify clusters of symptoms that define major independent dimensions of difference among the diagnostic groups. Whereas the DSM-III includes specific, and sometimes rather arbitrary, criteria for a large number of childhood diagnoses, it is important to recognize that a relatively few major symptom and behavior dimensions separate those more numerous diagnostic groups. The BPRS-C is designed to characterize individual patients, and to evaluate treatment responses, in terms that are relevant for a variety of different diagnostic classifications. Thus, the multidimensional BPRS-C is considered appropriate for description of major differences among child and adolescent patients and for characterizing such patients according to major syndrome groupings, as well as for the evaluation of treatment responses in longitudinal research designs.

Factor Analysis

In the factor analysis that provided the basis for development of the BPRS-C, the original data consisted of descriptions of hypothetical typical patients in some 18 diagnostic groups recorded on the 63-item Children's Psychiatric Rating Scale (CPRS) (Guy, 1974) by five experienced child and adolescent psychiatrists. The 18 diagnostic groups were selected from the DSM-III in an attempt to represent the range of clinical conditions most likely to be seen in the practice of child psychiatry. The five judges were asked to record what they considered from personal clinical experience to be the most likely level of symptom severity for typical patients in each of the 18 diagnostic groups. This produced 5 × 18 = 90 symptom and behavior rating-scale profiles representing a range of different types of childhood disorders. It is relevant to note that the CPRS rating scale on which the diagnostic stereotypes were recorded antedates the newly revised DSM-III, and that it includes symptom and behavior manifestations that span a broad domain of childhood psychopathology. The factors resulting from the analysis are thus conceived to be primary dimensions of symptom and behavior manifestations useful for describing differences among childhood psychiatric disorders in terms other than the specific diagnostic criteria of the DSM-III.

Intercorrelations among the 63 CPRS symptom variables across the 5 × 18 = 90 diagnostic profiles provided by the five expert judges were first factor-analyzed by a cluster-oriented powered vector method (Overall & Porterfield, 1962) to identify seven relatively independent variables which represent distinct domains in the symptom measurement space. An oblique marker variable factor analysis (Overall, 1974) was then accomplished, starting with marker variables identified in the preliminary orthogonal powered vector factor analysis. This resulted in a good oblique simple structure in which most of the 63 variables projected substantially on only one of the seven oblique reference axes. The results from this factor analysis have been reported in some detail elsewhere (Pfefferbaum & Overall, 1981).

---

[1] This work was supported in part by USPHS Grant MH-32457-02.

[2] The University of Texas Medical School, Houston, TX 77025.

Requests for reprints should be addressed to: Dr. John E. Overall, Department of Psychiatry and Behavioral Sciences, The University of Texas Medical School, P.O. Box 20708, Houston, TX 77025.

The BPRS-C includes three key variables to represent each of the seven empirically-identified factors. Care was exercised to avoid logical redundancies in the selection of symptom variables associated with each factor. That is, the several variables that projected primarily on each factor were inspected, and three variables were chosen for incorporation into the BPRS-C that appear to represent conceptually distinct manifestations of psychopathology that should be susceptible of separate evaluation even though they relate to a single primary factor in the larger symptom domain. In some cases, highly related symptom variables were combined into a single new rating construct for inclusion into the BPRS-C. Each of the seven empirically identified factors is thus represented by three conceptually distinct symptom constructs which appear in consecutive sequence in the BPRS-C format. A facsimili of the 21-item BPRS-C is presented in Figure 1.

BRIEF PSYCHIATRIC RATING SCALE FOR CHILDREN (BPRS-C)

Patient ______________________________

Rater ______________________________

Date ______________________________

	Not Present	Very Mild	Mild	Moderate	Mod. Severe	Severe	Extremely Severe
1. **Uncooperativeness** - negative, uncooperative, resistant, difficult to manage.	☐	☐	☐	☐	☐	☐	☐
2. **Hostility** - angry or suspicious affect, belligerence, accusations and verbal condemnations of others.	☐	☐	☐	☐	☐	☐	☐
3. **Manipulativeness** - lying, cheating, exploitive of others.	☐	☐	☐	☐	☐	☐	☐
4. **Depressive Mood** - sad, tearful, depressive demeanor.	☐	☐	☐	☐	☐	☐	☐
5. **Feelings of Inferiority** - lacking self-confidence, self-depreciatory, feeling of personal inadequacy.	☐	☐	☐	☐	☐	☐	☐
6. **Suicidal Ideation** - thoughts, threats, or attempts of suicide.	☐	☐	☐	☐	☐	☐	☐
7. **Peculiar Fantasies** - recurrent, odd, unusual, or autistic ideations	☐	☐	☐	☐	☐	☐	☐
8. **Delusions** - ideas of reference, persecutory or grandiose delusions.	☐	☐	☐	☐	☐	☐	☐
9. **Hallucinations** - visual, auditory, or other hallucinatory experiences or perceptions.	☐	☐	☐	☐	☐	☐	☐
10. **Hyperactivity** - excessive energy expenditure, frequent changes in posture, perpetual motion.	☐	☐	☐	☐	☐	☐	☐
11. **Distractibility** - poor concentration, shortened attention span, reactivity to peripheral stimuli.	☐	☐	☐	☐	☐	☐	☐
12. **Speech or Voice Pressure** - loud, excessive, or pressured speech.	☐	☐	☐	☐	☐	☐	☐
13. **Underproductive Speech** - minimal, sparse inhibited verbal response pattern, or weak low voice.	☐	☐	☐	☐	☐	☐	☐
14. **Emotional Withdrawal** - unspontaneous relations to examiner, lack of peer interaction, hypoactivity.	☐	☐	☐	☐	☐	☐	☐
15. **Blunted Affect** - deficient emotional expression, blankness, flatness of affect.	☐	☐	☐	☐	☐	☐	☐
16. **Tension** - nervousness, fidgetiness, nervous movements of hands or feet.	☐	☐	☐	☐	☐	☐	☐
17. **Anxiety** - clinging behavior, separation anxiety, preoccupation with anxiety topics, fears or phobias.	☐	☐	☐	☐	☐	☐	☐
18. **Sleep Difficulties** - inability to fall asleep, intermittant awakening, shortened sleep time.	☐	☐	☐	☐	☐	☐	☐
19. **Disorientation** - confusion over persons, places or things.	☐	☐	☐	☐	☐	☐	☐
20. **Speech Deviance** - inferior level of speech development, underdeveloped vocabulary, mispronunciations.	☐	☐	☐	☐	☐	☐	☐
21. **Stereotypy** - rhythmic, repetitive, manneristic movements or posture.	☐	☐	☐	☐	☐	☐	☐

© 1981 Overall and Pfefferbaum

FIGURE 1

Factor Scoring of the BPRS-C

The 21 symptoms of the BPRS-C are rated for severity on 7-point scales ranging from "not present" to "extremely severe." The items are grouped into subsets of three to form a basis for the scoring of the composite factors which are conceived to represent the major ways in which one type of childhood disorder differs from another. Factor scores are calculated by summing the ratings on the successive subsets of three consecutive scales. This consecutive grouping of items representing each factor was chosen, not only to facilitate factor scoring, but to provide for considered comparison of the relative levels of severity of closely related symptoms. Although the symptoms within each group of three relate to the same factor, it is important to recognize that they may differ in severity in individual patients. Such differences are easier to consider when the symptom constructs are adjacent in the rating scale format. Each symptom should be rated separately, with severity in relation to associated symptoms considered carefully.

The breadth of the domain of psychopathology spanned by the BPRS-C suggests that not all factors are relevant for description of each type of patient. The seven major factor constructs and the symptom rating variables that are combined to define the associated factor scores are presented on the left-hand side of the Table. The DSM-III childhood diagnoses for which each major factor is considered to be particularly relevant are listed on the right. These diagnostic relevances were identified empirically from factor score profiles in the original 63-item data set that was analyzed to define the seven factors.

Table

Factor Scoring of the Brief Psychiatric Rating Scale for Children and the Childhood Psychiatric Diagnoses in Which Each Factor Is Represented

Factors	Diagnoses
I. *Behavior Problems* Uncooperativeness Hostility Manipulativeness	Conduct Disorders (all types) Attention Deficit Disorders Oppositional Disorders Pervasive Developmental Disorder Infantile Autism Schizophrenic Disorder Major Depression
II. *Depression* Depressive Mood Feelings of Inferiority Suicidal Ideation	Major Depression Agitated Depression Retarded Depression Depression (other)
III. *Thinking Disturbance* Peculiar Fantasies Delusions Hallucinations	Pervasive Developmental Disorder Infantile Autism Schizophrenic Disorder
IV. *Psychomotor Excitation* Hyperactivity Distractibility Speech or Voice Pressure	Attention Deficit Disorder Pervasive Developmental Disorder Infantile Autism Schizophrenic Disorder Agitated Depression
V. *Withdrawal Retardation* Underproductive Speech Emotional Withdrawal Blunted Affect	Avoidant Disorder Schizoid Disorder Elective Mutism Retarded Depression
VI. *Anxiety* Tension Anxiety Sleep Difficulties	Separation Anxiety Overanxious Disorder Identity Disorder Anorexia Nervosa Agitated/Anxious Depression
VII. *Organicity* Disorientation Speech Deviance Stereotypy	Traumatic Brain Injury Organic Brain Disorder (other) Infantile Autism Pervasive Developmental Disorder Schizophrenic Disorder

Brief Psychiatric History for Children

For both research and clinical purposes, it is useful to have selected history and demographic information recorded in a standard format. The relevant background data in the case of children with emotional and behavioral problems include demographic characteristics of the family as well as the child. In our own research, the background data form shown in Figure 2 is used to ensure the systematic recording of at least these minimum items of background information. The Brief Psychiatric History for Children (BPH-C) is printed on the reverse side of the BPRS-C for convenience in use. As the data base grows, numerous interesting questions concerning the relationships of manifest psychopathology in children to background characteristics and family context can be answered. For comparative purposes, it may be useful to have similar information collected in different settings.

It will be noted that a section has been included for recording a tentative DSM-III diagnosis. Although a diagnosis made on the basis of brief contact with the child and parents is at best tentative, such a diagnostic impression is another way of characterizing or describing the patient. The fact that the symptom description recorded on the BPRS-C is not intended to be sufficient for diagnosis is emphasized. In children, as in adults, symptom descriptive classification and diagnosis are two different things. Examination of the phenomenological heterogeneity within major diagnostic categories may lead to eventual refinement of diagnostic concepts. The relationships between manifest psychopathology in children and DSM-III diagnosis should in fact be an interesting focus of future research with the BPRS-C.

Interviews with Parent and Child

The interviews used to obtain information necessary for completing the BPH-C and the BPRS-C rely heavily on the interviewing skills of the experienced clinician, who may be a child psychiatrist, child clinical psychologist, or other mental health professional with training and experience in working with children. The interviewer will be described as a psychiatrist in this discussion simply to avoid redundancy in reciting a list of qualified professionals.

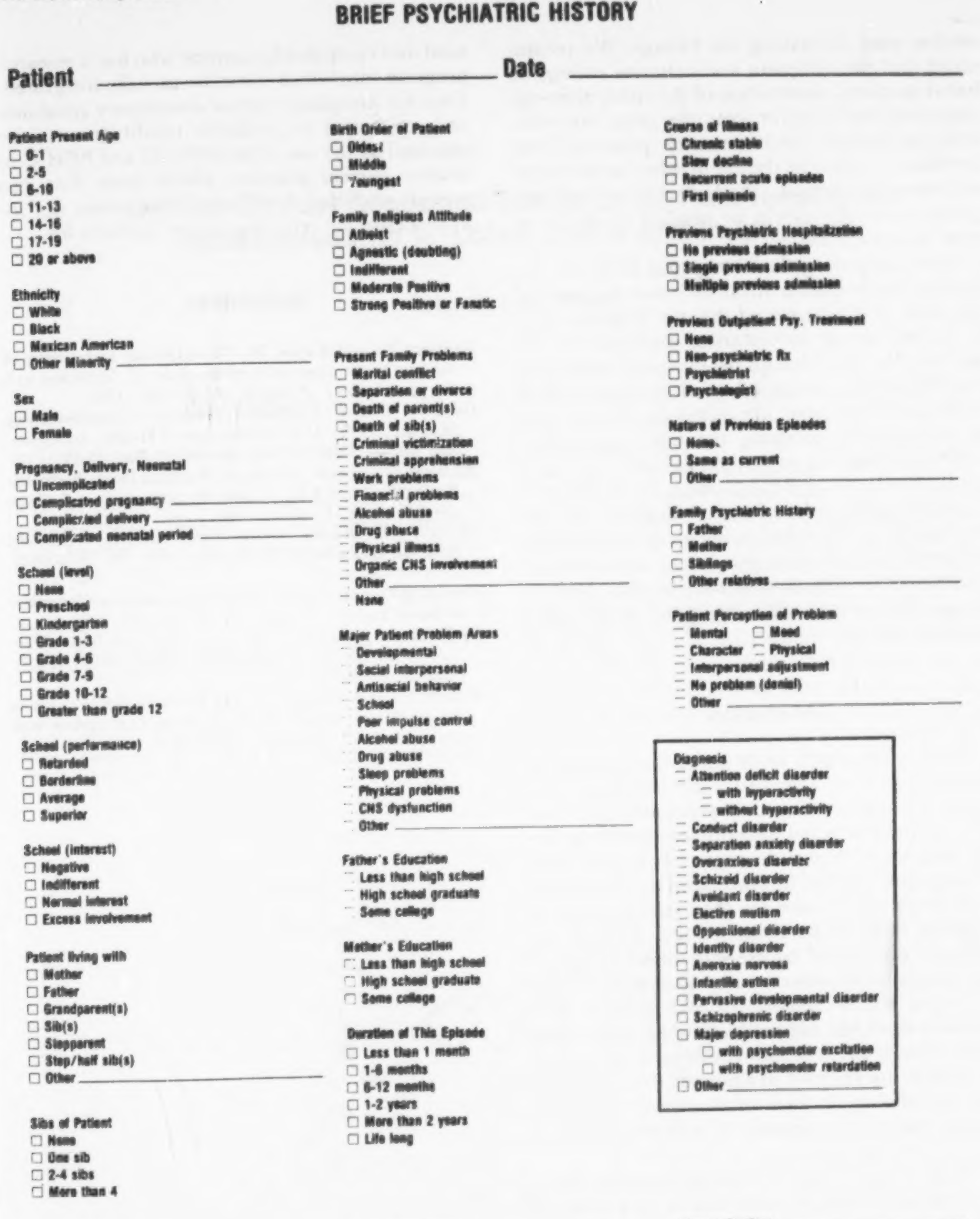
An individualized style which allows the interviewer to maximize rapport is considered most important. Clinical skills unique to the individual can be capitalized on in a flexible semi structured interview. Nevertheless, a format that may help to eliminate extreme variation in the mode of data acquisition will be proposed here. It should allow ample opportunity for assessment in a reasonably short period of time. The use of such flexible, semistructured interviews has been documented to produce adequate reliability and validity in the assessment of children (Graham & Rutter, 1968; Rutter & Graham, 1968) as well as adults (Hedlund & Vieweg, 1980).

An interview with one or both parents, or a guardian, is required. The interviewer is encouraged to begin with open-ended questions regarding the child's presenting emotional and/or behavioral problems. Each identified problem is covered in depth with specific regard to onset, duration, and severity of symptoms. Once each problem has been discussed, a more structured format is used to obtain information for the BPH-C and the various symptoms to be rated on the BPRS-C. Specific queries should relate to activity level, attention span, speech development and possible abnormalities, emotional relationships, mood, suicidal ideation, self-concept, tension or anxiety, vegetative symptoms, fantasies, and delusions or hallucinations. A medication history should also be obtained in the interview with the parent. This interview can usually be completed in 35 minutes.

The interview with the child includes an assessment of the child's perception of his problems and an age appropriate mental status examination. As with the parent interview, this interview begins in an unstructured format allowing the interviewer to establish rapport and observe the child's behavior. Play or other modes of relating may be used depending on the child's age and condition. In the unstructured portion of the interview, the clinician can pay particular attention to activity level, attention span, peculiar mannerisms, speech production and abnormalities, manner of relating, mood, affect, self-concept, preoccupations, tension or anxiety, and delusional thinking or hallucinations that are spontaneously manifest.

During the structured portion of the examination, specific tasks may be assigned to the child in order to ascertain the child's developmental level, attention span, and ability to accept direction. Specific questions regarding friendships, school progress, mood, suicidal ideation, preoccupations, fears, fantasies, and unusual experiences or perceptions should be asked. The nature and severity of any positive findings should be explored in detail.

Since the BPRS-C is intended for research use, it is important to standardize the source of infor-



BRIEF PSYCHIATRIC HISTORY

Patient ______________________ Date ______________________

Patient Present Age
☐ 0-1
☐ 2-5
☐ 6-10
☐ 11-13
☐ 14-16
☐ 17-19
☐ 20 or above

Ethnicity
☐ White
☐ Black
☐ Mexican American
☐ Other Minority ______________

Sex
☐ Male
☐ Female

Pregnancy, Delivery, Neonatal
☐ Uncomplicated
☐ Complicated pregnancy ______________
☐ Complicated delivery ______________
☐ Complicated neonatal period ______________

School (level)
☐ None
☐ Preschool
☐ Kindergarten
☐ Grade 1-3
☐ Grade 4-6
☐ Grade 7-9
☐ Grade 10-12
☐ Greater than grade 12

School (performance)
☐ Retarded
☐ Borderline
☐ Average
☐ Superior

School (interest)
☐ Negative
☐ Indifferent
☐ Normal interest
☐ Excess involvement

Patient living with
☐ Mother
☐ Father
☐ Grandparent(s)
☐ Sib(s)
☐ Stepparent
☐ Step/half sib(s)
☐ Other ______________

Sibs of Patient
☐ None
☐ One sib
☐ 2-4 sibs
☐ More than 4

Birth Order of Patient
☐ Oldest
☐ Middle
☐ Youngest

Family Religious Attitude
☐ Atheist
☐ Agnostic (doubting)
☐ Indifferent
☐ Moderate Positive
☐ Strong Positive or Fanatic

Present Family Problems
☐ Marital conflict
☐ Separation or divorce
☐ Death of parent(s)
☐ Death of sib(s)
☐ Criminal victimization
☐ Criminal apprehension
☐ Work problems
☐ Financial problems
☐ Alcohol abuse
☐ Drug abuse
☐ Physical illness
☐ Organic CNS involvement
☐ Other ______________
☐ None

Major Patient Problem Areas
☐ Developmental
☐ Social interpersonal
☐ Antisocial behavior
☐ School
☐ Poor impulse control
☐ Alcohol abuse
☐ Drug abuse
☐ Sleep problems
☐ Physical problems
☐ CNS dysfunction
☐ Other ______________

Father's Education
☐ Less than high school
☐ High school graduate
☐ Some college

Mother's Education
☐ Less than high school
☐ High school graduate
☐ Some college

Duration of This Episode
☐ Less than 1 month
☐ 1-6 months
☐ 6-12 months
☐ 1-2 years
☐ More than 2 years
☐ Life long

Course of Illness
☐ Chronic stable
☐ Slow decline
☐ Recurrent acute episodes
☐ First episode

Previous Psychiatric Hospitalization
☐ No previous admission
☐ Single previous admission
☐ Multiple previous admission

Previous Outpatient Psy. Treatment
☐ None
☐ Non-psychiatric Rx
☐ Psychiatrist
☐ Psychologist

Nature of Previous Episodes
☐ None.
☐ Same as current
☐ Other ______________

Family Psychiatric History
☐ Father
☐ Mother
☐ Siblings
☐ Other relatives ______________

Patient Perception of Problem
☐ Mental ☐ Mood
☐ Character ☐ Physical
☐ Interpersonal adjustment
☐ No problem (denial)
☐ Other ______________

Diagnosis
☐ Attention deficit disorder
  ☐ with hyperactivity
  ☐ without hyperactivity
☐ Conduct disorder
☐ Separation anxiety disorder
☐ Overanxious disorder
☐ Schizoid disorder
☐ Avoidant disorder
☐ Elective mutism
☐ Oppositional disorder
☐ Identity disorder
☐ Anorexia nervosa
☐ Infantile autism
☐ Pervasive developmental disorder
☐ Schizophrenic disorder
☐ Major depression
  ☐ with psychomotor excitation
  ☐ with psychomotor retardation
☐ Other ______________

Past medications ______________

Current medications ______________

New medications ______________

Figure 2

mation used in making the ratings. We recommend that the symptom and behavior ratings be based on direct observation of the child, although important leads derive from the prior interview with the parent. Some research protocols may specifically authorize the use of information derived from other sources; however, in general, the psychopathology should be verified in the interview with the child.

After completing the history and BPRS-C, the psychiatrist is asked to make an initial diagnosis of the child. It is understood that the diagnosis may be based on all information available to the psychiatrist, even though the symptom ratings on the BPRS-C are restricted to information verified in the child interview. The initial diagnosis should be recorded by checking the most appropriate DSM-III diagnosis in the box at the lower right-hand corner of the BPH-C form. In addition to providing past and current medication use, the psychiatrist is also asked to list medications which he intends to start after this initial assessment. If he decides to discontinue any current medications, that should also be noted under new medications.

Conclusion

Much work needs to be done to establish the BPRS-C as a reliable and valid instrument for characterizing childhood psychopathology. We believe that the initial development based on factor analyses of ratings descriptive of a wide range of diagnostic entities has produced an instrument with desirable balance for the representation of different types of psychopathology. Because the BPRS-C is intended for use with different types of patients, it is not expected that all symptoms and behaviors will be present in each patient. Preliminary work has suggested, however, that some of the symptoms, and their combinations into factor scores, are relevant in assessing the severity of psychopathology in each of the major diagnostic groups that were considered in development of the instrument.

Because appropriate evaluation of a new assessment device is best accomplished in the context of ongoing research, we have chosen to present the BPRS-C at this time so that it can be considered in the public domain — an instrument that can be used and evaluated by anyone who has a research program into which it can be usefully integrated. Data for assessing internal consistency reliability and concurrent or predictive validity can also be obtained by the use of the BPRS-C and BPH-C in routine clinical practice, where those data can provide standard descriptive information not inappropriate for retention in the patient's file.

References

Graham, P., and Rutter, M. The reliability and validity of the psychiatric assessment of the child. II. Interview with the parent. *Br. J. Psychiatry*, 114:581-592, 1968.

Guy, W. *ECDEU Assessment Manual for Psychopharmacology* (Revised, 1976). U.S. Department of Health, Education, and Welfare, DHEW Publication No. (ADM) 76-338, 1976.

Hedlund, J.L., and Vieweg, B.W. The Brief Psychiatric Rating Scale (BPRS): A comprehensive review. *J. Operational Psychiatry*, 11:48-65, 1980.

Overall, J.E. Marker variable factor analysis: A regional principal axes solution. *Multivariate Behav. Res.*, 9:407-422, 1974.

Overall, J.E., and Porterfield, J. The powered vector method of factor analysis. *Psychometrika*, 28:415-422, 1963.

Pfefferbaum, B., and Overall, J.E. Diagnostic factor structure of the Children's Psychiatric Rating Scale (CPRS). (Submitted, 1981)

Rutter, M. and Graham, P. The reliability and validity of the psychiatric assessment of the child. I. Interview with the child. *Br. J. Psychiatry*, 114:563-579, 1968.

Vol. 18, No. 2, April 1982

On the Clinical Response/Serum Level Relationship for Antidepressants II: Lofepramine and Imipramine

John E. Dutt, Ph.D.[1]

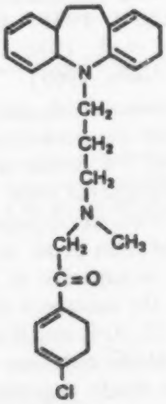
Introduction

In a recent paper by the author (Dutt, 1981), five clinical studies involving amitriptyline (A) and its main metabolite nortriptyline (N) were retrospectively evaluated. In that report, attention was focused on three subgroups of responders, since they tended to be more homogeneous than the full study population. The three groups of responders were:

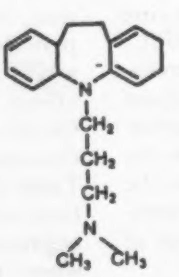
1) *ALL* responders—Defined as at least a 40% reduction in Hamilton Depression Scale (%Ham– =l≥40%) scores and a final Ham-D score of 16 or less.
2) Responders for which nortriptyline levels were higher than amitriptyline levels.
3) Responders for which amitriptyline levels were higher than nortriptyline levels.

In the responder groups, there was a pattern of higher correlations between clinical response and steady-state serum level parameters involving both amitriptyline and its metabolite nortriptyline.

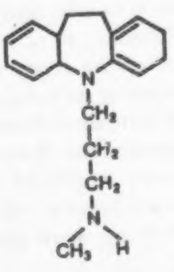
The focus of this paper is on two tricyclic antidepressants, imipramine and lofepramine (Eriksoo & Rohte, 1970; Ply n Forshell, Siwers, & Tuck, 1976; Siwers, Freyschuss, Hamberger, et al., 1970). These compounds have structures similar to desmethylimipramine (DMI), the main metabolite of each drug. The chemical structures of all three compounds are shown below:



Lofepramine



Imipramine



Desipramine

---

[1] E.M. Laboratories, Inc. (Associate of E. Merck, Darmstadt, Germany), Hawthorne, NY 10532.

Three studies are re-evaluated here—the studies of Gram, Reisby, Ibsen, et al. (1976) and Olivier-Martin, Marzin, Buschsenschutz, et al. (1975) involving imipramine alone, and the double-blind study of D'Elia, Borg, Hermann, et al. (1977) and Siwers, Borg, D'Elia, et al. (1977) comparing lofepramine and imipramine. Individual patient data from a fourth study, the Glassman, Perel, Shostak, et al. (1977) study of imipramine, were unavailable.

In comparing data from different studies, it is essential that there be comparable inclusion criteria, comparable operational definitions of clinical response, uniform handling of data, and a population that can, in fact, respond to the drug (Dutt, 1981; Feighner, Robins, Guze, et al., 1972). Clinical response, which is operationally defined as percent reduction of total depression score from pretreatment to the appropriate posttreatment period, is identified by either percent reduction in Ham-D (Hamilton, 1960) or percent reduction in Cronholm-Ottosson Depression Scale (CODS) (Cronholm & Ottosson, 1960). Depending on the availability of data in each study, the clinical response/steady-state serum level relationship was examined for those most frequently encountered parameters—parent drug (lofepramine or imipramine), the metabolite desmethylimipramine (DMI), metabolite to parent drug ratio (DMI/parent drug), and total serum level (DMI + parent drug).

Additionally, in the double-blind study (D'Elia et al., 1977; Siwers et al., 1977) of imipramine and lofepramine, relationships involving percent norepinephrine (NE) reuptake inhibition after treatment were examined. This latter parameter, which relates to the role of NE as a neurotransmitter in central monoamine nerve terminals, has been found to correlate well in in vivo and in vitro studies with DMI (Plym Forshell, et al., 1976).

The lack of homogeneity of the study populations is again handled by focusing on subgroups of responders, since they tend to be more homogeneous than the full study population. Because responders are used, however, it should not be assumed that significant correlations will inevitably be obtained. The following three groups of responders are considered:

1) *ALL* responders—Defined as at least a 40% reduction in Hamilton Depression Scale (%Ham-D$\downarrow \geq 40\%$) scores and a final Ham-D score of 16 or less, or a 40% reduction or more in the CODS scores and a final CODS score of 7 or less.
2) Responders for which the percent of DMI to the parent drug is greater than or equal to 1.
3) Responders for which the percent of DMI to the parent drug is less than 1.

The data are further treated uniformly across studies by imposing the intake criteria of either Ham-D equal or greater to than 18 or CODS equal or greater than 12, and by employing identical statistical methods.

Method

Four studies with adequate sample sizes examined the relationship of clinical response/serum level in patients treated with imipramine for primary depression. These are the studies of Glassman et al. (1977), Gram et al. (1976), Olivier-Martin et al. (1975), and Siwers et al. (1977), which are summarized (Sets 1-4) along with the lofepramine part of the Siwers et al. double-blind study (D'Elia et al., 1977; Siwers et al., 1977) (Set 5). Two desipramine studies (Friedel, Veith, Bloom, & Bielski, 1979; Khalid, Amin, & Ban, 1978) (Sets 6 and 7) are included in Table 1 for discussion purposes. In addition to the Glassman et al. study (1977), there are several other imipramine studies with either insufficient or unavailable data (Malitz & Kanzler, 1969; Moody, Tait, & Todrick, 1967; Muscettola, Goodwin, Potter, et al., 1978; Nagy & Treiber, 1973; Sathananthan, Gershon, Almeida, et al., 1976; Walter, 1971; Watt, Crammer, & Elkes, 1969).

In the four study sets (Nos. 2-5) under evaluation, both in- and outpatients were treated for periods of 3-6 weeks with a fixed dosage except where reductions were necessary because of side effects. With the exception of a subgroup in the Olivier-Martin et al. study (1975), the reported outcome is negative in all four sets. As noted in Table 2, the numbers of nonresponder/nonqualifiers are 12, 9, 6, and 8 in Sets 2-5, respectively. A negative study outcome seems assured, therefore, when the study population contains proportionately large numbers of nonresponder/nonqualifiers. A similar observation was noted with amitriptyline studies (Dutt, 1981).

Table 1

Summary of Significant Results from Seven Study Sets

Study Sets	*N*	Sample (In/Out Pts)	Treatment Period	Efficacy Parameter	Serum Level Parameters[1] Parent	DMI	Parent + DMI	Time of Signif.
1. Imipramine (Glassman et al.)	60	Full In	4 wks	Global (Wk 4)	—	—	Sig[2]	Wk 4
		42[3] In			—	—	0.48**	Wk 4
2. Imipramine (Gram et al.)	24	In	4-5 wks	Tot Ham-D[4] (Endpoint)	—	—	N.S.	Endpoint
3. Imipramine (Olivier-Martin et al.)	24	Full In	3 wks	%Ham-DI (Wk 3)	N.S.	N.S.	—	Wk 3
		11[7] In			N.S.	0.70*	Sig[2]	Wk 3
4. Imipramine (Siwers et al.)	19	In/Out	3-5 wks	CODS[5] Amelior. (Wk 3)	—	N.S.	—	Wk 3
					Additional Findings[6] at Wk 3			
					%NE+ vs. DMI $(r = 0.86^{***})$			
					%NE+ vs. %CODS+ (N.S.)			
5. Lofepramine (Siwers et al.)	20	In/Out	3-5 wks	CODS Amelior. (Wk 3)	N.S.	N.S.	N.S.	Wk. 3
					Additional Findings[6] at Wk 3			
					%NE+ vs. DMI $(r = 0.82^{***})$			
					%NE+ vs. %CODS+ (N.S.)			
6. Desipramine (Friedel et al.)	25	Out	3 wks	Tot Ham-D (Wk 3)	/	−0.365*	/	Wk 3
7. Desipramine (Khalid et al.)	20	Out	6 wks	Ham-D Amelior. (Wk 4)	/	0.57* ($N = 15$)	/	Wk 4
				(Wk 6)	/	N.S. ($N = 10$)	/	Wk 5

---

[1] Little or no attention was given to ratios, either D/I or D/L.

[2] Exact figures were not reported.

[3] Significant global response/I + DMI relationships were also found for unipolar nondelusional depressives ($r = 0.436^{*}$, $N = 30$) and bipolar depressives ($r = 0.882^{*}$, $N = 12$).

[4] Total Ham-D was reported to be well correlated with %Ham-D.

[5] Cronholm-Ottosson Depression Scale (CODS).

[6] %NE = % norepinephrine (NE) reuptake inhibition from Week 0.

[7] Endogenous depressives who did not receive concomitant medication.

*, **, and *** denote significance at $p <$ .05, .01, and .001 levels, respectively.

Table 2

Responder/Nonresponder Numbers in Relation to Intake Depression Score and Reported Study Outcome in the Seven Study Sets Under Discussion

Study Sets	Median Score at Intake	Responders[1]	Non-Responders	Non-Qualifiers[2]	Reported Outcome
1. Imipramine (Glassman et al.)	— (N = 60)	31	29	—	Positive
	— (N = 42)[4]	25	17		
2. Imipramine (Gram et al.)	21.5 (N = 24)	12	9	3	Negative
3. Imipramine (Olivier-Martin et al.)	27.9[3] (N = 24)	15	8	1	Negative
	— (N = 11)[4]	10	1	—	Positive
4. Imipramine (Siwers et al.)	16 (N = 19)	13	5	1	Negative
5. Lofepramine (Siwers et al.)	16 (N = 20)	12	4	4	Negative
6. Desipramine (Friedel et al.)	16[6] (N = 26)	16	10	—	Negative (Inverse Relation)
7. Desipramine (Khalid et al.)	24 (N = 10)	4	6	—	Negative[5]

[1] Based on the uniform criterion (improvement ≥ 40%; Final score ≤ 16 [Ham-D] or ≤ 7 [CODS]) except study sets #1 and #3. In study sets #1 and #7, the responder/nonresponders are as reported by the authors, and in study #3, according to %Ham-D↓ ≥ 40% only.

[2] A nonqualifier failed to have a score at intake of either Ham-D ≥ 18 or CODS > 12.

[3] Mean score reported by authors.

[4] Subgroup.

[5] As noted in Table 1, a positive outcome was reported for Week 4.

[6] Median score reported by authors.

Statistical analyses included the Spearman correlation coefficient (Conover, 1971) as in Tables 3-5, and the 95% confidence interval for medians as in Figure 1. When statistical significance was found with the Spearman correlation coefficient, this was checked with three additional correlation coefficients:

1) A Pearson based on clinical response as measured by %Ham-D↓ or %CODS↓. These scores were correlated with the logarithms of the serum level parameters.
2) A Spearman based on clinical response as measured by total Ham-D or CODS at treatment endpoint.
3) A Pearson based on clinical response as measured by total Ham-D or CODS at treatment endpoint and logarithms of the serum level parameters.

Table 3

Comparison of Correlation Coefficients Based on Steady-State Serum Levels Averaged over Weeks 4 and 5 for Imipramine Responders from the Gram et al. Study

Time Period	%Ham-D↓ vs. I	%Ham-D↓ vs. D	%Ham-D↓ vs. (I + D)	%Ham-D↓ vs. D/I
Week $3^{1,2}$ ($N = 9$)	+0.62*	N.S.	N.S.	N.S.
Endpoint^{1,2} [Wk 4 or 5] ($N = 1$)	+0.84**	N.S.	0.47†	N.S.

[1] Because of a 1-week placebo period, Weeks 3, 4, and 5 correspond to Days 28, 35, and 42, respectively.

[2] For all responders except one, D/I > 1.

†, *, and ** denote significance at $p < .10$, .05, and .01 levels, respectively.

Table 4

Comparison of Correlation Coefficients with Serum Level Parameters at Week 3 for Imipramine Responders from the Olivier-Martin et al. Study

Grouping	%Ham-D↓ vs. I	%Ham-D↓ vs. D	%Ham-D↓ vs. (I + D)	%Ham-D↓ vs. D/I
D/I < 1 ($N = 4$)	0.90*	0.80*	0.90*	N.S.
D/I ≤ 1 ($N = 11$)	N.S.	N.S.	N.S.	N.S.
ALL ($N = 15$)	N.S.	0.41†	0.36†	0.41†
Endog^1 ($N = 10$)	N.S.	0.52†	0.58*	N.S.

[1] Subgroup of endogenous depressive patients identified by Olivier-Martin et al.

† and * denote significance at $p < .10$ and .05 levels, respectively.

(manu. 48)

Table 5

Comparison of Correlation Coefficients with Serum Level Parameters at Week 3 for the Imipramine^1 and Lofepramine^2 Responders from the Siwers et al. Study

	Lofepramine			Imipramine		
	With Min. Intake (CODS ≥ 12)	Without Min. Intake		With Min. Intake (CODS ≥ 12)	Without Min. Intake	
Relationships	Resp. ($N = 12$)	Resp. ($N = 15$)	Total ($N = 20$)	Resp. ($N = 13$)	Resp. ($N = 14$)	Total ($N = 19$)
1. (%NE^1) vs. (DMI)	0.80**	0.86***	0.89***	0.92***	0.92***	0.92***
2. (%CODS^1) vs. (DMI)	0.55*	0.24	0.30†	0.20	-0.11	0.8
3. (%NE^1) vs. (%CODS^1)	0.71**	0.36†	0.33†	0.23	0.26	0.14
4. (%NE^1) vs. (DMI/Parent Drug)	0.90***	0.85***	0.80***	Not Available		
5. (%CODS^1) vs. (DMI/Parent Drug)	0.62**	0.40†	0.40*	Not Available		
6. (%CODS^1) vs. (DMI + Parent Drug)	0.51*	0.25	0.29	Not Available		

[1] Imipramine was not measured in serum.

[2] For all lofepramine responders, D/L ≥ 1.

%NE^1 = %Norepinephrine (NE) reuptake inhibition from baseline (Week 0).

%CODS^1 = %Total Cronholm-Ottosson Depression Score (CODS) reduction from baseline (Week 0).

†, *, **, and *** denote significance at $p < .10$, .05, .01, and .001 levels, respectively.

manu. 49

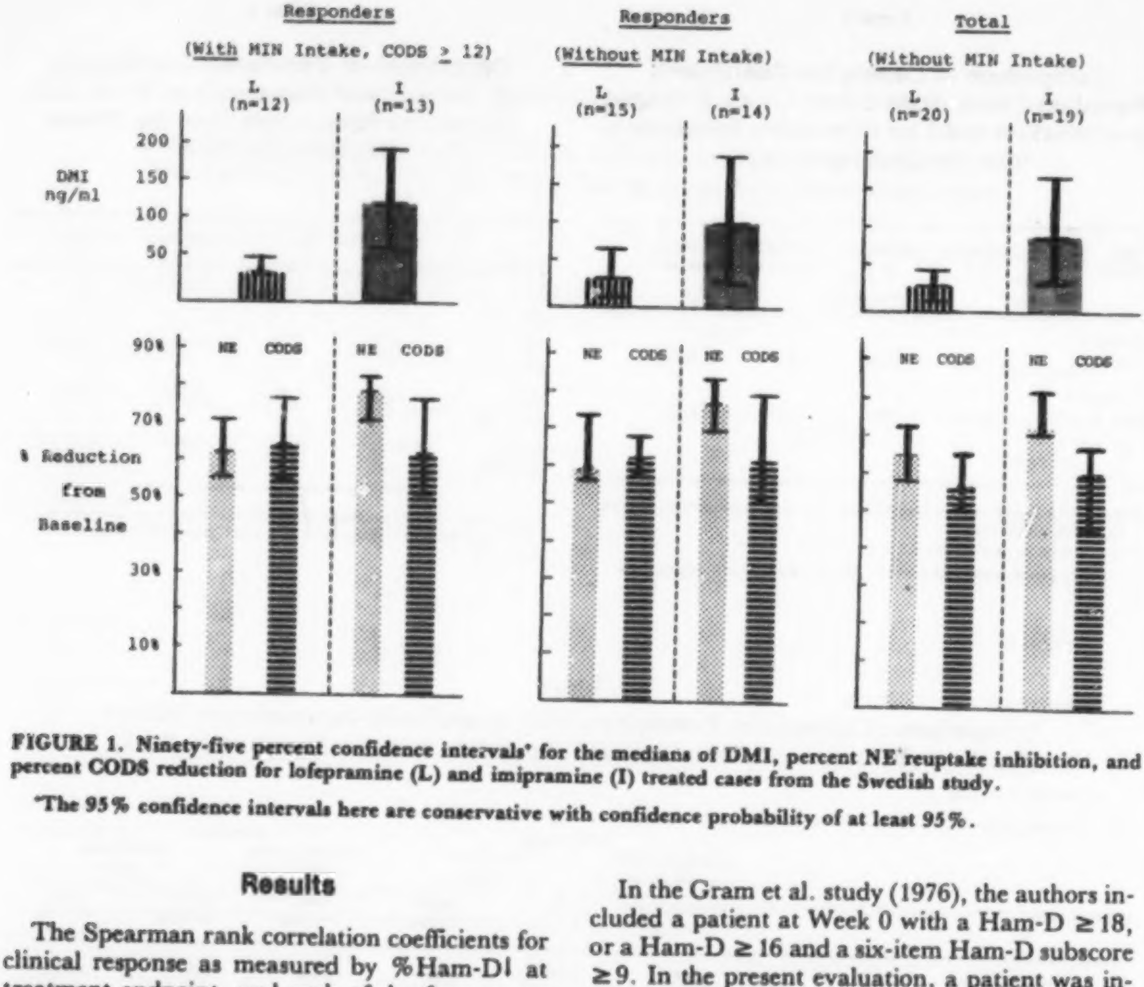


FIGURE 1. Ninety-five percent confidence intervals* for the medians of DMI, percent NE reuptake inhibition, and percent CODS reduction for lofepramine (L) and imipramine (I) treated cases from the Swedish study.

*The 95% confidence intervals here are conservative with confidence probability of at least 95%.

Results

The Spearman rank correlation coefficients for clinical response as measured by %Ham-D↓ at treatment endpoint, and each of the four serum level parameters I, DMI, I+DMI, and DMI/I are given in Tables 3 and 4, corresponding to Studies No. 2 (Gram et al., 1976) and No. 3 (Olivier-Martin et al., 1975), respectively. For the imipramine and lofepramine responders from the Swedish study (Siwers et al., 1977), a comparison of Spearman correlation coefficients for six relationships, with and without a minimum intake condition of CODS≥12, is available in Table 5. Correlations are primarily computed for ALL responders, without breakdown into DMI/parent drug subgroups, since either imipramine (Swedish study) was not measured or the proportions of (DMI/parent drug < 1) responders were relatively few.

In the Gram et al. study (1976), the authors included a patient at Week 0 with a Ham-D ≥18, or a Ham-D ≥16 and a six-item Ham-D subscore ≥9. In the present evaluation, a patient was included if the average of Ham-D at the beginning (Day 0) and end (Day 7) of the 1-week pretreatment placebo period was >18. Average Ham-D was also used in computing the %Ham-D↓ at Week 3, and at endpoint for Table 3. Because of the 1-week placebo period, Weeks 3, 4, and 5 here correspond to Days 28, 35, and 42, respectively.

In the Olivier-Martin et al. study, unfortunately, intake depression scores are not available so that the number of nonqualifiers with Ham-D ≥18 could not be identified. Because the authors reported a statistically significant correlation for an endogenous depression subgroup of 11 patients, results for responders (10 out of 11) are given in the last row of Table 4.

In Set No. 2 (Gram et al. study), as noted in

Table 3 for ALL responders, statistically significant correlations were found with imipramine (I) serum levels both at Week 3 ($r=0.62^{*}$) and at treatment endpoint ($r=0.84^{**}$). A considerably weaker correlation ($r=0.47$) was found with total serum level. Correlations with D or D/I were not significant.

In Set No. 3 (Olivier-Martin et al. study), for ALL responders weak statistically significant correlations are indicated in Table 4 with D, I+D, and D/I. When ALL responders are subdivided into D/I subgroups, significant correlations are found when D/I <1 with I, D, and I+D but for small sample sizes ($N=4$). For the endogenous depression responders, significance is found with D and (I+D) which is consistent with the findings of Olivier-Martin et al., as noted in Table 1. A computational check reveals that somewhat higher correlations are obtained in this case with Pearson's method, which was used by Olivier-Martin et al., than with the Spearman rank order correlation.

In the Swedish study, in which imipramine (Set No. 4) and lofepramine (Set No. 5) are compared, the invoking of a minimum intake depression score (CODS ≥ 12), as indicated in Table 5, seems to have significant beneficial effects for the lofepramine responders. With the minimum intake requirement, for ALL responders the correlations for all six relationships in Table 5 are statistically significant. In particular, with regard to clinical response and %NE↓, DMI/L was found to correlate better than DMI. Lofepramine itself did not correlate with any parameter.

The picture is less clear for the imipramine responders, partly because imipramine was not measured in serum. Outside of the relationship of DMI and %NE↓, which was found to be significant for both imipramine and lofepramine (Siwers et al., 1977), no significant results were found.

The median values of DMI, %NE↓, and %CODS↓ with their 95% confidence limits for the total groups and ALL responders are given in Figure 1. Within each treatment, the parameter medians for responders are not appreciably different from those of the total group.

The median DMI levels, however, are significantly lower for lofepramine (37-38 ng/ml) than for imipramine (87-114 ng/ml). Correspondingly, the median %NE↓ values are somewhat lower for lofepramine (61-66%) than for imipramine (75-78%). Only minor differences were noted between the two treatments in the medians of %CODS↓, 59-63% for the total groups, and 64-66% for responders. Therefore, the responders achieved a median clinical response of about 65%, with median DMI levels of about 37 ng/ml (lofepramine group) and about 114 ng/ml (imipramine group).

In an effort to tie together clinical response with both %NE↓ and DMI, the difference Δ = (% reduction of CODS − % NE reuptake inhibition) is plotted against DMI for each of the lofepramine and imipramine responders in Figure 2. The graph is divided into four quadrants depending on DMI levels <50 ng/ml or ≥ 50 ng/ml together with values of $\Delta > 0$ or $\Delta \leq 0$.

From Table 6, it is noted that without regard to $\Delta > 0$ or $\Delta \leq 0$, most lofepramine cases had DMI levels ≤ 50 ng/ml, while most imipramine patients had DMI levels ≥ 50 ng/ml, and this difference is statistically significant (Part A). Although the sample sizes are small, there are higher proportions of responders for DMI levels ≥ 50 ng/ml (Part B).

Table 6

Proportions of Patients and Responders with DMI < 50 ng/ml and DMI ≥ 50 ng/ml in the Siwers et al. Study†

A. Proportion of Patients

Drug	<50 ng/ml	≥50 ng/ml
Lofepramine	13	3
Imipramine	5	13

$\chi^2 = 7.69$, significant at $p < .01$

B. Proportion of Responders

Drug	<50 ng/ml	≥50 ng/ml
Lofepramine	69.2% (9/13)	100% (3/3)
Imipramine	60.0% (3/5)	76.9% (10/13)

†All numbers denote the number of patients that satisfied intake CODS ≥ 12.

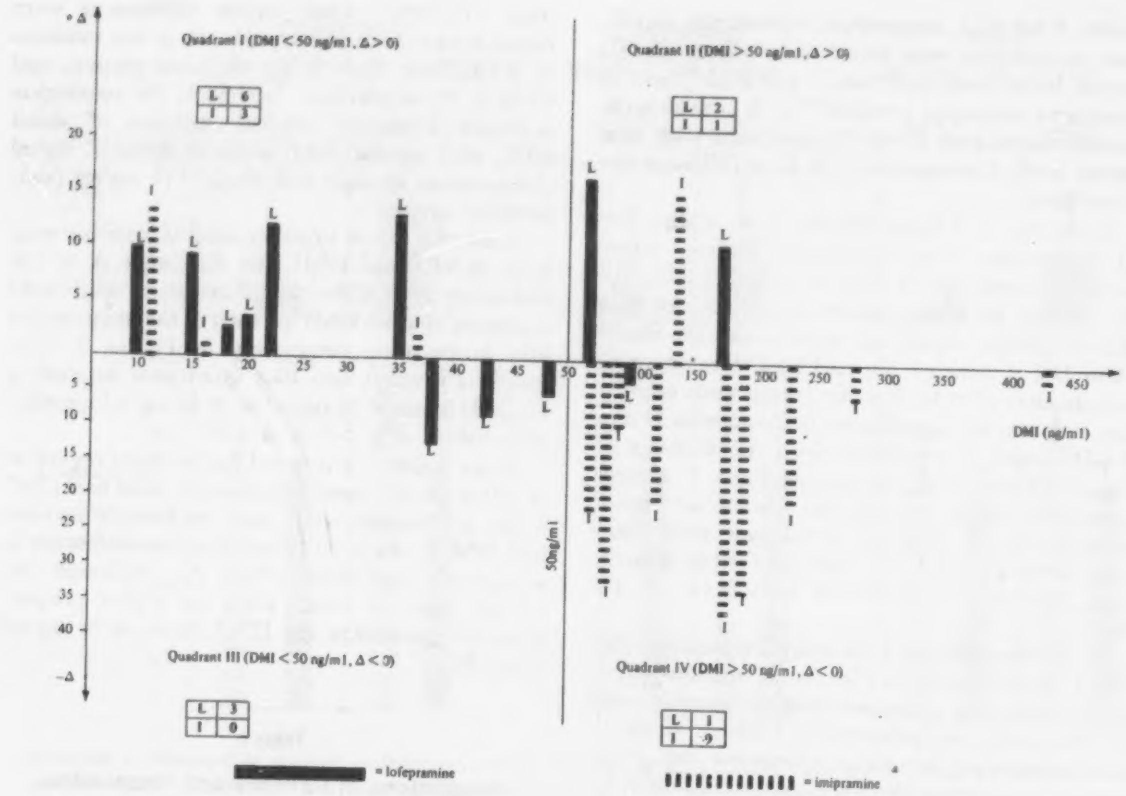


FIGURE 2. The difference Δ (% CODS reduction − % NE reuptake inhibition) as a function of DMI for the responders in the Swedish study.

Table 6 (cont'd.)

C. Proportion of Responders in Quadrants I and IV

Drug	Quadrant I (< 50 ng/ml, Δ < 0)	Quadrant IV (≥ 50 ng/ml, Δ < 0)
Lofepramine	6	1
Imipramine	3	9

$\chi^2 = 4.33$, significant at $p < .05$

D. Proportion of Responders as a Function of Δ

Drug	Δ > 0	Δ > 0
Lofepramine	8	4
Imipramine	4	9

When Δ >0 or Δ ≤0 is taken together with DMI levels <50 ng/ml or ≥50 ng/ml, most lofepramine responders are in quadrant I (<50 ng/ml and Δ >0) and most imipramine responders are in quadrant IV (≥50 ng/ml and Δ ≤0), and this difference is statistically significant (Part C). In terms of Δ alone, most lofepramine responders have Δ >0, and most imipramine responders have Δ ≤0, but the separation is not statistically significant (Part D).

This discrimination property of Δ stems from the fact that the same level of clinical response (median 65%) was achieved with each drug but with substantially lower DMI levels after lofepramine treatment. Since DMI and %NE↓ are highly correlated (Table 5—Relationship 1), and since DMI is lower after lofepramine treatment, %NE↓

is also lower. With the same clinical response but lower %NEI, Δ, therefore, tends to be positive more often with lofepramine treatment. Alternatively, with imipramine treatment, Δ tends to be negative more often.

Discussion

In the past (Asberg & Sjoqvist, 1978; Glassman, Hurwic, & Perel, 1973; Gram, 1977; Hammer, Martens, & Sjoqvist, 1968; Hollister, 1969; Kupfer, Pickar, Himmelhoch, & Detre, 1975; Petit, Spiker, Ruwitch, et al., 1977; Poldinger & Stille, 1969; Preskorn & Biggs, 1978), there has been considerable emphasis on the role and associated problems of serum/plasma/blood-level monitoring of tricyclic antidepressants. The resolving of study inconsistencies that obscure the clinical outcome/serum level relationship, however, is necessary if the value of serum level monitoring is to be realized. The pattern of difficulties, noted previously (Dutt, 1981) in the amitriptyline studies, is also evident in the imipramine studies evaluated here, as may be seen from Table 7.

Table 7

Proportion of Responders/Nonresponders' as a Function of Total Serum Levels (DMI + I) or (DMI + L)

Study	R/NR	DMI/Parent < 1		DMI/Parent ≥ 1		ALL	
		< 220	≥ 220	< 220	≥ 220	< 220	≥ 220
Imipramine	R	0	1	(5	5)†	(5	6)†
(Gram et al.)	NR	3	1	3	2	6	3
Imipramine	R	1	3	4	7	5	10
(Olivier-Martin et al.)	NR	—	—	—	—	1	7
Imipramine	R	—	—	—	—	8	6
(Siwers et al.)	NR	—	—	—	—	4	1
Lofepramine	R	0	0	(12	0)*	(12	0)*
(Siwers et al.)	NR	1	0	3	0	4	0

'The nonqualifiers are not included.

†Confirmed significant clinical response/serum level relationship with only the parameter I.

*Confirmed significant clinical response/serum level relationships with parameters DMI, DMI/L, and DMI + L.

In the three imipramine study sets, it was only possible to obtain confirmed statistical significance with one parameter in the Gram et al. study. The numbers of responders with total serum level ≥ 220 ng/ml in those three studies are relatively large, viz., 6, 10, and 6. On the other hand, with the lofepramine responders, confirmed statistical significance occurred in three parameters: DMI, DMI/L, and (DMI + L), while for any responder the total serum level did not exceed 220 ng/ml. These results are consistent with what was previously reported for amitriptyline studies. In other words, there is a greater likelihood of confirmed significant results when the number of responders for which total serum level ≥ 220 ng/ml is small (Dutt, 1981).

With regard to the two desipramine studies (Friedel et al., 1979; Khalid et al., 1978) summarized in Tables 1 and 2, again, the large numbers of nonresponders present a problem. In the Friedel et al. (1979) study, an inverse relationship ($r = -.365$) between clinical response and DMI and hence a negative outcome was reported for the full study group. Dropping the large number (10) of nonresponders and focusing on responders (10) with 50 ng/ml < DMI < 200 ng/ml, a positive outcome is possible. In the Khalid et al. (1978) study, there are too few responders for analysis.

The analyses with the lofepramine responders revealed a number of interesting findings. For example, the use of the somewhat stringent intake criterion (CODS ≥ 12) appeared to substantially improve the likelihood of finding statistically significant clinical response/serum level relationships. It is recalled from Table 5 that all six relationships were significant. In addition, the ratio DMI/L was found to correlate better than DMI. It is not clear why this occurred. All lofepramine responders had DMI/L > 1.

The relationship of NE reuptake inhibition and clinical response needs to be explored further in patients that respond to other antidepressant drugs. The finding that most lofepramine responders have Δ > 0 while most imipramine responders have Δ < 0 is certainly interesting. It would be useful to see if Δ, as a function of metabolite serum levels, has a discriminating role with other tricyclics. On the other hand, as is always the case, it would be desirable to see if these findings could be duplicated in additional studies with lofepramine and imipramine.

This evaluation suggests again the desirability of having large numbers of patients who respond to the drug. Stringent intake criteria for all patients and subsequent dosage adjustment for those patients with total serum levels ≥ 220 ng/ml can increase the likelihood of predicting clinical outcome from serum levels. Hopefully, with these and other measures to improve sample homogeneity, there will be a greater body of consistent study results for tricyclic antidepressants.

Acknowledgments: The author is grateful to Dr. Karl Rickels, University of Pennsylvania, for helpful discussion and, at EM Labs, to Ms. Amy Huang and Ms. Shiow Chen for the computer results. Thanks also to Dr. Lothar Herrmann at Leo in Sweden for details on the lofepramine data and to Dr. Khalid for his raw data on desipramine. Finally, the author acknowledges the efforts of the Editor to improve the clarity of this paper.

References

Asberg, M., and Sjoqvist, F. On the role of plasma level monitoring of tricyclic antidepressants in clinical practice. *Commun. Psychopharmacol.*, 2:381-391, 1978.

Conover, W.J. *Practical Nonparametric Statistics*. New York: John Wiley & Sons, 1971.

Cronholm, B., and Ottosson, J. O. Experimental studies of the therapeutic action of electroconvulsive therapy in endogenous depression. *Acta Psychiatr. Scand. (Suppl.)*, 145:169, 1960.

D'Eliz, G., Borg, S., Hermann, L., et al. Comparative clinical evaluation of lofepramine and imipramine: Psychiatric aspects. *Acta Psychiatr. Scand.*, 55:10-20, 1977.

Dutt, J. E. On the clinical response/serum level relationship for antidepressants I: Amitriptyline. *Psychopharmacol. Bull.*, 17(2):42-55, 1981.

Eriksoo, E., and Rogte, O. Chemistry and pharmacology of a new potential antidepressant. *Arzneim-Forsch.*, 20:1561-1569, 1970.

Feighner, J. P., Robins, E., Guze, S. B., et al. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry*, 26:57-63, 1972.

Friedel, R. O., Veith, R. C., Bloom, V., and Bielski, R. J. Desipramine plasma levels and clinical response in depressed outpatients. *Commun. Psychopharmacol.*, 3:81-87, 1979.

Glassman, A. H., Hurwic, M. J., and Perel, J. M. Plasma binding of imipramine and clinical outcome. *Am. J. Psychiatry*, 130:1367-1369, 1973.

Glassman, A. H., Perel, J. M., Shostak, M., et al. Clinical implications of imipramine plasma levels for depressive illness. *Arch. Gen. Psychiatry*, 34:197-204, 1977.

Gram, L. F. Plasma level monitoring of tricyclic antidepressant therapy. *Clin. Pharmacokinet.*, 2:237-251, 1977.

Gram, L. F., Reisby, N., Ibsen, I., et al. Plasma levels and antidepressive effect of imipramine. *Clin. Pharmacol. Ther.*, 19:318, 1976.

Hamilton, M. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry*, 23:56-62, 1960.

Hammer, W., Martens, W., and Sjoqvist, F. A comparative study of the metabolism and desmethylimipramine, nortriptyline, and oxyphenylbutazone in man. *Clin. Pharmacol. Ther.*, 10:44-49, 1968.

Hollister, L.E. Relationship between blood levels of centrally-acting drugs and clinical effects, in the present status of psychotropic drugs – pharmacological and clinical aspects. International Congress Series No. 180, Amsterdam, Excerpta Medica Foundation, 1969, pp. 90-93.

Khalid, R., Amin, M.M., and Ban, T.A. Desipramine plasma levels and therapeutic response. *Psychopharmacol. Bull.*, 14(1):43-44, 1978.

Kupfer, D. J., Pickar, D., Himmelhoch, J. M., and Detre, T. P. Are there two types of unipolar depression? *Arch. Gen. Psychiatry*, 32:866-871, 1975.

Malitz, S., and Kanzler, M. Onset of action and clinical effectiveness of desmethylimipramine vs. imipramine in a double-blind study of depressed patients, in the present status of psychotropic drugs—pharmacological and clinical aspects. International Congress Series No. 180, Amsterdam, Excerpta Medica Foundation, 1969, pp. 522-525.

Moody, J. P., Tait, A. C., and Todrick, A. Plasma levels of imipramine and desmethylimipramine during therapy. *Br. J. Psychiatry*, 113:183-193, 1967.

Muscettola, G., Goodwin, F. K., Potter, W. Z., et al. Imipramine and desipramine in plasma and spinal fluid. *Arch. Gen. Psychiatry*, 35:621, 1978.

Nage, A., and Treiber, L. Quantitative determination of imipramine and desipramine in human blood plasma by direct densitometry of thin-layer chromatograms. *J. Pharm. Pharmacol.*, 25:599-603, 1973.

Olivier-Martin, R., Marzin, D., Buschsenschutz, E., et al. Concentrations plasmatiques de l'imipramine et de la desmethylimipramine et effet anti-depresseur au cours d'un traintment controle. (Plasma concentrations of imipramine and desmethylimipramine and anti-depressant effects in the course of a control treatment) *Psychopharmacologia (Berlin*, 41:187-195, 1975.

Petit, J.M., Spiker, D.G., Spiker, D.G., Ruwitch, J.F., et al. Tricyclic antidepressant plasma levels and adverse effects after overdose. *Clin. Pharmacol. Ther.*, 21:47-51, 1977.

Plym Forshell, G., Siwers, B., and Tuck, J. R. Pharmacokinetics of lofepramine in man: Relationship to inhibition of noradrenaline uptake. *Eur. J. Clin. Pharmacol.*, 9:291-298, 1976.

Poldinger, W., and Stille, G. Concerning the possibility of correlating pharmacological and clinical data of psychotropic drugs,, in the present status of psychotropic drugs—phamacological and clinical aspects. International Congress Series No 180, Amsterdam, Excerpta Medica Foundation, 1969, pp. 529-531.

Preskorn, S. H., and Biggs, J. T. Use of tricyclic antidepressant blood levels. *New Engl. J. Med.*, 298:166, 1978.

Sathananthan, G. L., Gershon, S., Almeida, M., et al. Correlation between plasma and cerebrospinal levels of imipramine. *Arch. Gen. Psychiatry*, 33:1109-1110, 1976.

Siwers, B., Borg, S., D'Elia, G., et al. Comparative clinical evaluation of lofepramine and imipramine—Pharmacological aspects. *Acta Psychiatr. Scand.*, 55:21-31, 1977.

Siwers, B., Freyschuss, U., Hamberger, B., et al. A quantitative approach to the initial clinical trial of tricyclic antidepressants—A comparison of Leo 640 and nortriptyline. *Eur. J. Clin. Pharmacol.*, 3:12-17, 1970.

Walter, C. J. S. Significance of plasma imipramine levels. *Proc. R. Soc. Lond. (Med.)*, 64:282-285, 1971.

Watt, D. C., Crammer, J. L., and Elkes, A. The relations of side effects to therapeutic outcome of imipramine in depressive illness, in the present status of psychotropic drugs. International Congress Series 180, Amsterdam, Excerpta Medica Foundation, 1969, pp. 553-555.

Models of Cognitive Impairment: Cognitive Changes in Depression[1]

Herbert Weingartner, Ph.D.,[2] and Edward Silberman, M.D.[2]

Introduction

Cognitive dysfunctions are an integral aspect of the behaviors evident in depression. One of the most obvious clinical expressions of depression is reflected in how these patients experience and describe themselves, significant others, and their environment. These subjective as well as observed cognitive changes can appear as alterations in the perception, organization, interpretation, and meaning of a large variety of events or stimuli. Past events, stimuli in the present, as well as future events are appreciated in qualitatively different ways from the nondepressed state. Depressed patients also experience and demonstrate difficulties in concentration, attention, memory, and other aspects of information processing. That is, while depressed, there appear not only qualitative changes in cognition, but quantitative changes as well, and the efficiency or effectiveness of information processing is compromised in the depressed state. The clinical and experimental studies reviewed here demonstrate that these qualitative and quantitative changes in cognition are complex and highly variable in form. The purpose of this review is to outline and structure what we have learned about cognition in depression. Some of these findings can be clinically useful. They also may teach us some things about the psychobiology of mood and cognition. Finally, we consider some of the questions that remain to be answered and propose some directions for further study and research.

A remarkable diversity of studies has been completed to date. Some of the findings come from clinical studies using clinical assessment tools. In other studies, patient populations have been examined using laboratory based methods and procedures. Still other studies have tested unimpaired subjects, manipulated their mood, and then examined changes in cognition. Methods have varied with respect to the types of subjects studied, the definition of depression, the theoretical framework that has been used to interpret cognitive responses, and the nature of the cognitive response that has been used as the target behavior.

The structure of this review is as follows. The findings that describe changes in the *form* of cognition (qualitative changes) and the *effectiveness* of those cognitive processes (quantitative changes) in depression will be reviewed separately. Some of these cognitive changes will then be compared to the changes in cognition apparent in other disorders, particularly those evident in early-stage dementia. An underlying theme throughout the review is whether there are distinctive features to the cognitive changes in depression that differentiate them from forms of cognitive impairment associated with other states. We then consider why it is difficult to integrate the available data base on cognition in depression. A framework is provided that may be useful both in integrating aspects of cognitive processes apparent in depression and in providing methods and interpretative schemes for further study. Finally, we describe some of the major questions that remain to be answered by such future study.

---

[1] To be published as a chapter in *Neurobiology of Manic Depressive Illness.* R. Post and J. C. Ballenger (eds.), Baltimore, MD: Williams and Wilkins Co.

[2] Laboratory of Psychology and Psychopathology, National Institute of Mental Health, Bethesda, MD 20205.

Qualitative Changes in Cognition in Depression

Three types of findings have supported the contention that depressed patients think about, interpret, and remember events in a manner that is different from processes apparent in the undepressed state. Psychodynamic formulations of depression have been one basis of these findings. Cognition in depression is considered in terms of a recapitulation of processing strategies used during some early developmental stage. Observed cognitive behaviors in depression, such as helplessness, passivity, and dependence, are then interpreted within a context of the consequences of a developmental history, and disruptions in stages of that history. This view of cognitive processing in depression has been reformulated on the basis of versions of experimentally based learning theories (operant theories, behavior modeling theories, and cognitive versions of behaviorism) as developed within experimental psychology, and have served as an important basis for describing the qualitative changes in cognition in depression. A second basis for describing qualitative changes comes from studies in which mood is manipulated, using a variety of laboratory procedures. Here the strategy is to model or mimic the types of mood changes evident in depression and then characterize related changes in cognition. A third source of data has been generated from studies that have used information processing models to examine alterations in the form of cognition in depression. In these studies, mood-state is viewed as a form of context for encoding processes and retrieval processes. In other terms, mood states are defined in terms of their stimulus properties, in much the same way that a drug manipulation is associated with unique stimulus properties. A mood-state then serves to bias the form of cognitive processing in a unique manner.

During the past two decades there have appeared a number of different kinds of studies, each demonstrating that life events, a particular developmental history, and other factors result in a pattern of cognitive behaviors which are then related, or determine the experience of depression (Brown, Sklair, Harris, & Burley, 1973; Forrest, Fraser, & Priest, 1965; Jacobs, Prusoff, & Paykel, 1967; Paykel, 1975; Paykel, Myers, Drenelt, et al., 1969). In these studies, it would appear that depressed patients think about past, present, and future events differently from what is apparent in the undepressed state. In some instances, these studies have served as a basis for formulations of cognitively focused theories that would describe the etiology of depression and what maintains depressive symptoms. For example, Beck has conceptualized the cognitive aspects of depression as reflecting a negative view of self, lowered self-esteem and decreased motivation, and related specific and systematic distortions that serve as a primary integrative theme for depressed cognition (Beck, 1967, 1971, 1974). Beck has argued that dysfunctional cognitions are, in fact, at the heart of what constitutes the experience of being depressed. Cognitively, depressed patients overgeneralize, selectively abstract information, are susceptible to some arbitrary forms of interference and, most important, minimize positive consequences and maximize negative consequences. These last issues or observations have been used by Seligman (1971) in his reformulation of Beck's theory. This has taken the form of the "learned helplessness" theory in depression. The phenomenon has been produced in animals (Maier & Seligman, 1976) and manipulated or modeled in man as well as used to describe cognition in depressed subjects. Depression is viewed as the result of learned helplessness or the expectation that outcome or consequences are response-independent. Feelings of helplessness are considered the focal behavior in depression and are operationalized as expecting consequences to be independent of what one does in some situation (Abramson, Seligman, & Teasdale, 1968; Seligman, 1971, 1975). In depression, patients expect unfavorable events to occur, feel they have no control over those negative consequences and, as a result, demonstrate passivity and a negative cognitive set. Another type of cognitive-theoretical formulation that is superficially similar to a learned helplessness description deals with internal vs. external loci of control and how these are altered in the depressed state (Hiroto, 1974). Such a theoretical position has been used to interpret attributing failure to self, and self-blame for some outcomes as particularly characteristic of depressed patients (Klein & Seligman, 1976; Rizley, 1978).

Another form of cognitive theory that seems to account for the uniqueness of cognitive processes in depression deals with perceived competence or ability to effectively cope with the environment. Lewinsohn has described the cognitive experience of depression in terms of impairments in social competence. Depressed patients are less interpersonally and socially skilled (Lewinsohn, Mischel, Chaplain, & Barton, 1980), and, therefore, less interpersonally effective. Yet another theory about the nature of the qualitative changes in depressive cognition has been suggested by Bandura in terms of the notion of self-efficacy. He argues that individuals have cognitive schemas that involve their conviction about whether they can successfully execute some behavior that is required of them, one that would produce some desired outcome. Expectations of personal mastery effects both the initiation and persistence of such coping behaviors. The strength of an individual's conviction about his own effectiveness will determine how much effort he will extend and how long he will persist in the face of obstacles and adverse experiences. The stronger the perceived self-efficacy, the more active will be his efforts in dealing with a stressful situation. Successful performance encourages a positive view of self and, in turn, the more positive the view, the more likely is the individual to attempt further tasks and be successful. Self-efficacy then becomes a concept that ties an individual's view of himself with his ability to master situations, and both of these determine his perception of his previous and recent history of success and failure.

These behaviorally oriented theories of depression formulated by Lewinsohn, Seligman, Bandura, and others have spurred a good deal of interest, empirical study, and further theoretical refinement and reformulation (Abramson et al., 1968; Huesmann, 1978; Seligman, 1978). Such theories have also been criticized as too simplistic and inexact descriptions of cognitive processes, since learned helplessness models predict patterns of cognitive symptoms that do not in fact occur in depression (Buchwald, Coyne, & Cole, 1978; Costello, 1978). In addition, much of the theorizing and empirical findings in support of these cognitive theories of depression assume that a manipulation of dysphoric mood in an unimpaired subject is like depression in a mood-disorder patient. Clearly, this is an oversimplification (Wortman & Dintzer, 1978). In fact, most of the empirical studies of these cognitive models of depression have been accomplished in laboratory tests in unimpaired subjects rather than in depressed patients. For example, learned helplessness has been manipulated by altering outcome, e.g., success or failure on skill tasks, which then produces impairments in performance, cognitive and motivational changes, and alterations in the expectation of contingent reinforcement (Abramson et al., 1968). What a subject attends to after some manipulation may also be a consequence of laboratory-based failure manipulations, rather than an alteration of expectations of success and related changes in mood (Coyne, Metalsky, & Lavelle, 1980). That is, manipulation of success or failure on some complex task may primarily alter focus of attention and only in a secondary way alter expectation of success or mood. In general, however, the cognitive behaviors that follow the experience of failure have been interpreted as learned helplessness or loss of perceived competence, and these cognitive changes appear to mimic depression. Critics of these behavioral-cognitive theories point out some of their shortcomings, including the circularity in some of the reasoning. Although the theories may be descriptively useful, they nevertheless explain little about the nature of the cognitive experience of depression (Diener & Dweck, 1978). Furthermore, the major type of manipulation that has been used as an empirical basis for learned helplessness has also served to account for anxiety (Lucas, 1952), stress (Lazarus, Deese, & Osler, 1952), frustration (Lawson & Marx, 1958), and schizophrenia (Garmezy, 1966). It is also not clear from such theories why a negative cognitive set can be induced in some people and not others. Nor do these theorists specify the presence or role of these altered forms of cognitive processes in the various stages that mark the development and maintenance of depression (Blaney, 1977).

The above theories and related methods and procedures used to test them have also been used to generate strategies for cognitive manipulations in altering depressive behaviors, or forms of cognitive therapies. These cognitive therapies have been designed to reverse or alter the mediational styles and behaviors that presumably maintain depression. That is, they are formulated and used to alter the way depressed individuals think about themselves, their competence, and their expectations of success or failure. Consistent with behavioral views of psychopathology, where symptoms are the targets of change, cognitive therapies have been used to change the thinking and cognition of depressed patients. If cognitive changes are produced, it is expected to be reflected in alterations in behavior, thereby effecting changes in depression. Personal mastery initiation and persistence training in coping behaviors are just some of the manipulations that have been used to alter mood in depressed patients. These techniques have also included attentional redeployment (Coyne et al., 1980), and direct cognitive manipulations of self-esteem (Coleman, 1975; Raps, Reinhard, & Seligman, 1980), as well as manipulations of reinforcing consequences that would be expected to alter cognitive behaviors related to depression.

All of these behaviorally oriented theories and studies imply that cognition is qualitatively altered in the depressed state. This has not been tested directly in an effective manner. That is, relatively little research has been explicitly directed at characterizing empirically, qualitative, mood-state specific encoding of events, how information is organized, and how memory for past and recent events is scanned and recalled. Instead, it has been anecdotal, clinical data which has served as a basis for describing changes in how depressed patients interpret information about self, others, their environment, and their past histories. Some of these inferred qualitative changes in cognition have, in fact, been the starting point of some of the cognitive theories of depression as described by Beck (1967, 1971, 1974), Seligman (1971, 1975, 1978), Lewinsohn, Mischel, and Chaplain (1980), and Bandura (1977). Despite extensive laboratory studies in which mood is manipulated in unimpaired subjects or altered by affective illness, there is, nevertheless, little clear and direct evidence that cognition is qualitatively altered in depression. Some studies have shown that when depressed, people recall qualitatively different past events than those that they remember under normal mood-state conditions (Lishman, 1972). That is, positively charged past events are less likely to be remembered when depressed and, instead, depressed patients selectively recall negatively charged events. There are similar findings that have been reported on the basis of laboratory studies of mood and its effects on selective recall of previously processed events. For example, in laboratory studies in which mood is manipulated by a success-failure condition (on a skill task), there appears to be selective and biased recall of positive and negative feedback that differentiates depressed patients from control subjects (Nelson & Craighead, 1977). Depressed patients selectively underestimate the frequency of positive reinforcement even while accurate in estimating the frequency of contingent negative consequences received during the performance of some skill task. A similar type of finding has been obtained in tests of depressed subjects in estimating correct responses on a pseudo-social intelligence task (Wener & Rehm, 1975). Unimpaired subjects who are induced into experiencing a depressive-like mood, as opposed to experiencing a happy mood, required a longer time to retrieve pleasant memories when happy and demonstrate decreased response latencies in recalling unpleasant memories when happy (Teasdale & Fogarty, 1979). All of these studies suggest that mood-states bias the accessibility and retrieval of information already in memory (Weingartner, Miller, & Murphy, 1977). Depressed patients, in recalling recent biographical (episodic) events, are far less likely to recall positively valent material than either neutral or negatively charged information (Breslow, Kocis, & Belkin, 1981). There are also aspects of the cognitive styles of depressed patients that are employed in recalling recent events, that differentiate them from subjects with normal mood. The depressed patient is far more likely to be preoccupied with, or attend to, past events than events that occur either in the present, recent past, or future (Wyrick & Wyrick, 1977). Other studies have been designed to examine the perception of recent life-stress events and have found that depressed patients report more stressful recent events than controls (Brown et al., 1973; Forrest et al., 1965; Hammen & Cochran, 1981; Jacobs et al., 1967; Paykel et al., 1969), although this may not relate to the actual occurrence of more frequent prior life stresses. The depression-related cognitive style, and changes in how past and present events are scanned and interpreted, are also reflected in alterations in self-schemata or perception of self. These self-schemata changes then also result in alterations in how information about self is organized in the depressed mood-state. Together, these findings seem to all suggest that the cognitive styles of depressed patients are, in fact, different from those apparent under normal mood-state conditions. The kinds of attributes of stimuli that are attended to, the types of past events, the valence of those past events, all seem altered in depression. These qualitative changes may also play a role in defining the nature of the quantitative changes that are apparent in depression. What is less clear is whether such qualitative cognitive changes are also evident in patients even after they have recovered from their depression.

The other form of empirical and theoretical evidence that suggests that cognitive process in depression is qualitatively different from that used normally, comes from studies of state-dependent or dissociative learning under mood-altered condition. State-dependent or dissociative studies were first accomplished in animal learning paradigms, comparing performance under a variety of acquisition and retrieval conditions. These studies have shown that the stimulus properties of drugs can serve as discriminative stimuli biasing the type of response that is elicited from some repertoire (Overton, 1968, 1971). Animals taught a response in a drugged state seemed to "forget" that response in the undrugged state. These dissociative effects have been attributed to discriminative stimulus properties of the drug, where responses are uniquely tied to stimuli represented by some drug-altered state. Similar effects have been demonstrated in drug-state-dependent learning studies in man (Goodwin, Powell, & Bremer, 1969; Weingartner, 1977; Weingartner, Adefris, Eich, & Murphy, 1976). On the bases of these studies in man, it has been possible to demonstrate that memory dissociations occur when events are poorly processed, and when recall is attempted by freely remembering information (Eich, Weingartner, Stillman, & Gillin, 1975; Weingartner, 1977). A number of studies have also demonstrated that the depressed mood state represents a state much like a drug state. It acts as a form of an informational context that, much like a drug, biases or determines how information is processed, encoded, and organized in memory. For example, when a patient in a depressed mood tries to remember previously processed events under normal mood conditions, there appears a form of dissociative learning and memory which is very much like that evident under drug-altered conditions. Sequences of events, such as past biographical experiences, are less likely to be remembered under a disparate mood condition, especially under free remembering conditions, but not when recall is attempted in the presence of strong cues that would ordinarily aid recall. Events that were stored while depressed are less likely to be recovered under normal mood-state conditions, and those events that were stored under normal mood-state conditions are less accessible in the depressed state (Weingartner et al., 1977; Weingartner, Murphy, & Stillman, 1978). That mood states can serve to produce dissociations which are mainly apparent in freely remembering information has been used as evidence for a change in how events are encoded or interpreted in the depressed state.

In summary, a variety of types of convergent findings have been used to infer that depressed patients process events qualitatively differently from how information is processed under undepressed mood-state conditions. However, what is lacking is direct evidence or measurement of cognitive processes themselves, rather than inferences drawn from subjects, levels of learning and memory. The types of findings that suggest qualitative changes in cognition in depression relate to the sorts of biographical experiences that come to mind, recall of reinforcing consequences (success and failure), expectations of future reinforcement, how events are organized, information about the self, and how events are encoded and tied to some mood context. These factors all serve to differentiate the cognitive processes in depression from those evident under normal mood conditions.

Quantitative Changes in Cognition

Depressed patients frequently complain of impairments in cognition. These are frequently verbalized as problems in attention, concentration, memory, and learning, and can be reflected in difficulties in solving problems, persisting on some cognitive tasks, thinking clearly, and distractability. Any or all of these experienced cognitive impairments can be evident on clinical examination, although both their expression and severity may vary widely as a function of the severity of depression and also perhaps the type of depression. In fact, the cognitive dysfunction may be severe enough so that it can resemble the profound cognitive impairments evident in progressive dementia patients.

Although there are considerable anecdotal data describing changes in the effectiveness of cognitive processes in depression, relatively little systematic empirical research has been accomplished to date. Most studies confirm the clinical description of a cognitive impairment in depression, but have not, as yet, defined a) the structure and specificity of these cognitive changes, b) the mechanisms that determine them, and c) the features of cognition during depression that distinguish them from the cognitive dysfunctions associated with other syndromes.

Most of the empirical tests or studies of quantitative changes in cognition apparent in depression have used standard psychometric or laboratory procedures to document and quantify the presence of a deficit (Stromgren, 1977). These procedures have primarily focused on attention, or memory and learning, although rarely together in the same study. Mediation or rehearsal processes that might account for changes in attention, learning, and memory have not been studied systematically. In large part, this is due to the fact that while there are many "ready-made" pretested procedures for measuring attention, learning, and memory, it is much more difficult to measure changes in underlying mediational or rehearsal processes that are hypothesized to determine the effectiveness of various types of cognitive operations.

Investigators have used one of three types of models of information processing as a basis for exploring the cognitive impairment in depression. Each of these models includes methods of approach as well as interpretative schemes for defining or describing cognitive findings. Most of the information processing studies in depression have implicitly or explicitly used some version of a stage theory or model of information processing (Atkinson & Shiffrin, 1968). These theories assume that information processing occurs in discrete stages in which the control or operating processes are different for each stage in processing and storing events, and the nature of the trace of experience is different for each stage of information processing. Aspects of attention, short- and long-term memory, retention, and retrieval are considered to be determined by different psychobiological mechanisms. Any impairment, in any single stage of information processing, would result in a failure to adequately record or recall ongoing events. This model has been used in several studies describing cognitive changes in depression. An alternative theoretical view of how information processing succeeds or fails considers learning, memory retention, and retrieval along a single continuum (Craik & Lockhardt, 1972; Craik & Tulving, 1975). This single process (or "levels of processing") framework for describing information processing has also begun to be used to describe cognitive changes in depression (Weingartner, Cohen, Martello, & Gerdt, 1981). The assumptions in this theoretical approach are very different from stage theory descriptions of information processing. Acquisition, retention, and retrieval are defined not by different mechanisms. Instead, the completeness of encoding or processing at the time of acquisition, and the relationship between retrieval context and encoding context at the time of acquisition, define the probability that learning has taken place and remembering is possible. In many instances it has been possible to show that memory fails because encoding operations have been weak or incomplete. A third type of theoretical model used to explore the nature of cognition in depression considers the events that follow information processing to be important in defining whether or not a trace of experience, a memory, is established in some relatively permanent form. The basic notion is that biological events that succeed acquisition will determine the consolidation of trace events in memory (McGaugh, 1966; McGaugh, Zornetzer, Gold, & Landfield, 1972). This model has been used almost exclusively in studies of the biology of animal learning and only more recently in studies of information processing in man (Parker, Birnbaum, Weingartner, et al., 1980; Weingartner, Hall, Murphy, & Weinstein, 1976).

A number of studies have demonstrated a relationship between the intensity or severity of depression and the extent of cognitive impairment (e.g., memory) that is present (Harness, Bental, & Carmon, 1977). In some studies, the severity of depression is directly related to impairments in long-term memory (Henry, Weingartner, Murphy, & Murphy, 1973), while other studies have shown this relationship with short-term memory functions (Sternberg & Jarvik, 1976). This difference may be one of semantics, or type of descriptors used to measure such cognitive impairments. By contrast to the above studies, it appears in some reports that the cognitive dysfunction in depression is a highly generalized nonspecific impairment in memory (Stromgren, 1977). Other interpretations of cognitive findings have suggested that memory impairment that is evident in depressed patients may simply be a function of the depressed individual using a more conservative response strategy, one that underestimates what the patient has learned and could potentially remember (Miller, 1975). It would appear that at least some aspects of the cognitive failures evident in depression are accounted for by retrieval failures in the form of increased reaction time, response inhibition, conservative response biases, or output failures, rather than an inability to attend to and acquire new information (Hale & Strickland, 1976; Harness et al., 1977).

A number of studies have also demonstrated that depressed patients demonstrate types of cognitive "blurring" in the form of illogical thinking—failures to accomplish detailed, analytic thinking—and also demonstrate difficulties abstracting, forming concepts, and organizing their experience. These same types of cognitive failures may be reflected in the form of inaffective mediational processes. It is plausible that memory changes that are apparent in depressed patients are a direct result of disruptions in those cognitive processes involved in the encoding of information at the time of acquisition. This may be reflected in the depressed patient being unable to perceive or use structure inherent to some informational input, thereby failing to acquire new information which is then ultimately reflected in failures in recall. In fact, some direct evidence substantiates the hypothesis of impaired analytic cognition, leading to memory changes. One form of this evidence is that depressed patients cluster related events less completely than unimpaired controls (Koh, Kayton, & Berry, 1973; Russell & Beekhuis, 1976). Other findings have demonstrated that depressed patients are less able to process and remember unrelated events, but are indistinguishable from controls in processing and recalling related information (Weingartner et al., 1981a).

Another category of investigation which has yielded information about quantitative cognitive changes in depression is that of neuropsychological testing. The Halstead-Reitan battery, for example, has been reported to show evidence of "right-hemisphere impairment" in two studies of depressed populations (Flor-Henry, 1979; Goldstein, Filskow, Weaver, & Ives, 1977). Such a conclusion is inferred from a pattern of test results characterized by relatively greater deficits in performance of spatial or holistic tasks compared to verbal, numerical, or sequential tasks. When tested in the remitted state, however, depressives have not shown deficits or lateralizing signs on the Halstead-Reitan battery (Small, Small, Milstein, & Moore, 1972). Other investigators have found quantitative deficits on spatial rather than verbal neuropsychological tests (Kronfol, Hamsher, deS. Digre, & Wazir, 1978), but have failed to find deficits on simultaneous as compared to sequential methods of information processing (Gur, 1979). One study has examined the Categories Test, a measure of abstract reasoning and logical ability used as part of the Halstead-Reitan battery, to compare cognitive changes in bipolar vs. unipolar depressed patients (Savard, Rey, & Post, 1980). The study concluded that while both groups showed impairment, the deficits in bipolars were much greater and, in the case of older bipolars, often fell below performance levels expected in brain-damaged subjects. Further analysis of the Savard data subsequently revealed that the greatest differences between depressed and control groups occurred on the portion of the test which is most dependent on processing of spatial information (Silberman & Weingartner, unpublished data).

A number of studies have suggested that the cognitive impairment evident in depression occurs in those situations or tasks that require effort, particularly sustained effort. For example, depressed patients are more likely to demonstrate impaired cognitive performance in freely remembering information rather than on tests of recognition memory. Memory-learning failures are also more likely when depressed patients are asked to accomplish tasks requiring elaborative processing and analysis of information, rather than conditions that require superficial processing of information. In a similar vein, memory failures in depression are less obvious on tests of immediate recall from short-term memory rather than delayed recall (Stromgren, 1977). Furthermore, when depressed patients are administered amphetamine, there is facilitation that is selective and restricted to tasks that require more effort (Reus, Silberman, Post, & Weingartner, 1979). In summary, it would appear that effortful processing tasks, those that require active and sustained cognitive activity, are the particular targets of disruption in depression. Recent cognitive studies have, in fact, suggested that different types of mechanisms are involved in automatic vs. effortful information processing (Hasher & Zacks, 1979). These processes are mediated by different psychobiological determinants (Lewis, 1979) and are disrupted differentially in different syndromes (Stromgren, 1977; Weingartner, Gold, et al., 1981b; Weingartner, Kaye, Smallberg, et al., 1981c). This hypothesis, namely that the cognitive information processing impairment in depression is related to an inability to sustain effort on some level, has been tested directly and confirmed. The ability of depressed patients to sustain motor effort is almost perfectly correlated with the intensity of the memory impairment evident in these patients and, together, these are highly correlated with the patient's intensity of depression (Cohen, Weingartner, Smallberg, & Murphy, in press).

While it remains for further study to clarify the psychobiological mechanisms that link effortful (or automatic processes) to cognitive failures in depression, a line of evidence with potential explanatory power is that of changes in balance between the cerebral hemispheres. There is considerable evidence to support characterization of the left hemisphere cognitive style as detailed, serial, or intentional, and that of the right as holistic, parallel, and incidental. In such terms, one might speculate that depressive deficits in effortful processing, that is, deficits in relatively deep analysis of semantic and organizational aspects of stimuli, may represent a decrement in left hemisphere cognitive functions. In support of such a speculation is a body of independent data, gathered in normal and brain-lesioned subjects, associating the left hemisphere with mediation of positive affective states, and the right hemisphere with mediation of negative affective states. Evidence for this hypothesis comes from such diverse experimental sources as lateral eye movement (Ahern & Schwartz, 1979), electroencephalographic (Davidson, Schwartz, Saron, et al., 1979), and electromyographic (Schwartz, Ahern, & Brown, 1979) studies in normals, and observation of patients with unilateral pharmacologic or anatomical brain lesions (Alema, Rosadini, & Rossi, 1961; Gainotti, 1972; Rossi & Rosadini, 1967). Thus, the hypothesis arises that depression may be a manifestation of right hemisphere activity.

In depression itself, there are also data which more directly suggest shifts in hemispheric balance or function as a concomitant of the ill state. Such diverse procedures as electroencephalography, dichotic listening, galvanic skin response, and lateral eye movements have shown results suggestive of a shift in the balance of hemispheric activity away from the left and toward the right hemisphere (d'Elia & Perris, 1973; Flor-Henry, 1979; Myslobodsky & Horesh, 1978). Such studies, as well as the neuropsychological testing described above, also suggest that the right hemisphere may not only be abnormally activated, but also pathological in its functioning during the depressed state (Buchsbaum, Carpenter, Jr., Fedio, et al. 1979; Rochford, Swartzburg, Chaudhery, & Goldstein, 1976; Roemer, Shagass, Straumanis, & Amadeo, 1978; Yozawitz, Bruder, Sutton, et al., 1979). While such lateralized changes might provide one conceptual framework for understanding cognitive deficits in depression, the evidence is as yet preliminary (Biegel & Murphy, 1971; Donnelly, Murphy, & Goodwin, 1976; Donnelly, Murphy, & Scott, 1975), without contradictions. A great deal more data need to be collected before the presence of laterality changes in depression is firmly established, or their relationship to the origin of the illness understood.

Distinctive Features in the Cognitive Changes in Depression: Clinical and Diagnostic Implications

The cognitive impairment evident in patients in early states of a progressive dementia can appear to be superficially similar to the cognitive changes apparent in depressed patients. This similarity in the form of the cognitive impairment in depression and progressive dementia contributes to diagnostic uncertainty and consequent inappropriate treatment strategies. The fact that early-stage dementia patients are also likely to demonstrate depressive symptomatology in response to their perceived impairments compounds the difficulties involved in establishing an appropriate differential diagnosis. The laboratory findings that have established some of the mechanisms and determinants of cognitive failures in these two different types of disorders can be useful in appropriate differential diagnoses. That is, the determinants of cognitive failures in depression, as described in some of the studies reviewed above, are qualitatively different from those that account for memory-learning-attention failures in progressive dementia patients.

What are some of the distinctive features of cognitive failure in depression that might differentiate it from the cognitive changes apparent in an early stage of a progressive dementia? Depressed patients demonstrate learning and memory failures on tasks that lack easily discernible internal structure, and where the patient must impose organization for effective learning and memory to take place. For example, while recall of random words clearly differentiates the memory-learning performance of patients from undepressed controls, patients are as able as "normals" to learn and remember inherently organized information, such as semantically related words. That this characteristic of the memory-learning failure evident in depression is different from that evident in progressive dementia is illustrated by the findings in the following experiments. The details of these experiments are presented since the methods used, and the findings, can be easily translated into clinical tools for evaluating different types of cognitive impairments.

The learning-memory performance of a group of moderately depressed patients (10 males, 10 females), characterized on the basis of standard Research Diagnostic Criterian, standardized regular mood ratings, and standard psychometric testing, was compared to age-, sex-, and education-matched controls. Subjects learned and remembered different lists of 32 words including unrelated words, and organized word lists consisting of either 2 clusters of 16 words each (e.g., vegetables, parts of a house); 4 clusters of 8 words each, or 8 clusters of 4 words each. Depressed patients recalled significantly fewer words than controls [$F(1,18) = 9.4$; $p < .05$]. The interaction of type of list and groups (depressed vs. controls) was also statistically reliable using a standard repeated measures analysis of variance (ANOVA) and including all available degrees of freedom [$F(6,108) = 3.71$; $p < .01$], as well as by a conservative analysis using Winer's correction for degrees of freedom in a repeated measures design ($p < .05$). That is, depressed patients were most distinguishable from control subjects in recall of unrelated information, and this is illustrated in Figure 1.

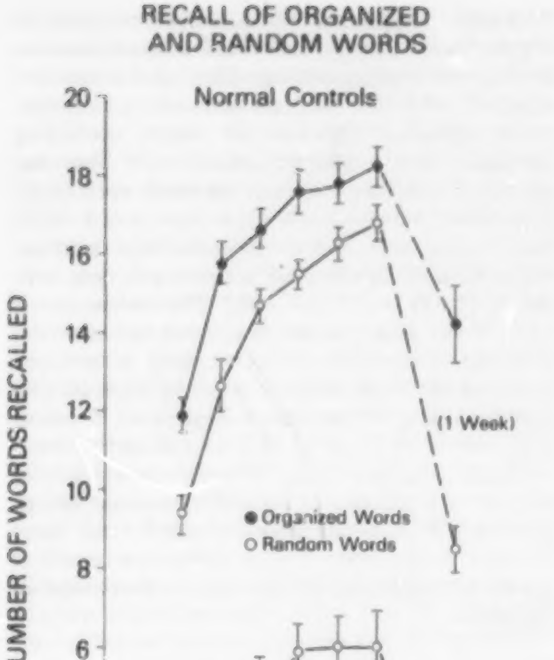


FIGURE 1. Learning and recall of random and related words by depressed patients and normal controls.

In contrast, progressive dementia patients could not use organizational or semantic relational properties of events as an aid in encoding information and, therefore, related events (words) are no more memorable than random words (Weingartner et al., 1981c). This is evident even in those patients who are no more cognitively impaired than depressed patients as measured by tests of IQ, Wechsler Memory Scale Scores, and recall of random words. Progressive dementia patients remembered about the same number of random and related events after a single exposure and after repeated presentation of information. Control subjects, as well as depressed patients, are far more successful in remembering related than random events, and this effect is enhanced with increased familiarization with that information, and also when memory is tested after a period of delay. The following experiment illustrates this aspect of the memory-learning failure in progressive dementia patients who are no more impaired than some depressed patients who have been studied using similar procedures. As will be evident, the form of the memory-learning impairment in these progressive dementia patients is quite different from that seen in depressed patients.

Fourteen patient volunteers (9 males and 5 females) were selected for further study from a much larger sample of patients after extensive systematic standardized clinical, psychometric, and neurological evaluation (for diagnostic purposes). On the basis of detailed historical, clinical, and laboratory data, a diagnosis of a progressive idiopathic dementia, probably of an Alzheimer's type, could be made. Patients, none over 65 years of age, were all in the earliest state of a progressive dementia (based on clinical data as well as psychometric findings, including IQ test scores of at least 100, and impairments in memory as measured by the Wechsler Memory Scale, normal digit span), were otherwise in good health, and were not being treated for other medical disorders. An equal number of age, education, and socioeconomic status matched control volunteers (where possible, the spouse of the patient) were also recruited and studied. Neither patients nor controls had any history of significant psychiatric disorder. Their average age was 61.2 (standard error ± 2.2), and education 14.1 years.

On separate occasions, subjects were presented with two different sets of very common words presented in a randomized sequence. One list consisted of 20 random words and the other was made up of words drawn from two superordinate categories (10 words each) of semantically related words, such as *vegetables* and *parts of the body*. After verbal presentation of each list, at a 3-second rate, immediate free recall was tested. The word list was then re—presented five times, always in a different random order, with a test of recall after each presentation. A delay period was included to measure and test the presence of information in long-term memory. Unimpaired subjects were retested 1 week after the last learning trial while progressive dementia patients attempted another recall after a delay of only 10 minutes. This shorter delay interval was a practical necessity when testing patients with significant memory impairments.

The inability of progressive dementia patients to effectively use organizational or relational properties of to-be-remembered words was evident on immediate recall, list learning, and delayed recall following multiple list presentations of random and related words. Controls consistently remembered more related than random words and this was evident on each presentation (learning) recall trial [$F(1,13) = 18.3$; $p < .001$]. This effect was increasingly evident as list learning continued (interaction of trial × lists [$F(4,5.2) = 53$; $p < .01$]. Recall of related words was also more complete than that of random words when memory was tested one day later [$F(1,13) = 17.5$; $p < .001$]. Progressive dementia patients thus demonstrated memory-learning failures when their cognitive performance is compared to unimpaired controls. More important, and unlike the pattern of cognitive failures in depression, organization did not significantly alter any aspects of learning or memory in these patients. These findings are summarized in Figure 2.

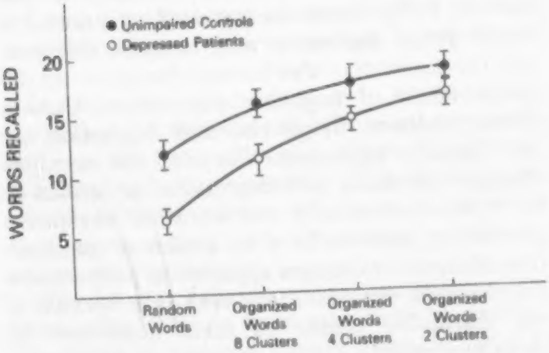


FIGURE 2. Learning and recall of random and semantically related words in patients with a progressive dementia and unimpaired controls.

As described above, laboratory studies of depressed patients demonstrate that learning and memory fail as a function of the difficulty, effort, or cognitive load required in some task. Compared to controls, depressed patients demonstrate more obvious and robust impairments when they are directed to learn and remember information (intentional learning) rather than for incidentally learned information (Weingartner et al., 1981a), when information must be "held" in memory for long rather than short time periods, for more difficult types of learning such as remembering serial order, or under more stringent and demanding remembering conditions such as free recall. As was pointed out above, the cognitive failures in depression are far less evident on "easier" cognitive tasks such as those that involve relatively "automatic," effortless, or passive operations. In contrast, progressive dementia patients fail to learn and remember despite their sustained efforts in performing cognitive operations. Unlike depressed patients, they are particularly distinguishable from controls on "passive" or "automatic" processing tasks such as estimating how often events had occurred, in contrast to freely remembering those events (a more active effortful task). The progressive dementia patient is also different from older controls, who may demonstrate changes in learning and memory requiring effortful processing but are indistinguishable from healthy young subjects on "automatic" processing tasks.

Despite the cognitive blurring and disrupted learning and memory that is apparent in depressed patients, they are able to effectively access knowledge structures such as the semantic relationships, and attributes and meanings of events, and relate this previous learning to ongoing events. For example, when either unimpaired or depressed subjects are asked to think about and say aloud words related to categories of information (such as types of flowers, parts of a house, etc.), they do so easily and are even more productive, over a 2-minute time period, than when thinking of words that might start with the same letter. On the other hand, progressive dementia patients, in generating appropriate associations to names of categories or words all starting with the same letter, are far less productive than controls or depressed patients but, more important, are particularly unproductive in generating words that are all members of the same category (Weingartner et al., 1981c). Their productivity in generating appropriate responses from semantic memory is highly correlated with the learning-memory performance of progressive dementia patients, but this relationship is not evident in depressed patients (Weingartner et al., 1981a).

Methodological Issues

Studies that have explored cognition in depression have differed from one another in three important ways. They have varied with respect to 1) the nature of the independent variable (what constitutes depression); 2) the type of dependent measure (the target cognitive response); and 3) the assumptions and models used to generate questions about cognition in depression. Because of these differences in design, focus of study, and theoretical models used to generate studies and interpret results, it has been difficult to form a general and integrated picture of cognitive changes in depression.

Two types of independent variables have been used in cognitive studies in depression. Comparison of subject groups represents the most frequent method of manipulating depression as an independent variable. Depressed patients are often compared to some control group or to themselves in an undepressed state. One of the problems in obtaining a clear picture of the nature of cognitive changes in depression results directly from the diversity in defining what constitutes depression in some population of subjects. That is, depressed patients studied have varied with respect to the intensity of depression, forms of depressive symptoms, and sub-diagnostic categories. Studies of clinically depressed subjects have included patients who are defined as Bipolar 1, Bipolar 2, or reactive depressions, as well as other forms of unspecified clinical depressions. What can be concluded about the nature of cognitive changes in depression may be quite dependent upon not only the intensity of depressive symptoms but also the type of clinical depression that is studied. There are, in fact, data that would suggest that with respect to quantitative changes in depression, bipolar patients are more likely to demonstrate more profound changes than any other subgroup of depressed patients. Unipolar and bipolar patients, for example, have been found to differ in presenting symptomatology, Rorschach response style, and Minnesota Multiphasic Personality Inventory (MMPI) profile.

It is also not clear to what extent cognitive changes in depressed patients are state vs. trait specific. Little work has been done examining the nature of cognitive processes in patients who have recovered from some depressed episode. This type of data represents just one source of information that is necessary for appropriate evaluation and definition of cognitive changes associated with depressed states.

Other studies have defined depression as the independent variable by choosing to contrast subjects that are drawn from other than clinical populations. These have examined essentially unimpaired subjects in the psychology laboratory. In general, subjects have been selected on the basis of large sampling strategies using some standard psychometric test instrument. Depression is then defined on the basis of statistical rather than clinical criterion. A large variety of scales have been used as methods for defining such subgroups of subjects. The MMPI, the Zung, and Hamilton Depression inventories, standard clinical interviews, life-stress event scales, hopelessness scales, as well as more behaviorally and less subjectively focused scales, were designed to measure cognitive bias in depressed mood (Blaney, Behar, & Head, 1980; Hammen, in press; Krantz & Hammen, 1979; Sarason, Johnson, & Siegel, 1978; Seligman, Abramson, Semmel, & von Baeyer, 1979). These measures of behaviors that would define depression may be quite different, and the scales may also be anticipated to tap different facets of cognitive experience. Unhappiness, sadness, dysphoria, and depression are not logically equivalent. Clearly, the cognitive changes associated with depression, as defined by some psychometrically and statistical evaluation procedure, may not be at all similar to the structure of cognitive changes apparent in patients who are clinically depressed and seek help because of the disruptive effects of their experience of dysphoric mood.

The other method of defining depression, the independent variable for study, is through some behavioral manipulation of mood. Those behavioral manipulations have primarily been directed at affecting mood changes in unimpaired normal controls under laboratory test conditions. These mood-induction procedures have been useful in inducing mild depression, which is presumed to model the kinds of dysphoric moods that are evident in depressed patients. Frequently, the manipulations used are conceptually tied to studies that would test behavior-oriented models of depression. Two types of manipulations have been used. One has involved the use of some informational context. For example, a subject may be asked to read statements that describe various moods. These are then used to provide a contextual mood-altered setting for processing information about self and others (Velton, 1968). Many subjects, when asked to read statements with dysphoric content, rate themselves as depressed, which may then be reflected in cognitive behaviors as measured by response latency and speech patterning (Natale, 1977) and other measures of cognitive efficiency. A second commonly used technique for altering mood has involved manipulations such as feedback on some task that requires skill, as in the form of a success vs. failure manipulation (Diener & Dweck, 1978; Hammen & Krantz, 1976) on a skill task. It can also involve a manipulation of reinforcing consequences or informational feedback on some task which may affect self-esteem (Coleman, 1975). Other behavioral manipulations may induce a form of helplessness through experimenter-induced failure (Abramson et al., 1968). In all of these approaches what is being tested is how a manipulation of mood, through informational or behavioral means, may affect aspects of information processing, problem solving, interpersonal perceptions, or perceptions about self. The assumption is, again, that these alterations in mood that are a product of behavioral manipulations are like those evident in depressed patients. Whether such manipulations of mood in unimpaired subjects mimic the types of cognitive changes associated with depression remains an unanswered question.

The nature of the dependent variable has also been quite different from one study to another. The kinds of cognitive measures that are used to assess performance in depressed patients, recovered patients, or normal subjects after some manipulation of mood have been quite variable. The cognitive response may be one that assesses how thoughts are organized, what is remembered, the meaning of prior-life events, how well a complex cognitive behavior is accomplished, the effectiveness in interacting with an information-rich environment, concept attainment, encoding of self, or significant others. Clearly, the kinds of changes in cognition that would occur in the depressed state would be expressed rather differently depending on the type of cognitive behaviors used as target measures for cognitive changes.

The theoretical models and assumptions that are used both to generate strategies for looking at depression and interpreting findings are also quite different from one another. These have included biological, behavioral, information processing, and psychodynamic models of depression. Unfortunately, both the nature of the findings that have been generated and their interpretation have not been easily integrated and synthesized. In part, this is due to the intrinsic differences in the language systems used to describe events in biological psychiatry, psychodynamic theory and application, and behavioral approaches to psychopathology. Investigators speak one of these languages and not others. It is, therefore, particularly difficult to relate findings generated from those very different conceptual schemes for the analysis of behavior.

There remain many unresolved questions about the psychobiology of cognitive processes in mood disorders. A good deal of work has been done, but more remains to be accomplished.

What might be some productive themes for future investigations? Clearly, cognitive changes that are apparent during periods of disordered mood must be evaluated and contrasted with cognitive processes during normal mood states in these same patients. This requires following patients systematically over time. It may also be useful to evaluate first-degree relatives of these same patients or subjects who may be considered to be at risk for affective illness. Are cognitive processes in these patients, mood-state specific or trait specific, and do the types of cognitive processes used by these subjects, while unimpaired, predict or make these subjects vulnerable to a mood disorder? Further research in this area should allow for more effective and deliberate integration of clinical material, findings from unimpaired subjects where mood is manipulated, behavioral views of mood disorder, and information processing characterizations of cognition in mood-disorder patients. Without such integration of methods, findings, and interpretation of findings, this area of study will remain as a series of isolated efforts without the necessary research leverage that permits us to answer basic questions about cognitive processes in mood disorders.

Last, and a related issue, is the fact that although we have learned a great deal about the biology of mood disorder and about the psychology of disordered mood, surprisingly little research has been accomplished that would bring these two types of research endeavors together in a systematic manner. This may be most effectively accomplished in considering cognitive processes in the mood disorders.

References

Abramson, L.Y., Seligman, M.E.P., and Teasdale, J.D. Learned helplessness in humans. Critique and reformulation. *J. Abnorm. Psychol.*, 87:49-74, 1968.

Ahern, G.L., and Schwartz, G.E. Differential lateralization for positive versus negative emotions. *Neuropsychologia,* 17:693-697, 1979.

Alema, G., Rosadini, G.R., and Rossi, G.F. Psychic reactions associated with intracarotid Amytal injection and relation to brain damage. *Excerpta Medica,* 37:154-155, 1961.

Atkinson, R.C., and Shiffrin, R.M. Human memory: A proposed system and its control processes. In: Spence, K.W., and Spence, J.T. (eds.), *The Psychology of Learning and Motivation: Advances in Theory and Research* (Vol. 2). New York: Academic Press, 1968.

Bandura, A. Self-efficacy: Toward a unifying theory of behavioral change. *Psychol. Rev.*, 84(2):191-215, 1977.

Beck, A.T. *Depression: Clinical, Experimental, and Theoretical Aspects.* New York: Hoeber, 1967.

Beck, A.T. Cognition, affect, and psychopathology. *Arch. Gen. Psychiatry,* 24:495-500, 1971.

Beck, A.T. The development of depression: A cognitive model. In: Friedman, R.S., and Katz, M.M. (eds.), *The Psychology of Depression: Contemporary Theory and Research.* New York: John Wiley & Sons, 1974.

Biegel, A., and Murphy, D.L. Unipolar and bipolar affective illness: Differences in clinical characteristics accompanying depression in unipolar and bipolar illness. *Arch. Gen. Psychiatry,* 24:215-220, 1971.

Blaney, P.H. Contemporary theories of depression: Critique and comparison. *J. Abnorm. Psychol.*, 86:203-223, 1977.

Blaney, P.H., Behar, V., and Head, R. Two measures of depressive cognitions: Their association with depression and with each other. *J. Abnorm. Psychol.*, 89:678-682, 1980.

Breslow, R., Kocis, J., and Belkin, B. Contributions of the depressive perspective to memory function in depression. *Am. J. Psychiatry,* 138:227-230, 1981.

Brown, G.W., Sklair, F., Harris, T.O., and Burley, J.L.T. Life events and psychiatric disorders. Part I: Some methodological issues. *Psychol. Med.*, 3:74-87, 1973.

Buchsbaum, M.S., Carpenter, W.T., Jr., and Fedio, P. Hemispheric differences in evoked potential enhancement by selective attention to hemiretinally presented stimuli in schizophrenic, affective, and post-temporal lobectomy patients. In: Gruzelier, W.H., and Flor-Henry, P. (eds.), *Hemispheric Asymmetries of Functions in Psychopathology.* Amsterdam: Elsevier Press, 1979.

Buchwald, A.M., Coyne, J.C., and Cole, C.S. A critical evaluation of the learned helplessness model of depression. *J. Abnorm. Psychol.*, 87:180-193, 1978.

Cohen, R.M., Weingartner, H., Smallberg, S.A., and Murphy, D.L. Effort in cognitive processes in depression. *Arch. Gen. Psychiatry.* (In press)

Coleman, R.E. Manipulation of self-esteem as a determinant of mood of elated and depressed women. *J. Abnorm. Psychol.*, 84:693-700, 1975.

Costello, C.G. A critical review of Seligman's laboratory experiments on learned helplessness and depression in humans. *J. Abnorm. Psychol.*, 87:21-31, 1978.

Coyne, J.C., Metalsky, G.I., and Lavelle, T.L. Learned helplessness as experimenter-induced failure and its alleviation with attentional redeployment. *J. Abnorm. Psychol.*, 89:350-357, 1980.

Craik, F.I.M., and Lockhardt, R.S. Levels of processing: A framework for memory research. *J. Verb. Learning Verb. Behav.*, 11:671-684, 1972.

Craik, F.I.M., and Tulving, E. Depth of processing and the retention of words in episodic memory. *J. Exp. Psychol. Gen.*, 1:268-294, 1975.

Davidson, R.J., Schwartz, G.E., Saron, C., et al. Frontal vs. parietal EEG asymmetry during positive and negative affect. *Psychophysiology,* 16:202-203, 1979. (Abstract)

d'Elia, G., and Perris, C. Cerebral functional dominance and depression: An analysis of EEG amplitude in depressed patients. *Acta Psychiatr. Scand.*, 49:191-197, 1973.

d'Elia, G., and Perris, C. Cerebral functional dominance and memory functions: An analysis of EEG integrated amplitude in depressive psychotics. *Acta Psychiatr. Scand. (Suppl.),* 255:143-157, 1974.

Diener, C., and Dweck, C. An analysis of learned helplessness: Continuous changes in performance, strategy, and achievement cognitions following failure. *J. Pers. Soc. Psychol.*, 36:451-462, 1978.

Donnelly, E.F., Murphy, D.L., and Goodwin, F.K. Cross-sectional and longitudinal comparison of bipolar and unipolar depressed groups on the MMPI. *J. Consult. Clin. Psychol.*, 44:233-237, 1976.

Donnelly, E.F., Murphy, D.L., and Scott, W.H. Perception and cognition in patients with bipolar and unipolar depressive disorder. *Arch. Gen. Psychiatry,* 32:1128-1131, 1975.

Eich, J.E., Weingartner, H., Stillman, R.C., and Gillin, J.C. State-dependent accessibility of retrieval cues in the retention of a categorized list. *J. Verb. Learning Verb. Behav.*, 14:408-417, 1975.

Flor-Henry, P. On certain aspects of the localization of the cerebral systems regulating and determining emotion. *Biol. Psychiatry,* 14:677-698, 1979.

Forrest, A.D., Fraser, R.H., and Priest, R.G. Environmental factors in depressive illness. *Br. J. Psychiatry,* 111:243-253, 1965.

Gainotti, G. Emotional behavior and hemispheric side of the lesion. *Psychophysiology,* 16:561-573, 1979.

Garmezy, N. The prediction of performance in schizophrenia. In: Hoch, P.H., and Zubin, J. (eds.) *Psychopathology of Schizophrenia.* New York: Grune & Stratton, 1966.

Goldstein, S.G., Filskow, S., Weaver, L.A., and Ives, J.O. Neuropsychological effects of electroconvulsive therapy. *J. Clin. Psychol.,* 33:798-806, 1977.

Goodwin, D.W., Powell, B., Bremer, D., et al. Alcohol and recall: State-dependent effects in man. *Science,* 163:1358-1360, 1969.

Gur, R.E. Cognitive concomitants of hemispheric dysfunction in schizophrenia. *Arch. Gen. Psychiatry,* 36:269-274, 1979.

Hale, W.D., and Strickland, B.R. Induction of mood states and their effect on cognitive and social behaviors. *J. Consult. Clin. Psychol.,* 44:155, 1976.

Hammen, C.L. Assessment of depressive behaviors: A clinical and cognitive emphasis. In: Rehm, L.P. (ed.), *Behavior Therapy for Depression: Present Status and Future Directions.* New York: Academic Press. (In press)

Hammen, C.L., and Cochran, S.D. Cognitive correlates of life stress and depression in college students. *J. Abnorm. Psychol.,* 90:23-27, 1981.

Hammen, C.L., and Krantz, S. Effect of success and failure on depressive cognitions. *J. Abnorm. Psychol.,* 85:577-586, 1976.

Harness, B., Bental, E., and Carmon, A. Comparison of cognition and performance in patients with organic brain damage and psychiatric patients. *Acta Psychiatr. Belg.,* 73:339-347, 1977.

Hasher, L., and Zacks, R.T. Automatic and effortful processes in memory. *J. Exp. Psychol. Gen.,* 108:356-388, 1979.

Henry, G.M., Weingartner, H., and Murphy, D.L. Influence of affective states and psychoactive drugs on verbal learning and memory. *Am. J. Psychiatry,* 130:966-971, 1973.

Hiroto, D.S. Locus of control and learned helplessness. *J. Exp. Psychol.,* 102:187-193, 1974.

Huesmann, L.R. Cognitive processes and models of depression. *J. Abnorm. Psychol.,* 87:194-198, 1978.

Jacobs, S.C., Prusoff, B.A., and Paykel, E.S. Recent life events in schizophrenia and depression. *Psychol. Med.,* 4:444-453, 1974.

Klein, D.C., and Seligman, M.E.P. Reversal of performance deficits and perceptual deficits in learned helplessness and depression. *J. Abnorm. Psychol.,* 85:11-26, 1976.

Koh, S.D., Kayton, L., and Berry, R. Mnemonic organization in young nonpsychotic schizophrenics. *J. Abnorm. Psychol.,* 81:299-310, 1973.

Krantz, S., and Hammen, C. Assessment of cognitive bias in depression. *J. Abnorm. Psychol.,* 88:611-619, 1979,

Kronfol, Z., Hamsher, K., deS. Digree, K., and Wazir, R. Depression and hemisphere functions: Changes associated with unilateral ECT. *Br. J. Psychiatry,* 132:560-567, 1978.

Lawson, R., and Marx, M.H. Frustration: Theory and experiment. *Genet. Psychol. Monogr.,* 57:393-464, 1958.

Lazarus, R.S., Deese, J., and Osler, S.F. The effects of psychological stress on performance. *Psychol. Bull.,* 49:293-317, 1952.

Lewinsohn, P.M., Mischel, W., Chaplain, W., and Barton, R. Social competence and depression: The role of illusory self-perceptions? *J. Abnorm. Psychol.,* 89:203-212, 1980.

Lewis, D.J. Psychobiology of active and inactive memory. *Psychol. Bull.,* 88:1054-1083, 1979.

Lishman, W.A. Selective factors in memory. *Psychol. Med.,* 2:248-253, 1972.

Lucas, J.D. The interreactive effects of anxiety failure and interserial duplication. *Am. J. Psychol.,* 33:31-40, 1952.

Maier, S.F., and Seligman, M.E.P. Learned helplessness: Theory and evidence. *J. Exp. Psychol. (Gen.),* 105:3-46, 1976.

McGaugh, J.L. Time dependent processes in memory storage. *Science,* 153:1351-1358, 1966.

McGaugh, J.L., Zornetzer, S.F., Gold, P.E., and Landfield, P.W. Modification of memory systems: Some neurobiological aspects. *Q. Rev. Biophys.,* 5:163-186, 1972.

Miller, W.R. Psychological deficit in depression. *Psychol. Bull.,* 32:238-260, 1975.

Myslobodsky, M.S., and Horesh, N. Bilateral electrodermal activity in depressive patients. *Biol. Psychol.,* 6:111-120, 1978.

Natale, M. Effects of induced elation-depression on speech in the initial interview. *J. Consult. Clin. Psychol.,* 45:45-52, 1977.

Nelson, R.E., and Craighead, W.E. Selective recall of positive and negative feedback, self-control behaviors, and depression. *J. Abnorm. Psychol.,* 86:379-388, 1977.

Overton, D.A. Dissociated learning in drug states (state-dependent learning). In: Efron, D.H., Cole, J.O., Levine, J. and Wittenborn, R. (eds.), *Psychopharmacology: A Review of Progress, 1957-1967.* Washington, D.C.: U.S. Government Printing Office, 1963.

Overton, D.A. Discriminative control of behavior by drug states. In: Thompson, T., and Pickens, R. (eds.), *Stimulus Properties of Drugs.* New York: Appleton-Century-Crofts, 1971.

Parker, E.S., Birnbaum, I.M., Weingartner, H., et al. Retrograde enhancement of human memory with alcohol. *Psychopharmacologia (Berlin),* 69:219-222, 1980.

Paykel, E.S. Environmental variables in the etiology of depression. In: Flack and Draghi (eds.), *The Nature and Treatment of Depression.* New York: John Wiley & Sons, 1975.

Paykel, E.S., Myers, J.K., Drenelt, M.N., et al. Life events and depression. *Arch. Psychiatry,* 21:753-760, 1969.

Raps, C.S., Reinhard, K.E., and Seligman, M.E.P. Reversal of cognitive and affective deficits associated with depression and learned helplessness by mood elevation in patients. *J. Abnorm. Psychol.,* 89:342-349, 1980.

Reus, V.I., Silberman, E., Post, R.M., and Weingartner, H. d-Amphetamine: Effects on memory in a depressed population. *Biol. Psychiatry,* 14:345-356, 1979.

Rizley, R. Depression and distortion in the attribution of causality. *J. Abnorm. Psychol.,* 87:32-48, 1978.

Rochford, J., Swartzburg, M., Chaudhery, S.M., and Goldstein, L. Some quantitative EEG correlates of psychopathology. *Res. Com. Psychol. Psychiatry Behav.,*

1:211-226, 1976.

Roemer, R.A., Shagass, C., Straumanis, J.J., and Amadeo, M. Pattern-evoked potential measurements suggesting lateralized hemispheric dysfunction in chronic schizophrenics. *Biol. Psychiatry,* 13:185-202, 1978.

Rossi, G.F., and Rosadini, G.R. Experimental analyses of cerebral dominance in man. In: Millikan, D.H., and Darley, F.L. (eds.), *Brain Mechanisms Underlying Speech and Language.* New York: Grune & Stratton, 1967.

Russell, P.W., and Beekhuis, M.E. Organization in memory: A comparison of psychotics and normals. *J. Abnorm. Psychol.,* 85:527-534, 1976.

Sarason, I.G., Johnson, J.H., and Siegel, J.M. Assessing the impact of life change: Development of the Life Experiences Survey. *J. Consult. Clin. Psychol.,* 46:932-946, 1978.

Savard, R.J., Rey, A.C., and Post, R.M. Halstead-Reitan category test in bipolar and unipolar affective illness. Relationship to age and place of illness. *J. Nerv. Ment. Dis.,* 168:297-304, 1980.

Schwartz, G.E., Ahern, G.L., and Brown, S.L. Lateralized facial muscle response to positive and negative emotional stimuli. *Psychophysiology,* 16:561-573, 1979.

Seligman, M.E.P. Depression and learned helplessness. In: Freedman, R.J., and Katz, M.M. (eds.), *The Psychology of Depression: Contemporary Theory and Research.* New York: John Wiley & Sons, 1971.

Seligman, M.E.P. *Helplessness: On Depression, Development, and Death.* San Francisco: W.H. Freeman, 1975.

Seligman, M.E.P. Comment and integration. *J. Abnorm. Psychol.,* 87:165-179, 1978.

Seligman, M.E.P., Abramson, L.Y., Semmel, A., and von Baeyer, C. Depressive attributional style. *J. Abnorm. Psychol.,* 88:242-248, 1979.

Small, I.F., Small, J.G., Milstein, V., and Moore, J.E. Neuropsychological observations with psychosis and somatic treatment. *J. Nerv. Ment. Dis.,* 155:6-13, 1972.

Sternberg, D.E., and Jarvik, M.E. Memory functions in depression. *Arch Gen. Psychiatry,* 33:219-224, 1976.

Stromgren, L.S. The influence of depression on memory. *Acta Psychiatr. Scand.,* 56:108-128, 1977.

Teasdale, J.D., and Fogarty, S.J. Differential effects of induced mood on retrieval of pleasant and unpleasant events from episodic memory. *J. Abnorm. Psychol.,* 88:248-257, 1979.

Velten, E., Jr. A laboratory task for induction of mood states. *Behav. Res. Ther.,* 6:473-482, 1968.

Weingartner, H. Human state-dependent learning. In: Ho, B.T., Richards, D., III, and Shute, D.L. (eds.), *Drug Discrimination and State-Dependent Learning.* New York: Academic Press, 1977.

Weingartner, H., Adefris, W., Eich, J.E., and Murphy, D.L. Encoding-imagery specificity in alcohol state-dependent learning. *J. Exp. Psychol. (Hum. Learn.),* 2:83-87,1976.

Weingartner, H., Cohen, R.M., Martello, J.D.I., and Gerdt, C. Cognitive processes in depression. *Arch. Gen. Psychiatry,* 38:42-47, 1981a.

Weingartner, H., Gold, P.W., et al. Vasopressin enhances memory consolidation in man. *Science,* 217:601-603, 1981b.

Weingartner, H., Hall, B., Murphy, D.L., and Weinstein, M. Imagery, affective arousal, and memory consolidation. *Nature,* 263:311-312, 1976.

Weingartner, H., Kaye, W., Smallberg, S.A., et al. Memory failures in progressive idiopathic dementia. *J. Abnorm. Psychol.,* 90:187-196, 1981c.

Weingartner, H., Miller, H., and Murphy, D.L. Mood-state-dependent retrieval of verbal associations. *J. Abnorm. Psychol.,* 86:276-284, 1977.

Weingartner, H., Murphy, D.L., and Stillman, R.C. Mood-state-dependent learning. In: Colpaert, F.C., and Rose-crans, J.A. (eds.), *Stimulus Properties of Drugs: Ten Years of Progress.* Amsterdam: Elsevier/North Holland Biomedical Press, 1978.

Wener, A.E., and Rehm, L.P. Depressive affect: A test of behavioral hypotheses. *J. Abnorm. Psychol.,* 84:221-227, 1975.

Wortman, C.B., and Dintzer, L. Is an attributional analysis of the learned helplessness phenomenon viable? A critique of the Abramson-Seligman-Teasdale reformulation. *J. Abnorm. Psychol.,*87:75-90, 1978.

Wyrick, R.A., and Wyrick, L.C. Time experience during depression. *Arch. Gen. Psychiatry,* 34:1441-1443, 1977.

Yozawitz, A., Bruder, G., Sutton, S., et al. Dichotic perception: Evidence for right hemisphere dysfunction in affective psychosis. *Br. J. Psychiatry,* 135:224-237, 1979.

Electroconvulsive Therapy: Research Goals

Section Editors:

Richard Abrams, M.D., Professor and Vice-Chairman, Department of Psychiatry, University of Health Sciences/The Chicago Medical School, No. Chicago, IL 60064.

Jack Blaine, M.D., Research Psychiatrist, Pharmacologic and Somatic Treatments Research Branch, National Institute of Mental Health, Rockville, MD 20857.

This special section of the *Psychopharmacology Bulletin* is devoted to the proceedings of two conferences held in Chicago on November 13-15, 1980 and January 29-31, 1981.[1] The purpose of these meetings was to review the present "state-of-the-art" with regard to electroconvulsive therapy (ECT) research and to generate specific recommendations to the National Institute of Mental Health (NIMH) concerning the major research problems facing ECT investigators during the present decade. These conferences evolved from two prior NIMH-sponsored conferences on ECT. The first, "Psychobiology of Convulsive Therapy" (Fink, Kety, McGaugh, et al., 1974), attempted to define the cognitive, technical, physiological, and biochemical parameters of ECT as they were then known, drawing upon both human and animal studies. The conclusions of this conference were that there had been significant advances in ECT techniques, resulting in an overall reduction in the undesirable side effects of this treatment, and that the major unresolved issue concerned the mode of action of ECT.

The second conference, "ECT: Efficacy and Impact" (Autry, to be published), focused on the short- and long-term impact of ECT on the organism, and on an assessment of its clinical efficacy in a wide range of psychiatric disorders. This conference provided a comprehensive and detailed historical assessment of the convulsive therapy process, and concluded by addressing some of the critical research needs in the field, many of which served as foci for the 1980-1981 conferences.

After more than 40 years, ECT remains a widely used treatment in this country. An estimated 73,000 patients per year (4.4/10,000 population) receive this treatment (Fink, 1979) with greatest usage in the general hospital. About 72% of American psychiatrists believe it to be the safest, least expensive, and most effective treatment for many patients, and 22% of those sampled personally administer the treatment (APA, 1978).

This special section amply demonstrates that although much is known about ECT, more remains to be learned. It is our hope that these papers will stimulate others to investigate the problems detailed here, with the aim of developing a more rational and effective therapy.

References

American Psychiatric Association, Task Force Report #14 on Electroconvulsive Therapy. American Psychiatric Association, Washington, D.C., 1978.

Autry, J. ECT: Efficacy and Impact. Presented at conference in New Orleans, La., Feb. 22-25, 1978. (To be published)

Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy*. New York: V.H. Winston & Sons, 1974.

Fink, M. (ed.) *Convulsive Therapy: Theory and Practice*. New York Raven Press, 1979.

---

[1] Supported by Grant MH-35518 from the National Institute of Mental Health.

The Importance of Diagnostic Criteria for Depression in the Study of ECT

Michael Alan Taylor, M.D.[1]

The keystone to quality clinical research is proper patient selection based upon reliable, operationally defined diagnostic criteria. Despite the use of sophisticated laboratory procedures or potent psychotropic agents, data from studies which do not employ rigorous patient selection cannot be generalized with any assurance, and the investigators are likely to miss real effects or report spurious findings.

Prior to the 1970s, reliable psychiatric research criteria were not available. The conflicting and confusing findings of the literature of that era, in part, reflect the lack of reliable diagnostic instruments necessary to eliminate from study the false positive subject and select homogeneous samples for investigation.

Several sets of reliable and operationally defined research criteria were developed in the 1970s (Feighner, Robins, Guze, et al., 1972; Spitzer, Endicott, & Robins, 1975; Taylor & Abrams, 1978). These criteria have permitted greater precision in subject selection and have helped clarify some of the confusion generated by older studies. The exposure of the overdiagnosis of schizophrenia and the underdiagnosis of affective disorder in the pre-1970s is perhaps the most important effect of the introduction of modern criteria (Taylor & Abrams, 1978; Pope & Lipinski, 1978).

Several categories in the nosology of mental disorders remain controversial, despite the recent advances in diagnosis. This is particularly true for the category of depression. As depression is the primary indication for electroconvulsive therapy (ECT) (Taylor, in press), a clearly defined, generally accepted concept of depression is essential for research attempting to understand the ECT process. Much of the controversy revolves around the putative validity of the endogenous/nonendogenous depression dichotomy.

As initially proposed (Gillespie, 1929; Lange 1926; Kraepelin, 1921), endogenous depression referred to a syndrome reflecting some unknown morbid process characterized by a clear-cut episode of profound and unremitting sadness associated with early morning wakening, anorexia, dry-mouth, inability to cry, constipation, a diurnal cycle in which symptoms were most severe in the morning, psychomotor retardation or agitation, and feelings of hopelessness, worthlessness, and/or guilt which often resulted in delusional ideas and/or perceptional aberrations. Reactive depression referred to a less well-defined episode of dysphoria with anxiety which was responsive or reactive to environmental stimuli and was associated with weeping, initial insomnia, weight gain, and feelings of anger. The literature evaluating the efficacy of ECT and antidepressant. agents (Taylor, in press; Fink, 1978; Prusoff, Weissman, Klerman, & Rounsaville, 1980; Nelson & Charney, 1981) clearly demonstrates endogenous depression to be extremely responsive to somatic treatment, whereas few reactive depessives respond to biological therapy and many are made worse. Despite the clear-cut distinction between the severe endogenous and mild reactive syndromes and their different responsivity to treatment, several investigators (Kendall, 1968; Lewis, 1934; McConaghy, Joffe, Murphy, et al., 1967; Weckowicz, Cropley, & Muir, 1971) were unable to discriminate the boundary between the two putative groups and concluded that the overlap was so great that the dichotomy was not warranted. Perhaps the best known works in this area are Kendall's (1968; Kendall & Gourlay, 1970a) elaborate discriminant function studies.

In these studies, variation of depressive symptomatology is expressed by a score on a linear discriminant function found from analyses of a number of items measured from patients originally diagnosed endogenous or nonendogenous. The distribution of the scores is then used to make inferences about the homogeneity of depression with a bimodal distribution indicative of subtypes and a unimodal distribution indicative of a single syndrome. In Kendall's two series a unimodal distribution was demonstrated. This has become the primary evidence in refutation of the endogenous/nonendogenous dichotomy. There are, however, several problems in interpreting this work. First, despite presenting a unimodal curve, many of the discriminant functions were significantly weighted in the predicted direction, and Kendall was able to correctly classify 86% of the sample. Secondly, although the overall distribution of discrimant functions did not differ significantly from a normal distribution, the chi-square reported comes close to significance, suggesting that measurement errors in the design (such as the significant difference in the sizes of the endogenous/nonendogenous groups and the lack of diagnostic criteria for patient selection) could have resulted in a Type II error, i.e., failing to find a real difference. Thirdly, demonstrating a bimodal distribution may be difficult, even for clearly different groups, if the two groups share more characteristics than the number which separates them or if characteristics are not properly weighted when some characteristics are more important than others at discriminating groups. For example, men and women have more physical characteristics in common than the number which clearly distinguishes them, and some of their distinguishing characteristics are more important than others. A discriminant function distribution curve of the sexes not adequately considering the overlap of characteristics or not weighting some characteristics might well be unimodal despite clear sexual dimorphism. Certainly, Kendall and Gourley's (1970b) inability to find a bimodal distribution for a sample of patients with schizophrenia or affective disorder suggests that this kind of analysis has limited usefulness. Finally, as Murphy (1964) and Everett (1981) have pointed out, bimodal and unimodal distributions of discriminant scores can be obtained at will from the same group of patients by choosing variables appropriately when samples are small (as in Kendall's studies), when putative subgroups are not well separated, or when the predicted variable is poorly defined (as may be the case for nonendogenous depression) (Akiskal, Bitar, Puzantran, et al., 1978; Nelson, Charney, & Quinlan, 1981) and by manipulating the class intervals for the distribution histogram. Nevertheless, some studies evaluating the power of "classical" endogenous and reactive symptoms to predict treatment response (Coryell, Ziegler, & Biggs, 1980), and one study comparing morbidity risks for affective disorder in the first-degree relatives of endogenous and reactive probands (Winokur & Pitts, 1964) also failed to support the dichotomous classification of depression.

---

[1] Department of Psychiatry and Behavioral Sciences, University of Health Sciences/The Chicago Medical School, North Chicago, IL 60064.

Modern diagnostic criteria have been influenced significantly by these negative studies. The Research Diagnostic Criteria (RDC) and the Diagnostic and Statistical Manual-III (DSM-III) attempt to finesse the issue by permitting subtyping within the broad category of major depression, and by not requiring clear-cut exclusion criteria to prevent contamination between subgroups. The Feighner et al. (1972) criteria reject subtypes of depression and consider primary affective disorder homogeneous.

Nevertheless, there is significant evidence (Carroll, Feinberg, Greden, et al., 1980; Feinberg, Carroll, Steiner, & Commorato, 1979; Klerman, Endicott, Spitzer, & Hirschfeld, 1979; Nelson, Charney, & Vingaino, 1978) that the above sets of criteria select heterogeneous samples of depressives which fit more readily into the endogenous/nonendogenous classification. Feinberg's and Carroll's work (1979, 1980) typifies this literature. They and their associates challenged RDC and Feighner positive depressives, who were independently and blindly reclassified as endogenous or reactive, with dexamethasone, a highly sensitive and reliable test for discriminating depression. Forty percent of the endogenous patients failed to suppress their control levels in response to dexamethasone, whereas 98% of reactive patients showed suppression. From this and other studies, investigators estimate that of patients labeled depressed by RDC or Feighner criteria, 50 to 70% are inappropriately classified and unsuitable for research of present-day biological treatment. This estimate is supported by studies of bereavement (Bornstein, Clayton, Halikas, et al., 1973; Clayton, Halikas, & Maurice, 1972) in which nearly 50% of widowed subjects satisfied Feighner criteria for primary depression, although neither the investigators nor the "Feighner-positive" subjects felt that they were ill. There was also no evidence (e.g., past personal history of affective disorder, family history of affective disorder) that these Feighner-positive individuals were predisposed to a disease.

Further support for the endogenous/nonendogenous dichotomy derives from laboratory work studying the sedation threshold (Perez-Reyes, 1968; Perez-Reyes & Cochrane, 1967; Shagass, Neiman, & Mihalick, 1956) and growth hormone response to amphetamine (Langer, Heinze, Reim, & Matussek, 1975). The sedation threshold is defined as the amount of barbiturate given intravenously at a fixed rate which will produce specific changes in electroencephalograph (EEG) frontal fast activity consistent with a reduction in alertness. Shagass et al. (1956) first demonstrated a significantly lower-than-normal sedation threshold in endogenously depressed patients and a significantly higher-than-normal sedation threshold in reactive depressives. This work was replicated but with considerable difficulty. More recently, Perez-Reyes, in a double-blind, well-controlled study (1967, 1968) investigated the sedation threshold using the galvanic skin response (GSR) as a validating and reliable measure of sedation threshold EEG changes and found reactive depressives, normal controls, and endogenous depressives to differ significantly in the predicted direction in their response to barbiturate on both EEG and GSR inhibition. Similarly, Langer et al. (1976) in their investigation of the hypothalamic-pituitary axis in psychiatric disorders, demonstrated that peak human growth hormone release after a single intravenous administration of amphetamine was significantly lower in endogenous depressives and significantly higher in reactive depressives as compared to normal subjects and other psychiatric patients who did not differ from the normal controls.

Recent studies of the phenomenology of depression offer further support for the endogenous/nonendogenous dichotomy (Matussek, Soldner, & Nagel, 1981). Blashfield and Morey (1979) compared the results of 11 studies which used cluster analysis to discriminate subgroups of depressives. Their analysis rejected the continuum model of depression, in which the endogenous syndrome is considered the more severe form, and the investigators concluded that as a group, cluster analytic studies demonstrate two depressive syndromes, one consistent with endogenous and one consistent with nonendogenous depression. Nelson and Charney (1981) have reviewed in great detail studies employing factor analysis, cluster analysis, discriminant function analysis, symptom frequency comparisons, and objective instrumental measures correlated with behavior (e.g., EEG recording of sleep patterns, cognitive testing) and have concluded from their review and from their own data (1981) that endogenous depression is an autonomous pathophysiological state distinct from the nonendogenous syndrome. In contrast, Akiskal et al.(1978) have demonstrated the heterogeneity and instability of reactive depression.

Thus, from treatment response, symptom pattern, and biological data endogenous depression appears to be a distinct clinical entity that is particularly reponsive to somatic treatment. As the use of DSM-III, RDC, and Feighner criteria will result in the inclusion of many false positive patients who do not have the endogenous syndrome, it is important to modify these criteria for studies of affective disorder and biological therapies.

The data summarized above suggest that this modification of present research criteria for depression is best achieved by 1) selecting patients who satisfy the inclusion criteria for melancholia or endogenous depression, and 2) excluding those who demonstrate coexisting or past behaviors consistent with anxiety states or Briquet's syndrome, who have no evidence of coarse brain disease, drug ingestion, or systemic illness known to produce depressive symptoms, and who have no concurrent alcohol or drug abuse. The Table displays these suggested criteria.

The recommendation to use rigorous criteria to identify endogenous depressives for studies of affective disorder and biological treatments does not mean that all such patients have a common pathophysiology. However, if we are to progress further in our understanding of what makes people depressed and how ECT works, the best possible delineation of depressive disorder is an essential first step.

Table

Suggested Research Diagnostic Criteria for Depression (Modified from RDC)

Inclusion Criteria (all required)

1. Must have loss of pleasure in all or almost all activities, lack of reactivity to usually pleasurable stimuli (doesn't feel much better, even temporarily, when something good happens)
2. Distinct quality of depressed mood, i.e., the depressed mood is perceived as distinctly different from the kind of feeling experienced following the death of a loved one
3. Must have two of the following present nearly every day for a period of at least 2 weeks:
    - a) early morning wakening (at least 2 hours before usual time of awakening)
    - b) depression is regularly worse in morning
    - c) marked psychomotor retardation or agitation (but not merely subjective feelings of restlessness or being slowed down)
    - d) anorexia with at least 2.5 kg weight loss
    - e) excessive or inappropriate guilt (may be delusional)

Exclusion Criteria (all required)

1. No evidence of coexisting or past anxiety disorder, somatoform disorder, or disassociable disorder
2. No evidence of coarse brain disease, drug ingestion, or systemic illness known to produce depressive symptoms.

References

Akiskal, H.S., Bitar, A.H., Puzantran, V.R., et al. The nosological status of neurotic depression: A prospective three-to-four-year followup examination in light of the primary-secondary and unipolar-bipolar dichotomies. *Arch. Gen. Psychiatry,* 35:756-766, 1978.

Blashfield, R.K., and Morey, L.C. The classification of depression through cluster analysis. *Compr. Psychiatry,* 20:516-527, 1979.

Bornstein, P.E., Clayton, P.J., Halikas, J.A., et al. The depression of widowhood after thirteen months. *Br. J. Psychiatry,* 121:561-566, 1973.

Carroll, B.J. Feinberg, M., Greden, J.F., et al. Diagnosis of endogenous depression. *J. Affect. Disord.,* 2:177-194, 1980.

Clayton, P.J., Halikas, J.A., and Maurice, W.L. The depression of widowhood. *Br. J. Psychiatry,* 120:71-78, 1972.

Coyrell, W., Ziegler, V.E., and Biggs, J.T. Symptoms as predictors of response to amitriptyline and nortriptyline. *J. Affect. Disord.,* 2:27-35, 1980.

Everett, B.S. Bimodality and the nature of depression. *Br. J. Psychiatry,* 138:336-339, 1981.

Feighner, J.P., Robins, C., Guze, S.B., et al. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry,* 26:57-63, 1972.

Feinberg, M., Carroll, B., Steiner, M., and Commorato, A.J. Misdiagnoses of endogenous depression with Research Diagnostic Criteria. *Lancet,* 1:267, 1979.

Fink, M. Efficacy and safety of induced seizures (ECT) in man. *Compr. Psychiatry,* 19:1-18, 1978.

Gillespie, R.D. The clinical differentiation of types of depression. *Guy's Hosp. Rep.,* 79:306-344, 1929.

Kendall, R.E. *The Classification of Depressive Illness.* London: Oxford University Press, 1968.

Kendall, R.E., and Gourlay, A.J. The clinical distinction between psychotic and neurotic depression. *Br. J. Psychiatry,* 117:257-260, 1970a.

Kendall, R.E., and Gourlay, A.J. The clinical distinction between the affective psychoses and schizophrenia. *Br. J. Psychiatry,* 117:261-266, 1970b.

Klerman, G.L., Endicott, J., Spitzer, G., and Hirschfeld, R.M.A. Neurotic depression: A systematic analysis of multiple criteria and meanings. *Am. J. Psychiatry,* 136:57-61, 1979.

Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* Barclay, R.M. (Trans.), 8th Ed. Edinburgh: Livingston, 1921.

Lange, J. Uber Melancholie (Concerning melancholia). *Z. Ges. Neurol. Psychiatry,* 101:293-319, 1926.

Langer, G., Heinze, G., Reim, B., and Matussek, N. Reduced growth hormone responses to amphetamine in "endogenous" depressive patients. *Arch. Gen. Psychiatry,* 33:1471-1475, 1976.

Lewis, A.J. Melancholia: A clinical survey of depressive states. *J. Ment. Sci.,* 80:277-378, 1934.

Matussek, P., Soldner, M., and Nagel, D. Identification of endogenous depressive syndrome based on the symptoms and the characteristics of the course. *Br. J. Psychiatry,* 138:361-372, 1981.

McConaghy, N., Joffe, A.D., Murphy, B., et al. The independence of neurotic and endogenous depression. *Br. J. Psychiatry,* 113:479-484, 1967.

Murphy, E.A. One cause? Many causes? The argument from the bimodal distribution. *J. Chronic Dis.,* 17:301-324, 1964.

Nelson, J.C., Charney, D.S., and Vingaino, A.W. False-positive diagnosis with primary affective disorder criteria. *Lancet,* 2:1252-1253, 1978.

Nelson, J.C., and Charney, D.S. The symptoms of major depressive illness. *Am. J. Psychiatry,* 138:1-13, 1981.

Nelson, J.C., Charney, D.S., and Quinlan, D.M. Evaluation of the DSM-III criteria for melancholia. *Arch. Gen. Psychiatry,* 38:555-559, 1981.

Perez-Reyes, M. Differences in sedative susceptibility between types of depression—Clinical and neurophysiological significance. *Arch. Gen. Psychiatry,* 19:64-71, 1968.

Perez-Reyes, M., and Cochrane, C. Differences in sodium thiopental susceptibility of depressed patients as evidenced by the galvanic skin reflex inhibition threshold. *J. Psychiatric Res.,* 5:335-347, 1967.

Pope, H.G., and Lipinski, J.F. Diagnosis in schizoprenia and manic-depressive illness: A reassessment of the specificity of "schizophrenic" symptoms in the light of current research. *Arch. Gen. Psychiatry,* 35:811-828, 1978.

Prusoff, B.A., Weissman, M.M., Klerman, G.L., and Rounsaville, B.J. Research diagnostic criteria subtypes of depression. *Arch. Gen. Psychiatry,* 37:796-801, 1980.

Shagass, C., Naiman, J., and Mihalick, J. An objective test which differentiates between neurotic and psychotic depression. *Arch. Gen. Psychiatry,* 75:461-471, 1956.

Spitzer, R.L., Endicott, J., and Robins, E. *Research Diagnostic Criteria (RDC) for a Selected Group of Functional Disorders.* 2d ed. New York: Biometrics Research, New York State Psychiatric Institute, 1975.

Taylor, M.A., and Abrams, R. The prevalence of schizophrenia: A reassessment using modern diagnostic criteria. *Am. J. Psychiatry,* 135:945-948, 1978.

Taylor, M.A. Indications for electroconvulsive treatment. In: Abrams, R., and Essman, W.B. (eds.), *Electroconvulsive Therapy in Theory and Practice.* New York: Spectrum Publications. (In press)

Weckowicz, T.E., Cropley, A.J., and Muir, W. An attempt to replicate the results of a factor analytic study in depressed patients. *J. Clin. Psychol.,* 27:30-31, 1971.

Clinical Prediction of ECT Response in Depressed Patients

Richard Abrams, M.D.[1]

Before signing consent for electroconvulsive therapy (ECT), a therapeutic measure popularly believed to be both drastic and a last resort, patients and their families want to know the likelihood of recovery with this form of treatment and whether its potential benefits outweigh its risks. Thus the need arises for practicing clinical psychiatrists to be able to predict which depressed patients are most (and which least) likely to respond to ECT.

Hobson (1953) was the first to assess the relation of various clinical and historical features to the outcome of depressed patients treated with ECT. He recorded the presence or absence of 121 clinical features in 127 patients ("almost all" depressed), eschewing diagnostic classification as "too ill-defined and too widely inclusive" for prognostic purposes. Two weeks after a course of ECT, patients were assigned to good (62%) or poor (38%) outcome groups and each of the 121 clinical features was tested for its correlation with outcome. Thirteen features were correlated significantly with outcome: five favorable (sudden onset, good insight, obsessional previous personality, self-reproach, and duration of illness less than 1 year), and eight unfavorable (mild-moderate hypochondriasis, depersonalization, emotional lability, neurotic traits in adult life, hysterical attitude toward symptoms, intelligence above average, fluctuating course, and neurotic traits in childhood). By adding to this list three "very suggestive" features (pronounced retardation being favorable, and the ill-adjusted premorbid personality, and hysterical previous personality being unfavorable), a checklist of 16 clinical and historical features was constructed to rate each patient, assigning one point for the absence of a favorable feature or the presence of an unfavorable one. The scores ranged from 1 to 14, with lower scores indicating the more favorable outcome. When the frequency distribution of scores was compared for the good and poor outcome cases, a score of 7.5 provided the least misclassification. For example, had a good outcome been predicted for each patient with a score less than 7.5, and a poor outcome for those with a score over 7.5, outcome would have been predicted successfully in 79.7% of the cases.

Roberts (1959) correctly predicted outcome after ECT in 78% of his cases using Hobson's index, but Hamilton and White (1960) found no correlation for the Hobson score and clinical outcome in 49 depressed men receiving ECT. They applied instead the technique of multiple regression analysis to the problem, choosing five variables individually correlated with outcome: duration of illness, weight, the body index, initial depression scale score, and the fall in blood pressure with methacholine, and derived a multiple correlation with improvement of +0.62 for these combined items.

Nyström(1964) selected 24 variables correlated with outcome after ECT and calculated individual prognostic values for each patient based on the partial regression coefficients of the items. Outcome was correctly predicted in 76% of the cases. Favorable features included early morning waking, retardation, and profound depression in mood; unfavorable features included seclusiveness, ideas of reference, depersonalization, obsessionality, and histrionic behavior.

Carney, Roth, and Garside (1965) constructed a predictive index (the Newcastle Scale) for patients receiving ECT by applying multiple regres-

---

[1] Department of Psychiatry, University of Health Sciences/The Chicago Medical School, North Chicago, IL 60064.

sion analyses to find the weights for each of 35 clinical items which best predicted outcome 3 months after treatment. They selected five favorable features (weight loss, pyknic physique, early morning waking, somatic delusions, and paranoid delusions) and five unfavorable features (anxiety, worsening of mood in the evening, self-pity, hypochondriasis, and hysterical traits). Assigning appropriate regression weights to each item yielded for each patient a score that had a multiple correlation with outcome of ±0.67. Each item that correlated positively with a good therapeutic outcome also correlated with the diagnosis of endogenous depression. The Newcastle Scale was subsequently tested on a new sample of 97 depressed patients by Carney and Sheffield (1972) and found to have a 76% predictive accuracy.

Mendels (1965a) found the Hobson score to predict outcome correctly 1 month after ECT in 34 of 50 depressed patients (78%). He then constructed his own index from variables selected by item analysis for their association with a significant reduction in depression scale score after ECT (1965b). Favorable items were a family history of depression, early morning waking, delusions, and psychomotor retardation. Unfavorable items included neurotic traits in childhood or adulthood, inadequate premorbid personality, precipitating factors, and emotional lability. Mendels correctly predicted the response to ECT at 1 month in 90% of his cases and, in a subsequent study with an additional 50 cases, a slight modification of the index yielded a predictive accuracy of 86% (1967).

A few individual variables have been reported to predict a favorable response to ECT, including cyclothymic personality (Abrams & Taylor, 1974; Ottosson, 1962) and pyknic physique (Abrams & Taylor, 1974). Perris (1966) observed that bipolar patients had a better response to ECT than unipolar patients, but our own study failed to confirm this (Abrams & Taylor, 1974).

The prognostic accuracy reported for the various indices may be statistically inflated. Selecting items significantly correlated with outcome from a larger group of items tested and combining them in a coefficient of multiple correlation overestimates the relationships involved. The problem is compounded when the indices are then used to predict outcome in the sample from which they were derived. It is also necessary to consider the accuracy of the predictive indices in comparison with simply giving ECT to all depressed patients referred for treatment or only to those with the diagnosis of endogenous depression. In Hobson's study (1953), a 61.8% predictive accuracy would have been achieved simply by giving ECT to every patient. In Mendels' study (1965b), this procedure would have been correct 60% of the time. If ECT were given only to patients with well-defined symptoms of endogenous depression, the predictive accuracy would have been 72% in Mendels' study (1965b) and 73% in Carney and Sheffield's study (1972).

Abrams, Fink, and Feldstein (1973) tested the predictive value of the indices of Hobson (1953), Carney et al. (1965), and Mendels (1965b) in a sample of 76 hospitalized primary depressives referred for ECT. They found no relation between any of the three indices and improvement as measured by the residual post-ECT Hamilton Depression Scale score, adjusted to account for the variance of the pre-ECT score. In addition to the individual items needed to calculate the three indices, they assessed the presence or absence of a number of other features possibly related to outcome with ECT, including a history of mania or hypomania, cyclothymic personality, endogenous mood swings, a history of prior depression, and impaired concentration. There were 22 variables in all, none of which demonstrated a significant correlation with outcome.

In retrospect, it is felt that negative results obtained by Abrams et al. (1973) were probably due to selection bias. He studied an older group of hospitalized patients (mean age = 63.7 years) who were much more likely to fit the category of endogenous rather than reactive depression, thus virtually eliminating the powerful negative predictive variables associated with reactive depression. To test this hypothesis, an analysis was done of the data on all depressed patients who participated in a series of ECT studies conducted by Taylor and the author over a period of 10 years (Abrams & Taylor, 1973, 1974, 1976; Abrams, Taylor, Faber, et al., in press). Each patient satisfied research criteria for endogenous depression and each was blindly rated before and after a course of ECT using a modified Hamilton Rating Scale for Depression. Hierarchical multiple regression analysis was used to examine the relation between each of the depression scale items and the post-ECT depression score, which was adjusted to account for the variances of the pretreatment depression score, treatment electrode placement, sex, and the total number of treatments received. In a sample of 97 endogenous depressives, a significant correlation was found only between one individual item (gastrointestinal symptoms) and the adjusted post-ECT depression score, well within the boundaries of chance. It would appear, then, that once a population of endogenous depressives is specified, there is simply not enough variability left from which to predict outcome.

In summary, the various clinical predictive indices have only limited application today. The individual clinical features comprising each index are, after all, only manifestations (epiphenomena) of an underlying disorder of presumed biological origin, variously termed endogenous depression or melancholia. Patients with this disorder have been universally demonstrated to respond to ECT, and the predictive indices probably do little more than attempt to identify such patients more systematically than is usual. What is needed is a biological measure of melancholia which is independent of the vagaries of clinical presentation. The dexamethasone suppression test is an important first step in the development of such a measure and will doubtless be further refined, or followed by other more accurate procedures, to ultimately yield a specific test for the prediction of response to ECT. The thrust of future research into the prediction of ECT response should be along these lines.

References

Abrams, R., Fink, J., and Feldstein, S. The prediction of clinical response to ECT. *Br. J. Psychiatry,* 122:457-460, 1973.

Abrams, R., and Taylor, M.A. Anterior bifrontal ECT: A clinical trial. *Br. J. Psychiatry,* 122:587-590, 1973.

Abrams, R., and Taylor, M.A. Electroconvulsive therapy and the diencephalon: A preliminary report. *Compr. Psychiatry,* 15:233-236, 1974a.

Abrams, R., and Taylor, M.A. Unipolar and bipolar depressive illness: Phenomenology and response to electroconvulsive therapy. *Arch. Gen. Psychiatry,* 30:320-321, 1974b.

Abrams, R., and Taylor, M.A. Diencephalic stimulation and the effects of ECT in endogenous depression. *Br. J. Psychiatry,* 129:482-485, 1976.

Abrams, R, Taylor, M.A., Faber, R., et al. Bilateral vs. unilateral ECT: Efficacy in melancholia. *Am J. Psychiatry.* (In press)

Carney, M.W.P., Roth, M., and Garside, R.F. The diagnosis of depressive syndromes and the prediction of ECT response. *Br. J. Psychiatry,* 111:659-674, 1965.

Carney, M.W.P., and Sheffield, B.F. Depression and the Newcastle scales. Their relationship to Hamilton's scale. *Br. J. Psychiatry,* 121:35-40, 1972.

Hamilton, M., and White, J. Factors related to outcome of depression treated with ECT. *J. Ment. Sci.,* 106:1030-1040, 1960.

Hobson, R.F. Prognostic factors in ECT. *J. Neurol. Neurosurg. Psychiatry,* 16:275-281, 1953.

Mendels, J. Electroconvulsive therapy and depression: II. Significance of endogenous and reactive syndromes. *Br. J. Psychiatry,* 111:682-686, 1965a.

Mendels, J. Electroconvulsive therapy and depression: III. A method for prognosis. *Br. J. Psychiatry,* 111:687-690, 1965b.

Mendels, J. The prediction of response to electroconvulsive therapy. *Am. J. Psychiatry,* 124:153-159, 1967.

Nyström, S. On relation between clinical factors and efficacy of ECT in depression. *Acta Psychiatr. Scand. (Suppl.),* 181, 1964.

Ottosson, J.O. Electroconvulsive therapy of endogenous depression: An analysis of various factors on the efficacy of the therapy. *J. Ment. Sci.,* 108:694-703, 1962.

Perris, C. A study of bipolar (manic-depressive) and unipolar recurrent depressive psychoses. *Acta. Psychiatr. Scand. (Suppl.),* 194, 1966.

Roberts, J.M. Prognostic factors in the electroshock treatment of depressive states. I. Clinical features from history and examination. *J. Ment. Sci.,* 105:693-702, 1959.

Predictors Of Outcome In Convulsive Therapy

Max Fink, M.D.[1]

With the introduction of treatments with inherent risk for the mentally ill, such as arsenicals and fever therapy for neurosyphilis, and insulin coma, convulsive therapy, and leucotomy for schizophrenia, predictors with specificity for a favorable outcome became matters of high priority. In studies of schizophrenia, both insulin coma and leucotomy were found to have limited ap-

---

[1] Department of Psychiatry and Behavioral Science, School of Medicine, State University of New York at Stony Brook, Long Island, NY 11794.

Supported in part by USPHS Grant MH-35518 to the International Association for Psychiatric Research, Inc., St. James, NY 11780.

plications. But convulsive therapy was effective in melancholia, mania, and catatonia. A search was focused on finding an analog of the Wasserman test for syphilis—a simple procedure with high specificity for a common pathogenesis. Such identification is essential to the development of a safe and rational therapy. It is the aim of this review to cite the principal studies in the search for predictors of outcome in convulsive therapy. While no recent measure fulfills the criteria of specificity, safety, and ease of administration of the Wasserman test, the variety of measures under study, when integrated with the present knowledge of the physiologic effects of induced seizures, and the objective methods of classification of the mentally ill, provide a basis for enthusiasm in the ongoing search.

The empirical nature of convulsive therapy has led investigators to seek specific predictors of outcome in three broad dimensions—clinical criteria, personality and psychologic tests, and biochemical and physiologic laboratory tests (Fink, 1968, 1979). Much of the data of studies done between 1938 and the early 1960s, prior to the introduction of modern psychotropic drugs, are no longer applicable. The argument in the early days was the selection of patients for convulsive therapy, leucotomy, and insulin coma, with hospitalization, moral, and milieu therapies as the principal alternatives. Not only did the treatments differ, but the population samples referred to research centers differed. The present samples reflect the residue of those severe mentally ill patients already treated with active psychotropic substances. Nevertheless, a review of the early concepts provides a basis for our present studies.

Clinical Criteria

The most widely used and best criterion for the selection of patients for convulsive therapy is clinical diagnosis—the type and severity of the pathology, and the recent medical history. Despite changes in clinical typologies, represented by the general acceptance of the Research Diagnostic Criteria and the Diagnostic and Statistical Manual-III (DSM-III) schemata, patients who are severely ill, with syndromes of melancholia (endogenous depression, primary depression), catatonia, and mania have the best prognosis for short-term outcome with electroconvulsive therapy (ECT) (APA, 1978; Fink, 1978, 1979; Scovern & Kilmann, 1980; Ottosson, 1981; Kendall, 1981). ECT is also the preferred treatment for those patients with recurrent depressions who have not responded to drug treatments in the past, and who have responded to ECT.

Within the broad syndrome of melancholia, two specific subtypes are especially responsive to convulsive therapy—patients with catatonic features (Roth & Rosie, 1953; Breakey & Kala, 1977; Regestein, Alpert, & Reich, 1977; Fink, 1979), and those with delusions of guilt or somatic delusions (Hordern, Holt, Burt, & Gordon, 1963; Glassman, Kantor, & Shostak, 1975; Avery & Winokur, 1977; Davidson, McLeod, Kurland, & White, 1977; Kantor & Glassman, 1977; Nelson & Bowers, 1978; Minter & Mandell, 1979a,b; Kaskey, Nasr, & Meltzer, 1980; Charney & Nelson, 1981). These patients respond poorly to tricyclic antidepressant medications (Rao & Coppen, 1979; Brockington, Kendell, Kellett, et al., 1978). There is also a subgroup of patients with confusional syndromes, such as the unusual cases of acute delirium, periodic confusional states, and delirious states complicating organic illnesses who respond dramatically to ECT, often to only a few treatments (Ottosson, 1981).

Many authors proposed prognostic indices, based primarily on symptoms and observable clinical signs (Hobson, 1953; Carney, Roth, & Garside, 1965; Mendels, 1965, 1967; Nyström, 1965; Pilowsky & Boulton, 1970; Weckowicz, Yonge, Cropley, & Muir, 1971). While these indices are useful in identifying the responsive subtypes in the initial samples, their application to new populations found them no more useful than clinical diagnosis alone, and they have not been generally adopted (Abrams, Fink, & Feldstein, 1973; Kiloh, 1977; Ottosson, 1981; Kendell, 1981). A good response is associated with the "endogenous features" of terminal insomnia, morning aggravation, self-denigration, weight loss and anorexia, retardation, and agitation. It is possible that the vegetative symptoms which are given the most weight in these indices reflect features in the pathogenesis of a syndrome of melancholia, which is particularly responsive to induced seizures. As these symptoms are associated with dysfunction of brainstem mechanisms, particularly hypothalamic-pituitary functioning, it is not unexpected that some recent concepts of the mode of action of ECT focus on dysfunctions of these structures (Fink, 1979; Fink & Ottosson, 1980).

Psychologic Tests and Personality Measures

Most clinicians note that an "adequate personality" is a good prognostic feature (Kiloh, 1977; APA, 1978; Ottosson, 1981). In some early studies of convulsive therapy, the relation of psychological tests to outcome was sought. Interest was shown in the syndrome of anosognosia and denial of illness—a syndrome which is seen in patients with generalized dysfunction of the brain. It is exaggerated by the administration of sedative drugs, like amobarbital (Weinstein & Kahn, 1955). In patients undergoing ECT, the development of an organic mental syndrome is easily documented, with the severity of the syndrome proportional to the number and frequency of seizures. In such patients, a denial personality (Kahn & Fink, 1959), high acquiescence score on social attitude scales (Kahn, Pollack, & Fink, 1959, 1960a), errors on figure-ground tests (Kahn, Pollack, & Fink, 1960b), and restricted performance on the Rorschach test (Kahn & Fink, 1960) were associated with a good clinical outcome (Fink, 1968, 1979). These studies also found that older patients of foreign birth had better prognoses with ECT than younger patients who were native born in the U.S. (Kahn et al., 1959). These tests never achieved general acceptance, in part because interest in ECT waned as antidepressant drugs were introduced, and, in part, because there was little evidence that these tests were useful in distinguishing the patients responsive to ECT from those who responded to other antidepressant treatments.

Physiologic and Biochemical Tests

In the almost 50 years since the introduction of convulsive therapy, many physiologic and biochemical measures have been examined in relation to a course of ECT. Most studies assessed the effects of repeated seizures on body physiology, but a few examined the possibility that dysfunctions in physiologic and biochemical measures were related to prognosis (Fink 1968, 1979).

Tests of autonomic reactivity were a feature of early studies. A common index was the change in blood pressure in response to subcutaneous or intramuscular methacholine or to intravenous epineprine. The rate of change, the peak change, and the rate at which the blood pressure returned to baseline were examined, with a systolic rise greater than 50mm Hg after epinephrine and a delayed return to baseline greater than 25 minutes after methacholine as good prognostic signs for ECT (Funkenstein, Greenblatt, & Solomon 1948, 1950, 1952). These observations were corroborated, but later reports noted that the correlations could largely be explained by age and the basal blood pressure (Blumberg, Cohen, & Miller, 1956; Roberts, 1959a,b; Hamilton & White, 1960; Rose, 1962; Thorpe, 1962). Correlations were best in older patients with defined hypertension.

Electrophysiologic Tests

Others studied the resting EEG before treatment and found better clinical results in those patients with normal (alpha) EEG records than in those with low voltage fast records (Turner, Lowinger, & Huddleson, 1945; Weil & Brinegar, 1947; Kennard & Willner, 1948; Mosovich & Katzenelbogen, 1948); but others failed to find such an association (Moriarty & Siemens, 1947; Chusid & Pacella, 1952). Indeed, Hoagland, Malamud, Kaufman, & Pincus (1946) found a positive relationship between the amount of EEG fast activity in the pretreatment electroencephalogram (EEG) and clinical outcome with ECT in a group of involutional depressed women.

The inflection point in the increase in EEG beta activity after the intravenous administration of amobarbital (0.5 mg/kg/40 sec) was defined as the "sedation threshold," with low thresholds being positively correlated with diagnoses of psychotic depression and good prognosis with ECT (Shagass 1954, 1957; Shagass & Naiman, 1956). These findings were confirmed by some observers (Nymgaard, 1959; Perris & Brattemo, 1963), but not by others (Ackner & Pampiglione, 1959; Roberts, 1959b).

Roth (1951) reported a better prognosis with ECT for patients in whom the resting EEG delta activity was enhanced by intravenous thiopental given a few hours after the first to third seizures. In a replication and followup study, Roth et al. (1957) reported that enhanced EEG slowing after pentothal was not related to the short-term evaluations of outcome, but to the likelihood of relapse after 3 and 6 months, with higher relapse rates in patients with lower EEG slow wave values. In parallel studies, Fink and Kahn (1957) found that the early and sustained development of high voltage EEG slow wave activity in the resting interseizure record was a good prognostic sign for short-term outcome evaluations with ECT. But this study also was not confirmed in a later series (Volavka et al., 1972; Volavka, 1974). We concluded that the earlier findings (like those with the sedation threshold and blood pressure studies) resulted from the mixed population samples (schizophrenic and depressed) studied at the time, and that such measures were not particularly useful in the more homogeneous depressed samples under study at present (Fink, 1979). The data still leave the possibility that such physiologic measures, when applied to mixed samples, identify subpopulations (such as depressed and catatonic patients) with characteristics that are particularly responsive in their behavior and physiology to induced seizures, in contrast to others (such as schizophrenic patients) who lack such responsivity.

Interest was also shown in the changes in averaged sensory-evoked responses, both as indices to identify subpopulations of the mentally ill and as indices to relate to outcome. Much of this work has been done by Shagass (1972, 1980), but its complexity and limited specificity has not encouraged its widespread use.

The sleep EEG, with measurement of rapid-eye-movement (REM) features, has been another source of indices of depressive illness and outcome with treatment. A prominent feature of depressive patients is a shortened time from sleep onset to the first REM period and a greater amount of REM activity. The changes in sleep characteristics are reversed by ECT (Kupfer et al., 1980, 1981).

One author has suggested that total seizure time may be an analog of the plasma level of antidepressant drugs, to provide a "therapeutic window" for a course of ECT (Maletzky, 1978). He noted that total seizure durations less than 210 seconds are much less effective than courses where the total seizure time was between 210 and 750 seconds.

Biochemical Measures

The biochemical effects of repeated seizures have been studied extensively and the reviews find consistent changes in brain tissues, CSF, blood, and urine (Essman, 1973; Fink, Kety, McGaugh, & Williams, 1974; APA, 1978; Fink, 1979). But the changes have not been related to clinical course, and none is useful as a predictor of clinical outcome. In studies of antidepressant medication, levels of urinary MHPG have been suggested as useful indices in the selection of different tricyclic antidepressants, but a study of its prognostic value in ECT did not confirm a relationship (Steiner et al., 1979). Studies of urinary cyclic AMP showed an increase with treatment (Hamadah et al., 1972; Moyes, 1972), while Choi, Taylor, and Abrams (1977) reported levels of calcium ATPase levels to be low in depression and to increase with treatment. In none of these studies is the relation to outcome defined.

An interesting relationship to outcome may be inferred from studies of calcium metabolism. A number of studies report decreased urinary, plasma, and CSF levels of calcium during a course of ECT, at a time when clinical improvement is noted, suggesting that the transfer of calcium into brain tissues is a feature of the therapeutic process (Flach, 1964; Faragalla & Flach, 1970; Carman & Wyatt, 1977). These observations suggest that monitoring plasma or urinary calcium may be a useful measure to relate to clinical outcome.

Neuroendocrine Measures

Recent studies of neuroendocrine relations in depressive illnesses provide the most interesting of the laboratory predictors. In some forms of depression, predominantly in endogenous depression or melancholia, neuroendocrine abnormalities are present in the absence of defined endocrinologic disease. The most extensively studied functions are those of the hypothalamic-pituitary-adrenal (HPA) axis (Carroll et al., 1976a,b), and the hypothalamic-pituitary-thyroid (HPT) axis (Loosen & Prange, 1980). An overactivity of the HPA axis is reflected in elevated plasma cortisol, loss of its diurnal rhythmicity, and its resistance to suppression (or early escape from suppression) by oral dexamethasone. This last abnormality has been reported in up to 50% of patients with melancholia, and is now seen as having diagnostic significance (Carroll et al., 1981). Hypoactivity of the HPT axis, as reflected in a blunted release of thyroid stimulating hormone (TSH) in response to intravenous thyrotropin releasing hormone (TRH), is also found in about 25% of patients with melancholia (Kirkegaard, 1981).

Normalization of the dexamethasone suppression test (DST) with clinical recovery is well documented (Greden & Carroll, 1979; Brown, Johnston, & Mayfield, 1979; Gold et al., 1980b; Greden et al., 1980; Papakostas et al., 1981). The DST and TSH tests in 50 hospitalized male veteran psychiatric patients with various psychiatric diagnoses were examined (Papakostas et al., 1981). Of 20 cases of unipolar melancholia, 17 exhibited hypercortisolism, and 14 failed to suppress plasma cortisol after dexamethasone. The measures were repeated in 14 unipolar depressed patients after a course of ECT. Improvement in psychopathology was directly related to normalization of the HPA functions. In the followup period at 9 months, the patients with normal HPA functions had better long-term prognoses than those with abnormal functions at the end of a course of ECT. It was concluded that normalization of HPA dysfunction could be used as an index of the end of a course of ECT, suggesting that clinicians should consider further treatment in those patients who continue to exhibit hypercortisolism or an abnormal DST after a series of ECT. Similar findings have been reported by others (Dysken et al., 1979; Albala & Greden, 1980; Greden et al., 1980; Albala et al., 1981). Similar neuroendocrine abnormalities and their response to ECT have been reported in patients with catatonia, suggesting that the tests are related to abnormalities in pathophysiology responsive to ECT, and not to a specific type of psychopathology (Brown, Johnston, & Mayfield, 1979; Dysken et al., 1979; Greden & Carroll, 1979).

Findings with the TRH test did not relate to psychopathology, nor did they change with ECT. The data are inconclusive, as the samples are small. Others found the TRH test to show similar changes with treatment for endogenous depression, and further study is needed (Mendlewicz et al., 1979; Kirkegaard & Bjørum, 1980; Asnis et al., 1980; Gold et al., 1980a; Loosen, & Prange, 1980; Kirkegaard, 1981).

Other indices of abnormal neuroendocrine response in patients with depression have been described (Fink, 1980). The release of growth hormone by hypoglycemia, L-dopa, and TSH is either reduced or lacking, and returns to normal with treatment. The prolactin response to carbidopa (Garfinkel et al., 1979), the corticosteroid response to methylamphetamine (Checkley, 1978, 1980), and the growth hormone response to amphetamine (Matussek, 1978) and to clonidine (Laakmann & Benkert, 1978; Matussek et al., 1980) characterize patients with severe depression. These studies, like those of the pituitary-thyroid axis, require additional work before their usefulness as prognostic indices can be fully assessed.

Conclusion

Many measures have been examined in the continuing search for a simple, specific, and safe laboratory test which may be used to identify patients for whom convulsive therapy may be helpful. There has also been some interest in using changes in some measures as endpoints to a therapeutic series. The degree of EEG slowing in the interseizure EEG, either at rest or after a challenge dose of a sedative drug; the onset of the first REM period in sleep; plasma and urine calcium levels; and neuroendocrine measures, particularly measures of plasma cortisol and some variation of steroid suppression tests, are of special interest in continuing studies. The TSH response to TRH, as a representative of other neuroendocrine systems, and the total seizure time are also of interest. The most compelling observation is the possibility that the DST, in those patients in whom it is abnormal before ECT, may be an index to the termination of a course of successful therapy.

References

Abrams, R., Fink, M., and Feldstein, S. Prediction of clinical response to ECT. *Br. J. Psychiatry*, 122:457-460, 1973.

Ackner, B., and Pampiglione, G. An evaluation of the sedation threshold test. *J. Psychosom. Res.*, 3:271-281, 1959.

Albala, A.A., and Greden, J.F. Serial dexamethasone suppression tests in affective disorders. *Am. J. Psychiatry*, 137:383, 1980.

Albala, A.A., Greden, J.F., Tarika, J., and Carroll, B.J. Changes in serial dexamethasone suppression tests among unipolar depressives receiving electroconvulsive treatment. *Biol. Psychiatry*, 16:551-560, 1981.

American Psychiatric Association. *Electroconvulsive Therapy*. Task Force Report #14. Washington, D.C., 1978, 200 pp.

Asnis, G.M., Nathan, R.S., Halbreich, U., et al. TRH tests in depression. *Lancet*, 1:424-425, 1980.

Avery, D., and Winokur, G. The efficacy of electroconvulsive therapy and antidepressants in depression. *Biol. Psychiatry*, 12:507-524, 1977.

Blumberg, A.G., Cohen, L., and Miller, J.S.A. The relation of mecholyl induced hypotension to the classification of psychiatric patients and its prognostic significance with electroshock therapy. *J. Hillside Hosp.*, 5:216-231, 1956.

Breakey, W.R., and Kala, A.K. Typhoid catatonia responsive to ECT. *Br. Med. J.*, 2:257-259, 1977.

Brockington, I.F., Kendell, R.E., Kellett, J.M., et al. Trials of lithium, chlorpromazine, and amitriptyline in schizoaffective patients. *Br. J. Psychiatry*, 133:162-168, 1978.

Brown, W.A., Johnston, R., and Mayfield, D. The 24-hour dexamethasone suppression test in a clinical setting: Relationship to diagnosis, symptoms, and response to treatment. *Am. J. Psychiatry*, 136:543-547, 1979.

Carman, J.S., and Wyatt, R.J. Alterations in cerebrospinal fluid and serum total calcium with changes in psychiatric state. In: Usdin, E., Hamburg, D., and Barchas, J. (eds.), *Neuroregulators and Psychiatric Disorders*. New York: Oxford University Press, 1977, pp. 488-494.

Carney, M.W.P., Roth, M., and Garside, R.F. The diagnosis of depressive syndromes and the prediction of ECT response. *Br. J. Psychiatry*, 111:659-674, 1965.

Carroll, B.J., Curtis, G.C., and Mendels, J. Neuroendocrine regulation in depression. I. Limbic system-adrenocortical dysfunction. *Arch. Gen. Psychiatry*, 33:1039-1044, 1976a.

Carroll, B.J., Curtis, G.C., and Mendels, J. Neuroendocrine regulation in depression. II. Discrimination of depressed from nondepressed patients. *Arch. Gen. Psychiatry*, 33:1051-1058, 1976b.

Carroll, B.J., Feinberg, M., Greden, J.F., et al. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry*, 38:15-22, 1981.

Charney, D.S., and Nelson, J.C. Delusional and nondelusional unipolar depression: Further evidence for distinct subtypes. *Am. J. Psychiatry*, 138:328-333, 1981.

Checkley, S.A. A new distinction between the euphoric and the antidepressant effects of methylamphetamine. *Br. J. Psychiatry*, 133:416-423, 1978.

Checkley, S.A. Neuroendocrine tests of monoamine function in man: A review of basic theory and its application to the study of depressive illness. *Psychol. Med.*, 10:35-53, 1980.

Choi, S.J., Taylor, M.A., and Abrams, R. Depression, ECT, and erythrocyte adenosinetriphosphatase activity. *Biol. Psychiatry*, 12:75-81, 1977.

Chusid, J.G., and Pacella, B.L. The electroencephalogram in electric shock therapies. *J. Nerv. Ment. Dis.*, 116:95-107, 1952.

Davidson, J.R.T., McLeod, M., Kurland, A.A., and White, H.L. Antidepressant drug therapy in psychotic depression. *Br. J. Psychiatry*, 131:493-496, 1977.

Dysken, M., Pandey, G.N., Chang, S.S., et al. Serial postdexamethasone cortisol levels in a patient undergoing ECT. *Am. J. Psychiatry*, 136:1328-1329, 1979.

Essman, W.B. *Neurochemistry of Cerebral Electroshock*. New York: Spectrum Publications, 1973, 181 pp.

Fink, M. Neurophysiological response strategies in the classification of mental illness. In: Katz, M.M., Cole, J.O., and Barton, W.E. (eds.), *The Role of Methodology of Classification in Psychiatry and Psychopathology*. Washington, D.C.: U.S. Government Printing Office, 1968, pp. 535-540.

Fink, M. Efficacy and safety of induced seizures (EST) in man. *Compr. Psychiatry*, 19:1-18, 1978.

Fink, M. (ed.), *Convulsive Therapy: Theory and Practice*. New York: Raven Press, 1979, 308 pp.

Fink, M. Neuroendocrinology and ECT: A review of recent developments. *Compr. Psychiatry*, 21:450-459, 1980.

Fink, M., and Kahn, R.L. Relation of EEG delta activity to behavioral response in electroshock: Quantitative serial studies. *Arch. Neurol. Psychiatry*, 78:516-525, 1957.

Fink, M., Kety, S., McGaugh, J., and Williams, T.A. (ed.), *Psychobiology of Convulsive Therapy*. Washington, D.C.: V.H. Winston & Sons, 1974, 312 pp.

Fink, M., and Ottosson, J.-O. A theory of convulsive therapy in endogenous depression: Significance of hypothalamic functions. *Psychiatr. Res.*, 2:49-61, 1980.

Flach, F.F. Calcium metabolism in states of depression. *Br. J. Psychiatry*, 110:588-593, 1964.

Flach, F.F., Liang, E., and Stokes, P.E. Effects of electric convulsive treatments on nitrogen, calcium, and phosphorous metabolism in psychiatric patients. *J. Ment. Sci.*, 106:638-647, 1960.

Funkenstein, D.H., Greenblatt, M., and Solomon, H.C. Autonomic nervous system changes following electric shock treatment. *J. Nerv. Ment. Dis.*, 108:409-422, 1948.

Funkenstein, D.H., Greenblatt, M., and Solomon, H.C. A test which predicts the clinical effects of electroshock treatment on schizophrenic patients. *Am. J. Psychiatry*, 106:889-901, 1950.

Funkenstein, D.H., Greenblatt, M., and Solomon, H.C. An autonomic nervous system test of prognostic significance in relation to electroshock treatment. *Psychosom. Med.*, 14:347-362, 1952.

Garfinkel, P.E., Brown, G.M., Warsh, J.J., and Stancer, H.C. Neuroendocrine responses to carbidopa in primary affective disorders. *Psychoneuroendocrinology*, 4:13-20, 1979.

Glassman, A.H., Kantor, S.J., and Shostak, M. Depression, delusions, and drug response. *Am. J. Psychiatry*, 132:716-719, 1975.

Gold, M.S., Pottash, A.L.C., Ryan, N., et al. TRH-induced response in unipolar, bipolar, and secondary depressions: Possible utility in clinical assessment and differential diagnosis. *Psychoneuroendocrinology*, 5:147-155, 1980a.

Gold, M.S., Pottash, A.L.C., Extein, I., and Sweeney, D.R. Dexamethasone suppression tests in depression and response to treatment (Letter). *Lancet*, 1:1190, 1980b.

Greden, J.F., Albala, A.A., Haskett, R.F., et al. Normalization of the dexamethasone suppression test. A laboratory index of recovery from endogenous depression. *Biol. Psychiatry*, 15:449-458, 1980.

Greden, J.F., and Carroll, B.J. The dexamethasone suppression tests as a diagnostic aid in catatonia. *Am. J. Psychiatry*, 136:1199-1200, 1979.

Hamadah, K., Holmes, H., Barker, G.B., et al. Effects of electric convulsion therapy on urinary excretion of 3′, 5′ cyclic adenosine monophosphate. *Br. Med. J.*, 3:439-441, 1972.

Hamilton, M., and White, J.M. Factors related to the outcome of depression treated with ECT. *J. Ment. Sci.*, 106:1031-1041, 1960.

Hoagland, H., Malamud, W., Kaufman, I.C., and Pincus, G. Changes in electroencephalogram and in excretion of 17-ketosteroids accompanying electroshock therapy of agitated depression. *Psychosom. Med.*, 8:246-251, 1946.

Hobson, R.F. Prognostic factors in electric convulsive therapy. *J. Neurol. Neurosurg. Psychiatry*, 16:275-281, 1953.

Hordern, A., Holt, H.F., Burt, C.G., and Gordon, W.F. Amitriptyline in depressive cases. *Br. J. Psychiatry*, 109:815-825, 1963.

Kahn, R.L., and Fink, M. Personality factors in behavioral response to electroshock therapy. *J. Neuropsychiatry*, 1:45-49, 1959.

Kahn, R.L., and Fink, M. Prognostic value of Rorschach criteria in clinical response to convulsive therapy. *J. Neuropsychiatry*, 1:242-245, 1960.

Kahn, R.L., Pollack, M., and Fink, M. Sociopsychologic aspects of psychiatric treatment in a voluntary mental hospital: Duration of hospitalization, discharge ratings, and diagnosis. *Arch. Gen. Psychiatry*, 1:565-574, 1959.

Kahn, R.L., Pollack, M., and Fink, M. Figure-ground discrimination after induced altered brain function. *Arch. Neurol.*, 2:547-551, 1960a.

Kahn, R.L., Pollack, M., and Fink, M. Social attitude (California F scale) and convulsive therapy. *J. Nerv. Ment. Dis.*, 130:187-192, 1960b.

Kantor, S.J., and Glassman, A.H. Delusional depressions: Natural history and response to treatment. *Br. J. Psychiatry*, 131:351-360, 1977.

Kaskey, G.B., Nasr, S., and Meltzer, H.Y. Drug treatment in delusional depression. *Psychiatr. Res.*, 1:267-277, 1980.

Kendell, R.E. The present status of electroconvulsive therapy. *Br. J. Psychiatry*, 139:265-283, 1981.

Kennard, M.A., and Willner, M.D. Significance of changes in the electroencephalogram which result from shock therapy. *Am. J. Psychiatry*, 105:40-45, 1948.

Kiloh, L.G. The use of electroconvulsive treatment in depressive illness. In: Burrows, G.D. (ed.), *Handbook of Studies on Depression*. Amsterdam: Excerpta Medica, 1977, pp. 229-252.

Kirkegaard, C. The thyrotropin response to thyrotropin-releasing hormone in endogenous depression. *Psychoneuroendocrinology*, 6:189-212, 1981.

Kirkegaard, C., and Bjørum, N. TSH response to TRH in endogenous depression (Letter). *Lancet*, 1:152, 1980.

Kupfer, D.J., Spiker, D.G., Doble, P.A., et al. Depression, EEG sleep, and clinical response. *Compr. Psychiatry*, 21:212-220, 1980.

Kupfer, D.J., Spiker, D.G., Doble, P.A., et al. Sleep and treatment prediction in endogenous depression. *Am. J. Psychiatry*, 138:429-434, 1981.

Laakmann, von G., and Benkert, O. Neuroendokrinologie und Psychopharmaka. (Neuroendocrinology and psychopharmacology). *Arzneim.-Forsch.*, 28:1277-1280, 1978.

Loosen, P.T, and Prange, A.J., Jr. Thyrotropin releasing hormone (TRH): A useful tool for psychoendocrine investigation. *Psychoneuroendocrinology*, 5:63-80, 1980.

Maletzky, B.M. Seizure duration and clinical effect in electroconvulsive therapy. *Compr. Psychiatry*, 19:541-550, 1978.

Matussek, N. Neuroendokrinologische Untersuchungen bei depressiven Syndromen. (Neuroendocrinology investigations in the depressive syndrome). *Nervenarzt*, 49:569-575, 1978.

Matussek, N., Ackenheil, M., Hippius, H., et al. Effect of clonidine on growth hormone release in psychiatric patients and controls. *Psychiatr. Res.*, 2:25-36, 1980.

Mendels, J. Electroconvulsive therapy and depression. III. A method for prognosis. *Br. J. Psychiatry*, 111:687-690, 1965.

Mendels, J. The prediction of response to electroconvulsive therapy. *Am. J. Psychiatry*, 124:153-159, 1967.

Mendelewicz, J., Linkowski, P., and Brauman, H. TSH responses to TRH in women with unipolar and bipolar depression. *Lancet*, 2:1079-1080, 1979.

Minter, R.E., and Mandel, M.R. The treatment of psychotic major depressive disorder with drugs and electroconvulsive therapy. *J. Nerv. Ment. Dis.*, 167:726-733, 1979a.

Minter, R.E., and Mandel, M.R. A prospective study of the treatment of psychotic depression. *Am. J. Psychiatry*, 136:1470-1472, 1979b.

Moriarty, J.D., and Siemens, J.C. Electroencephalographic study of electric shock therapy. *Arch. Neurol. Psychiatry*, 57:712-718, 1947.

Mosovich, A., and Katzenelbogen, S. Electroshock therapy, clinical and electroencephalographic studies. *J. Nerv. Ment. Dis.*, 107:517-530, 1948.

Moyes, I.C.A. ECT and cAMP excretion. *Br. Med. J.*, 3:829, 1972.

Nelson, J.C., and Bowers, M.B. Delusional unipolar depression—Description and drug response. *Arch. Gen. Psychiatry*, 35:1321-1328, 1978.

Nymgaard, K. Studies on the sedation threshold. A. Reproducibility and effect of drugs. B. Sedation threshold in neurotic and psychotic depression. *Arch. Gen. Psychiatry*, 1:530-536, 1959.

Nyström, S. On relation between clinical factors and efficacy of ECT in depression. *Acta Psychiatr. Scand. (Suppl.)*, 181:115-118, 1964.

Ottosson, J.-O. Convulsive therapy. In: van Praag, H.M., Lader, M.H., Rafaelson, O.J., and Sachar, E.J. (eds.), *Practical Applications of Psychotropic Drugs and Other Biological Treatments*. New York: Marcel Dekker, 1981, pp. 419-454.

Papakostas, Y., Fink, M., Lee, J., et al. Neuroendocrine measures in psychiatric patients: Course and outcome with ECT. *Psychiatr. Res.*, 4:55-64, 1981.

Perris, C., and Brattemo, C.-E. The sedation threshold as a method of evaluating antidepressive treatments. *Acta Psychiatr. Scand. (Suppl. 39)*, 169:111-119, 1963.

Pilowsky, I., and Boulton, D.M. Development of a questionnaire-based decision rule for classifying depressed patients. *Br. J. Psychiatry,* 116:647-650, 1970.

Rao, V.A.R., and Coppen, A. Classification of depression and response to amitriptyline therapy. *Psychol. Med.,* 9:321-325, 1979.

Regestein, Q.R., Alpert, J.S., and Reich, P. Sudden catatonic stupor with disastrous outcome. *JAMA;* 238:618-620, 1977.

Robert, J.M. Prognostic factors in the electroshock treatment of depressive states. I. Clinical features from history and examination. *J. Ment. Sci.,* 105:693-702, 1959a.

Robert, J.M. Prognostic factors in the electroshock treatment of depressive states. II. The application of specific tests. *J. Ment. Sci.,* 105:703-713, 1959b.

Rose, J.T. The Funkenstein test—A review of literature. *Acta Psychiatr. Scand.,* 38:124-153, 1962.

Roth, M. Changes in the EEG under barbiturate anesthesia produced by electroconvulsive treatment and their significance for the theory of ECT action. *Electroenceph. Clin. Neurophysiol.,* 3:261-280, 1951.

Roth, M., Kay, D.W.K., Shaw, J., and Green, J. Prognosis and pentothal-induced electroencephalographic changes in electroconvulsive treatment. *Electroenceph. Clin. Neurophysiol.,* 9:225-237, 1957.

Roth, M., and Rosie, J.M. The use of electroplexy in mental disease with clouding of consciousness. *J. Ment. Sci.,* 99:103-111, 1953.

Scovern, A.W., and Kilmann, P.R. Status of electroconvulsive therapy: Review of the outcome literature. *Psychol. Bull.,* 87:260-303, 1980.

Shagass, C. The sedation threshold. A method for estimating tension in psychiatric patients. *Electroenceph. Clin. Neurophysiol.,* 6:221-233, 1954.

Shagass, C. A measurable neurophysiological factor of psychiatric significance. *Electroenceph. Clin. Neurophysiol.,* 9:101-108, 1957.

Shagass, C. (ed.). *Evoked Brain Potentials in Psychiatry.* New York: Plenum Press, 1972, 274 pp.

Shagass, C. Brain potential studies of psychopathology. *Compr. Psychiatry,* 21:483-491, 1980.

Shagass, C., and Naiman, J. The sedation threshold as an objective index of manifest anxiety in psychoneurosis. *J. Psychosom. Res.,* 1:49-57, 1956.

Steiner, M., Radwan, M., Elizur, A., et al. Urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) excretion in depression. *Jpn. J. Exp. Med.,* 49:95-99, 1979.

Thorpe, J.G. The current status of prognostic test indicators for electroconvulsive therapy. *Psychosom. Med.,* 24:554-568, 1962.

Turner, W.J., Lowinger, L., and Huddleson, J.H. The correlation of pre-electroshock electroencephalogram and therapeutic results in schizophrenia. *Am. J. Psychiatry,* 102:299-300, 1945.

Volavka, J. Is EEG slowing related to therapeutic effect of convulsive therapy? In: Fink, M., Kety, S., McGaugh, J, and Williams, T.A. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston & Sons, 1974, pp. 35-40.

Volavka, J., Feldstein, S., Abrams, R., et al. EEG and clinical changes after bilateral and unilateral electroconvulsive therapy. *Electroenceph. Clin. Neurophysiol.,* 32:631-639, 1972.

Weckowicz, T.E., Yonge, K.A., Cropley, A.J., and Muir, W. Objective therapy predictors in depression: A multivariate approach. *J. Clin. Psychol. (Suppl.),* 27:3-29, 1971.

Weil, A.A., and Brinegar, W.C. Electroencephalographic studies following electric shock therapy. *Arch. Neurol. Psychiatry,* 57:719-729, 1947.

Weinstein, E.A., and Kahn, R.L. *Denial of Illness.* Springfield, IL: Charles C Thomas Publishers, 1955, 166 pp.

Relevance of Neuroendocrine Strategies Electroconvulsive Therapy Research

Roger F. Haskett, M.B.B.S.[1], and A. Ariav Albala, M.D.[1]

Introduction

Neuroendocrine strategies are a relatively recent addition to clinical psychiatry. The techniques developed from the observation that endocrine function was often altered in association with abnormal mental states. The theoretical rationale for the use of peripheral hormone measurements as biological markers of psychiatric illness was provided by the identification of functional links between the hypothalamus and anterior pituitary gland. These connections provided the mechanism whereby the limbic system dysfunction associated with psychiatric illness could directly interfere with neuroendocrine regulation. Like the clinical endocrinologists who developed these strategies, psychiatrists have found that measurement of basal hormone levels alone will not generally provide very specific information. Abnormalities of neuroendocrine regulation appear to be more precisely identified by dynamic studies of endocrine function such as stimulation or suppression tests.

A number of studies have demonstrated consistent abnormalities of the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-thyroid (HPT) axes in patients with melancholia. Evidence is accumulating that two neuroendocrine strategies, the Dexamethasone Suppression Test (DST) and the Thyrotropin-Releasing Hormone Stimulation Test (TRH Test), which examine the function of the HPA and HPT axes, respectively, have clinical utility in the study and management of melancholia.

---

[1] Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109.

The Desamethasone Suppression Test (DST)

This strategy evolved from a procedure described by Liddle (1960) for the evaluation of HPA axis dysfunction in Cushing's disease. When normal subjects receive a dose of 1 or 2 mg dexamethasone at midnight, plasma cortisol levels are suppressed for at least the next 24 hours. During the 1960s, several investigators reported that, in addition to secreting excessive amounts of corticosteroids, the HPA axis in some patients with melancholia is abnormally resistant to suppression by dexamethasone. Subsequent studies have confirmed this finding and developed the DST procedure to give optimal test results for the diagnosis of melancholia (Carroll, et al. 1981). Cortisol levels are measured at 4 p.m. and 11 p.m. after administration of 1 mg dexamethasone at 11:30 p.m. on the previous day. This form of the DST identified the syndrome of melancholia with a sensitivity of 67% and specificity of 96% when administered to psychiatric inpatients.

The Thyrotropin-Releasing Hormone Stimulation Test (TRH Test)

The TRH Test used in psychiatric studies is identical to the one devised by endocrinologists for the study of HPT disorders. The test is usually conducted at mid-morning, when spontaneous plasma TSH level fluctuations are least, after an overnight fast. After drawing one or two baseline blood samples, TRH is administered intravenously over a 30-second period. Subsequent samples are obtained 15, 30, 60, and 90 minutes after TRH administration. Most of the studies have used TRH doses of either 200 or 500 µg. TSH concentrations are determined by radioimmunoassay (RIA), and the maximal change in TSH (Δ TSH) is obtained by subtracting the baseline TSH value from the maximum TSH level after TRH administration.

Since the first reports showed that a proportion of depressed patients have blunted TSH responses to TRH (Kastin, Ehrensing, Schalch, & Anderson, 1972; Prange, Wilson, Lara, Alltop, & Breese, 1972), many investigators have replicated and extended those findings. Review of these studies reveals that between 25 and 30% of euthyroid depressed patients have blunted responses to TRH, regardless of whether a dose of 200 µg or 500 µg of TRH is used in the test. With so insensitive a test, the diagnostic utility of the test is probably low. Despite this limitation, there is some evidence that treatment-associated changes in the TRH Test may serve as predictors of outcome of the acute episode.

Questions For ECT Research

Since the syndrome of melancholia is the most widely accepted clinical indication for ECT, the information obtained from melancholic patients using these two strategies and their relevance to ECT research should be examined. Although similar techniques are likely to be helpful in defining the therapeutic mechanism of ECT, there have been few human studies on this subject. This discussion will be confined to the relevance of the DST and the TRH Test to the study of ECT in clinical practice.

The information provided by these neuroendocrine strategies may be used to examine three important questions. How can ECT-responsive patients be identified and, in particular, for which patients is ECT the *most* effective form of treatment? Can the therapeutic action of ECT be monitored by changes in biological markers and will these markers indicate the optimal endpoint for a course of ECT? Is it possible to predict which patients require continuation therapy to prevent relapse after a successful course of ECT?

Selection Of ECT-Responsive Patients

In addition to being a diagnostic aid in patients with melancholia, there are several reports which indicate that the presence of an abnormal DST may be useful as a predictor of response to treatment. Some studies suggest that patients with melancholia and an abnormal DST result have a better response to antidepressant treatment than similar patients with a normal DST result (Brown & Shuey, 1980; Greden et al. 1981). Another study reported that the DST result was more effective than clinician's judgment in predicting response of depressed catatonics to thymoleptics (Carman, Hall, Wyatt, & Crews, 1980).

It remains unclear whether the DST can identify particular melancholic patients who will respond better to ECT than antidepressant medication. There are two subgroups of patients with melancholia who generally have an excellent response to ECT and are more likely to be unresponsive to antidepressant medications. These are depressed patients with a catatonic syndrome and patients with an affective psyhcosis. Melancholic patients with psychosis may have a higher frequency of abnormal DST results than is generally present in melancholia (Carroll et al. 1980; Rudorfer, Hwu, & Clayton, 1982). In addition, retrospective examination of DST results in patients referred for ECT by clinical criteria alone shows a very high frequency of abnormal DST results (Papakostas, Fink, Lee, Irwin, & Johnson, 1981; Albala, unpublished data). These observations cannot demonstrate a relationship between an abnormal DST result in melancholia and good response to ECT. This possible association requires examination in a prospective study which controls for the psychotic and catatonic subtypes of melancholia, and compares the pretreatment DST result with the relative efficacy of antidepressant medication and ECT.

There have been no prospective studies to suggest that the TRH Test can be used to predict response to ECT. If the data reported by Papakostas, et al., (1981) are re-examined using the Δ TSH criterion of less than 7 μU/ml as suggested by Gold, Pottash, Extein, Martin, Howard, Mueller, and Sweeney (1981), it is evident that six out of seven patients with an abnormal TRH Test responded to ECT, whereas only one out of four patients with a normal TRH Test showed a good response. These data suggest that the relationship of the TRH test to prediction of ECT response deserves further examination.

Determination of Endpoint for a Course of ECT

One of the important problems faced by the clinician using ECT is to determine when a course is complete. In an attempt to lessen memory impairment, it is advisable to give the least number of ECT treatments necessary to induce relief of symptoms and prevent an early relapse. However, as discussed separately (*see* Haskett, pp. 75-78) no reliable criterion exists for determining the optimal number of ECT necessary to treat a specific patient. There are indications that the DST can provide some information on this subject.

Several investigators reported the results of serial DSTs performed throughout a course of ECT. Dysken, Pandey, Chang, Hicks, and Davis (1979) reported a case of a 56-year-old man with a diagnosis of major depressive disorder, psychotic and endogenous subtype, who was treated with ECT and had weekly DSTs throughout his treatment. They found that the abnormal DST results observed prior to treatment steadily normalized in association with clinical recovery. In another case report, Albala, Greden, and Carroll (1980) performed weekly DST assessments on a 69-year-old woman who was being treated with ECT. The abnormal pretreatment DST results normalized after the third ECT even though her depressive symptoms remained quite prominent. Further treatment resulted in good clinical recovery. More recently, Rothschild and Schatzberg (1982) reported the case of a 39-year-old man with a psychotic depression in whom the DST was performed serially during two courses of ECT. Each time, the DST normalized prior to complete, yet short-lived, clinical recovery.

Albala, Greden, Tarika, and Carroll (1981) selected a group of six unipolar endogenous depressives with abnormal DST results prior to treatment and who were treated with ECT. The DST was repeated every 5 to 7 days throughout treatment. Five out of the six patients responded favorably to ECT. The DST result in all responders normalized early in treatment despite only modest clinical improvement. Further ECT resulted in complete clinical recovery and a persistence of normal DST results. The single patient in whom DST normalization was not observed failed to respond to treatment. Similar results were reported by Schlesser and Rush (1981) who studied 12 endogenous depressives with abnormal DST results. They found that at mid-treatment six of the eventual 10 responders had normal DST results, and by the end of treatment the DST was normal in all 10 responders. In contrast, the two patients who did not respond to ECT continued to show abnormal DST results.

These findings seem to indicate that during the ECT-induced clinical improvement, the post-dexamethasone cortisol levels decrease and eventually normalize. This pattern is only observed among ECT responders and does not occur in patients who have a poor outcome to the treatment. This suggests that the DST can be used as a biological monitor of clinical response to ECT. Another aspect of these studies is the timing of the DST normalization in relation to clinical improvement. DST normalization precedes complete clinical recovery and accurately identifies the eventual ECT responders. This finding has important implications for the clinician who may be inclined to stop a course of ECT because of no apparent response. The presence of a normalized DST may indicate that extra treatments will eventually result in good clinical recovery.

Theoretically, serial TRH Tests may also yield information which is potentially useful in the clinical management of patients receiving ECT. This would particularly apply to those depressed patients who have a normal DST result and an abnormal TRH Test result. The existence of such a patient population has been demonstrated by Extein, Pottash, and Gold (1981) who conducted both DSTs and TRH Tests on patients diagnosed as major depressive disorder, primary subtype. They found that 34% of these patients had an abnormal TSH response to TRH in the presence of a normal DST result. Serial TRH Tests have been done in a group of 21 unipolar patients treated with clomipramine (Langer, Schönbeck, Koinig, Lesch, Schüssler, & Waldhäusl, 1980). The data suggested a significant statistical correlation between clinical improvement and increased TSH response to TRH. A similarly designed study with ECT-treated patients has not been reported and is necessary to evaluate the potential use of the TRH Test as a monitor of clinical response to ECT.

Prediction of Relapse After ECT

The incidence of relapse after successful treatment of ECT is reported to be very high. This is discussed in more detail elsewhere (*see* Haskett, page). It would be extremely valuable if tests could identify those patients who are more likely to experience an early relapse. This would permit a clinician to prescribe continuation therapy for those patients who require prophylaxis after completion of a course of ECT. Several studies suggested that lack of DST normalization may predict early relapse despite apparent clinical remission of the depression (Greden, Albala, Haskett, James, Goodman, Steiner, & Carroll, 1980; Goldberg, 1980; Gold, Pottash, Extein, & Sweeney, 1980; Papakostas et al., 1981).

In two of these studies specific data regarding ECT-treated patients are available. Greden et al. (1980) reported 14 patients with abnormal pretreatment DST results. Four of these patients were treated with ECT and all responded to treatment. Three responders had a normal DST after ECT and remained asymptomatic for at least 7 months. One patient clinically improved after the course of ECT, but did not show normalization of the neuroendocrine disturbance. She was admitted 6 weeks later for treatment of a relapse with a second ECT course which resulted in both clinical recovery and DST normalization. She subsequently remained asymptomatic for at least 1 year. Papakostas et al. (1981) presented a series of 14 unipolar depressed patients who were treated with ECT. Nine patients eventually responded to treatment and eight of these had pretreatment post-dexamethasone cortisol levels in excess of 5 μg/dl. At discharge, the DST result had normalized and all had a good outcome for 1 to 9 months. The three patients who responded clinically but still displayed abnormal DSTs had a poor outcome. Two were readmitted within 2 months and the third committed suicide 4 weeks after discharge.

These data suggest that persistently abnormal DST results after a course of ECT predict a poor outcome and a high risk for relapse, even where clinical recovery appears adequate. Conversely, clinical recovery accompanied by DST normalization may be a predictor of good outcome. An exception to this appears in a case report by Rothschild and Schatzberg (1982). Their patient was successfully treated with ECT, and normalization of the DST occurred. The patient, however, quickly relapsed and the DST again became abnormal. A second ECT course produced good clinical response and DST normalization. Still a second relapse occurred in association with an abnormal DST. Remission and DST normalization were eventually accomplished and maintained with the use of amoxapine. In this case DST normalization failed to predict a good outcome and was associated with rapid relapse. An alternative explanation is that this patient may have been a "rapid cycler" (Dunner, Patrick, & Fieve, 1977), and every relapse could have represented a new episode rather than a reemergence of the original episode. Greden, DeVigne, Albala, Tarika, Buttenheim, Eiser, and Carroll (1980) have shown that DST results can rapidly change in association with mood shifts in rapid cycling bipolar patients.

Several studies have reported on repeat TRH Tests after clinical recovery (Kirkegaard, 1981). It is apparent that some patients do not show a normalized TRH Test result despite clinical recovery. This suggests that, as mentioned in the previous section on the DST, antidepressant treatment can have a symptomatic effect in some patients without altering the neuroendocrine disturbance. Kirkegaard (1981) has reported that the persistence of abnormal TRH Test responses after clinical recovery predicts early relapse. In their study of 66 "clinically cured" patients, antidepressant therapy was withdrawn after clinical recovery and the patients were followed for at least 6 months or until relapse. They showed that $\Delta\Delta$ TSH values (Δ TSH at discharge - Δ TSH on admission) clearly distinguished good prognosis from poor prognosis patients. The $\Delta\Delta$ TSH criterion value of 2.0 μU/ml predicted cure in 27 out of 29 patients and relapse in 33 out of 37 patients. Most of the patients with little treatment-associated improvement in their neuroendocrine disturbance ($\Delta\Delta$TSH $< 2\mu$U/ml) relapsed within 4 months. In contrast, the patients with $\Delta\Delta$ TSHs > 2.0 μU/ml had a good outcome during the first 6 months after discontinuation of antidepressant treatment. This group of patients includes a subset of 35 patients with endogenous depression who were treated with ECT. All 19 patients with $\Delta\Delta$ TSH ≤ 2.0 μU/ml relapsed within 6 months of completing the ECT course. By comparison, only 3 out of 16 patients with $\Delta\Delta$ TSH > 2.0 μU/ml suffered a relapse. The relapse rates were similar among unipolars and bipolars (Kirkegaard & Bjorum, 1980). These results strongly suggest that normalization of the TRH Test, as defined by Kirkegaard, can be a reliable indicator of cure and therefore identify those patients who require maintenance antidepressant therapy to prevent relapse. A replication of this study is required.

In the series of patients presented by Papakostas et al. (1981), three of the nine ECT responders had blunted TRH Test results ($\leq$ 5.0 μU/ml) prior to treatment. In two of these cases the TRH Test was repeated and remained blunted (one with a $\Delta\Delta$TSH < 2.0 μU/ml and the other with a $\Delta\Delta$ TSH > 2.0 μU/ml). Neither relapsed during a 9-month followup period. The third patient with a blunted response on admission committed suicide 1 month after discharge. No repeat TRH Test was available in this case. The number of patients in this study is too small to draw any conclusions on the prognostic value of the TRH Test.

Conclusion

This review of neuroendocrine studies has been unable to provide definitive answers to the previously stated questions for ECT research. There is, however, much evidence that this area of investigation is likely to be helpful in the future. It is unlikely that a single neuroendocrine test will be able to select those patients requiring ECT in preference to other antidepressant treatment. Combination of neuroendocrine testing with other laboratory markers, or clinical subgrouping of syndromes, may however be successful in providing objective indications for ECT. The relationship of the normalization of neuroendocrine function to the therapeutic mechanism of ECT requires further examination. It may be possible to use these markers to more precisely determine the "adequate dosage" of treatment for individuals receiving ECT. Finally, it appears that changes in neuroendocrine tests during ECT may be of great assistance in the identification of patients with a high likelihood of relapse. There is a need for prospective studies to clarify these questions. The clinician using ECT may then be able to use objective criteria to support decisions on patient selection, duration of ECT course, and the need for continuation treatment.

References

Albala, A.A., Greden, J.F., and Carroll, B.J. Serial dexamethasone suppression tests in affective disorders. *Am. J. Psychiatry*, 137:383, 1980.

Albala, A.A., Greden, J.F., Tarika, J., and Carroll, B.J. Changes in serial dexamethasone suppression tests among unipolar depressives receiving electroconvulsive treatment. *Biol. Psychiatry*, 16:551-560, 1981.

Brown, W.A., and Shuey, I. Response to dexamethasone and subtype of depression. *Arch. Gen. Psychiatry*, 37:747-751, 1980.

Carman, J.C., Hall, K., Wyatt, E., and Crews, E.L. Dexamethasone non-suppression: Predictor of thymoleptic response in catatonic and schizoaffective patients. *Soc. Biol. Psychiatr. Sci. Proc.*, Abstr. #4:36, 1980.

Carroll, B.J., Greden, J.F., Feinberg, M., et al. Neuroendocrine dysfunction in genetic subtypes of primary unipolar depression. *Psychiatr. Res.*, 2:251-258, 1980.

Carroll, B.J., Feinberg, M., Greden, J.F., et al. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry*, 38:15-22, 1981.

Dunner, D., Patrick, V., and Fieve, R. Rapid cycling manic depressive patients. *Compr. Psychiatry*, 18:561-566, 1977.

Dysken, M.W., Pandey, G.N., Chang, S.S., et al. Serial post-dexamethasone cortisol levels in a patient undergoing ECT. *Am. J. Psychiatry*, 136:1328, 1979.

Extein, I., Pottash, A.L.C., and Gold, M.S. Relationship of thyrotropin-releasing hormone test and dexamethasone suppression test abnormalities in unipolar depression. *Psychiatr. Res.*, 4:49-53, 1981.

Gold, M.S., Pottash, A.L.C., Extein, I., and Sweeney, D.R. Dexamethasone suppression tests in depression and response to treatment. *Lancet*, 1:1190, 1980.

Gold, M.S., Pottash, A.L.C., Extein, I., et al. The TRH test in the diagnosis of major and minor depression. *Psychoneuroendocrinology*, 6:159-169, 1981.

Goldberg, I.K. Dexamethasone suppression test as indicator of safe withdrawal of antidepressant therapy. *Lancet*, 1:376, 1980.

Greden, J.F., Albala, A.A., Haskett, R.F., et al. Normalization of dexamethasone suppression test: A laboratory index of recovery from endogenous depression. *Biol. Psychiatry*, 15:449-458, 1980.

Greden, J.F., DeVigne, J.P., Albala, A.A., et al. Serial dexamethasone suppression tests among rapidly cycling bipolar patients. *Biol. Psychiatry*, 17:443-450 1982.

Greden, J.F., Kronfol, Z., Gardner, R., et al. Dexamethasone suppression test and selection of antidepressant medications. *J. Affect. Dis.*, 3:389-396, 1981.

Kastin, A.J., Ehrensing, R.H., Schalch, D.S., and Anderson, M.S. Improvement in mental depression with decreased thyrotropin response after administration of thyrotropin-releasing hormone. *Lancet*, 2:742, 1972.

Kirkegaard, C., and Bjørum, N.TSH responses to TRH in endogenous depression. *Lancet*, 1:152, 1980.

Kirkegaard, C. Thyrotropin response to thyrotropin-releasing hormone in endogenous depression. *Psychoneuroendocrinology*, 6(3):189-212, 1981.

Langer, G., Schönbeck, G., Koinig, G, et al. Antidepressant drugs and the hypothalamic-pituitary-thyroid axis. *Lancet*, 1:100-101, 1980.

Liddle, G.W. Tests of pituitary-adrenal suppressibility in the diagnosis of Cushing's syndrome. *J. Clin. Endocrinol. Metab.*, 20:1539-1560, 1960.

Papakostas, Y., Fink, M., Lee, J., et al. Neuroendocrine measures in psychiatric patients: Course and outcome with ECT. *Psychiatr. Res.*, 4:55-64, 1981.

Prange, A.J., Wilson, I.C.; Lara, P.P., et al. Effects of thyrotropin-releasing hormone in depression. *Lancet*, 2:999-1002, 1972.

Rothschild, A.J., and Schatzberg, A.F. Fluctuating post-dexamethasone cortisol levels in a patient with melancholia. *Am. J. Psychiatry*, 139(1):129-130, 1982.

Rudorfer, M.V., Hwu, H., and Clayton, P. Dexamethasone suppression test in primary depression: Significance of family history and psychosis. *Biol. Psychiatry*, 17:41-48, 1982.

Schlesser, M.A., and Rush, A.J. Serial changes in hypothalamic-pituitary-adrenal axis activity among depressives receiving ECT. *Soc. Biol. Psychiatr. Sci. Proc.*, Abstract #41:69, 1981.

Hemispheric Asymmetry in Affective Disorders

Henry A. Nasrallah, M.D.[1]

Introduction

Over the past 30 years, significant advances have been made in the understanding of the cerebral hemispheric and interhemispheric functions in the human brain. In contrast to previous notions that the two cerebral hemispheres were duplicate structures with one dominant/major (usually the left) and another nondominant/minor (usually the right) hemisphere, research over the

---

[1] Department of Psychiatry, University of Iowa College of Medicine and VA Medical Center, Iowa City, IA

Address Correspondence to:
Henry A. Nasrallah, M.D., Chief, Psychiatry Service, VA Medical Center, Iowa City, IA 52240.

past three decades has established that the two cerebral hemispheres are structurally and functionally asymmetrical, and that both have to be fully integrated to produce optimal mental activity.

The quantum leap in the understanding of hemispheric asymmetry was the product of the pioneering work of Sperry and others into the split brain of animals (Myers & Sperry, 1953; Sperry, Stamm, & Miner, 1956; Sperry, 1961) and humans (Gazzaniga, 1970) showing that the surgically separated hemispheres contain two independent spheres of consciousness, with different motor, perceptual, cognitive, conative, and emotive functions. The separated cerebral hemispheres can be trained to concurrently perform contradictory tasks, and cerebral dominance for a certain task (i.e., laterality) can be experimentally shifted from one hemisphere to the other. In the human brain, the left hemisphere is usually more specialized for verbal, analytical, logical, and propositional tasks while the right hemisphere is more specialized for spatial, synthetic, intuitive, and oppositional tasks. The monumental studies of split-brain patients have indeed revolutionized the scientific and philosophical conceptualization of brain, mind, and the unity of conscious awareness (Sperry, 1968; Puccetti, 1973; Sperry, 1977; LeDoux, Wilson, & Gazzaniga, 1977).

Inevitably, the new knowledge of the cerebral hemispheric asymmetry of function triggered novel areas of psychiatric research which over the past decade has created an impressive body of evidence linking psychopathology with normal and abnormal cerebral lateralization (Gruzelier & Flor-Henry, 1979). Laterality shifts have been found in psychosis (Wexler & Heninger, 1979) and have been shown to be related to many factors frequently associated with psychiatric illness such as stress (Tucker, Roth, Arneson, & Buckingham, 1977), alcohol ingestion (Chandler & Parsons, 1977), sleep (Goldstein, Stoltzfus, & Gardocki, 1972), hypnosis (Frumkin, Ripley, & Cox, 1978), orgasm (Cohen, Rosen, & Goldstein, 1976), psychotomimetic drugs (Goldstein & Stoltzfus, 1973), and neuroleptics (Serafetinides, 1972).

Most of the research into hemispheric asymmetries in psychiatric illness has focused on the major psychoses such as schizophrenia and affective disorders. The literature has tended to suggest that schizophrenia is associated with left hemispheric as well as interhemispheric dysfunction (Newlin, Carpenter, & Golden, 1981; Nasrallah, in press). In this paper, a selective review of the literature on cerebral laterality in affective disorders will be presented, with a special reference to implications for electroconvulsive therapy (ECT) research.

Hemispheric Asymmetries in Affective Disorders

Unilateral brain lesions: The clinical presentations of patients with neurological lesions in the right or left cerebral hemisphere provided the first clue of hemispheric asymmetry for affect. Babinski (1914) noted that patients with right hemispheric lesions behaved indifferently to the contralateral sensory-motor deficits. Goldstein (1939) noted that left hemispheric lesions were associated with a catastrophic reaction, whereas right hemispheric lesions were associated with indifference. Gainotti (1972) observed that the emotional and psychiatric symptoms accompanying a brain lesion depend on the side of the lesion.

Nasrallah and McChesney (1981) reported that tumors of the corpus callosum were significantly more likely to manifest clinical signs and symptoms of depression than tumors in either cerebral hemispheres. They suggested that interruption of interhemispheric interaction may be associated with affective symptoms.

Temporal lobe epilepsy: In a study of psychoses associated with temporal lobe epilepsy, Flor-Henry (1969) stated that left temporal lobe foci are more likely to be associated with a schizophrenia-like psychosis, while the right hemispheric foci are more likely to be associated with affective psychosis. Bear and Fedio (1977) reported that patients with right temporal lobe epilepsy had emotional tendencies and denied depression even when they appeared to have it, while patients with left temporal lobe foci had ideational traits and dyssocial behavior, and reported more depression even when they did not have it. They suggested that their findings indicate a hemispheric asymmetry for the expression of affect.

Intracarotid amytal effects: Terzian and Cecotto (1959) reported a differential response of the two cerebral hemispheres to intracarotid sodium amytal injections with "depressive-catastrophic" reaction following the inactivation of the right hemisphere. These findings were replicated (Rossi & Rosadini, 1967), except in patients with diffuse brain damage (Alema, Rosadini, & Rossi, 1961), and not replicated by Milner (1967).

Hommes and Panhuysen (1971) gave unilateral intracarotid amytal to patients hospitalized for depression, and found that more dysphasia occurred with right carotid amytal, and the severity of depression correlated negatively with dominance for speech in the left hemisphere, suggesting that left hemispheric dominance is reduced in depression. Elevation of mood was noted with injections on either side to varying extents, but depressive reactions were difficult to ascertain against the background of preexisting clinical depression.

ECT and laterality: A large literature appeared during the past 15 years suggesting that ECT applied only to the right hemisphere is as effective as bilateral ECT for the treatment of depression, but that ECT to the left hemisphere only was significantly less effective than bilateral or right hemispheric ECT (Halliday, Davison, Brown, & Kreeger, 1968; Abrams & DeVito, 1969; Cronin, Bodley, Potts, Matgher, Gardner, & Tobin, 1970; Costello, Belton, Abra, & Dunn, 1970) which has led to suggestions that depression may be associated with right hemispheric dysfunction. Deglin and Nikolaenko (1975) found more dysphoric reactions following left ECT and more euphoric reactions following right ECT and concluded that the left hemisphere plays a major role in the regulation of mood.

Kronfol, Hamsher, Digre, and Waziri (1978) reported that before treatment with ECT, depressed patients had more abnormalities in neuropsychological testing of right hemisphere functions compared to the left, and that after ECT (whether unilateral right or left) the right but not the left hemispheric functions were improved.

Nasrallah, McCalley-Whitters, and Keelor (submitted for publication) tested depressed patients for sensory and motoric lateralization before and after ECT to examine the effect of ECT on hemispheric dominance. All patients experienced shifts in either sensory or motor lateralization, but with equal frequency towards left and right hemispheric dominance.

EEG asymmetry: Using power spectrum EEG, Flor-Henry (1976) showed that schizophrenia is associated with left temporal EEG abnormalities, while affective illness is associated with right temporal abnormalities. Urstad (1979) found higher alpha activity on the left compared to the right temporal region in a group of schizophrenic and depressed patients, while the control group had a reverse pattern. After treatment, the depressed patients showed normal alpha predominance over the right hemisphere.

Abrams and Taylor (1979) examined 132 rigorously diagnosed patients with affective disorder and compared them to 27 schizophrenic patients. They found that the schizophrenic patients had a higher rate of abnormal EEG, particularly temporal slowing, whereas the affective group had more parieto-occipital abnormalities. They also noted that EEG abnormalities were lateralized, with predominantly left hemispheric abnormalities in schizophrenia and predominantly right hemispheric abnormalities in the affective group.

Skin conductance: Brain damage has been found to be associated with decreased skin conductance on the side ipsilateral to the lesion (Sourek, 1965). Gruzelier and Venables (1974) found decreased skin conductance on the right side in depressed patients and concluded that there is right hemispheric dysfunction in depression. Myslobodsky and Horesh (1978) reached the same conclusion, but with the findings of high conductance on the left side in depressed patients, which they interpret as evidence of contralateral brain dysfunction in the right hemisphere.

Dichotic listening: Dichotic listening has been shown to be a reliable method of indicating which cerebral hemisphere is dominant for language functions (Kimura, 1967). Yozawitz, Bruder, Sutton, et al. (1979), using verbal and nonverbal auditory stimuli, found that ear asymmetry of affectively ill patients was similar to patients with right temporal lobe lesions. They also found that neuroleptics worsen this asymmetry in affective patients but normalize it in schizophrenic patients.

Wexler and Heninger (1979) reported that the normal dichotic asymmetry diminished in both schizophrenic and depressed patients when the psychopathology was high and was restored when patients improved. They concluded that psychotic illness is associated with a shift in laterality from left to right.

Bruder and Yozawitz (1979) also found that dichotic asymmetry in depression is consistent with right hemispheric dysfunction. Caudry and Kirk (1979) found schizophrenic patients to have a right ear advantage, while depressed patients have a left ear advantage. They concluded that depressives have a higher tendency for speech to be located in the right hemisphere.

Lateral eye movements: Conjugate lateral eye movements have been hypothesized to reflect activation of the cerebral hemisphere contralateral to the direction of gaze (Bakan, 1971). Verbal tasks have been shown to activate the left cerebral hemisphere, and spatial and emotional tasks preferentially activate the right cerebral hemisphere (Kinsbourne, 1972; Schwartz, Davidson, & Maer, 1975).

Schweitzer (1979) reported that depressed patients initiated reflective tasks more often in the right hemisphere. Myslobodsky and Horesh (1978) found depressed patients to look more often to the left for various tasks, and concluded that there may be right hemispheric overactivity in depression.

Motoric lateralization: Handedness is a crude measure of cerebral dominance for motoric laterality, with right handedness indicating left hemisphere dominance, and left handedness or ambidexterity reflecting right hemisphere dominance, in some cases due to early brain insult and left cerebral impairment (Satz, 1972).

Left handedness has been reported to be high in schizophrenia (Dvirskii, 1976; Gur, 1977; Nasrallah, Schroeder, Keelor, & McCalley-Whitters, 1981), particularly the paranoid subtype (Nasrallah, Kuperman, McCalley-Whitters, & Keelor, 1981). An increased frequency of left handedness in affective disorders has been reported by some investigators (Lishman & McMeekan, 1976; Flor-Henry, 1979) but not by others (Fleminger, Dalton, & Standage, 1977; Nasrallah & McCalley-Whitters, in press).

Neuroanatomical measurements: Rosenthal and Bigelow (1972) reported an increase in the thickness of the corpus callosum (the largest interhemispheric commissure) in postmortem brains of chronic schizophrenic patients. This has been widely interpreted as possible evidence for interhemispheric dysfunction in schizophrenia.

In the only other study of corpus callosum thickness in schizophrenia (Nasrallah, Bigelow, Rauscher, & Wyatt, 1979), brains of patients with bipolar affective disorder were also studied. The mean corpus callosum thickness in the affective group was almost identical to that of the late onset (paranoid) schizophrenic group, but almost significantly less ($p < .08$) than the early onset (nonparanoid) schizophrenic group. Histological studies of the corpus callosum in affective disorders are also similar to the late onset schizophrenic group (Nasrallah, McCalley-Whitters, Bigelow, & Rauscher, 1982).

Positron emission tomography (PET): Very recent studies of brain glucose metabolism using PET scans suggest that in contrast to the hypofrontal pattern seen in schizophrenic patients, patients with bipolar disorder have a hyperfrontal pattern during the manic phase. Asymmetry was also noted in schizophrenic patients (more metabolism in the right hemisphere) but data are not yet available on affectively ill patients (Farkas, 1980).

Discussion

The above review reflects the various lines of evidence for hemispheric asymmetry in affective illness. Although some form of right hemispheric dysfunction is the leading model for understanding hemispheric asymmetry of function in affective disorders, more evidence is needed to confirm that hypothesis and the specific nature of the hemispheric dysfunction in affective illness has to be defined. Many of the studies in this area of research suffer from methodological flaws that limit the reliability and validity of the results. Perhaps the greatest source of error is diagnostic accuracy, particularly in light of the heterogeneity of affective disorders, and the overlap with the schizophrenias. Almost all the studies of laterality did not use accepted diagnostic criteria such as the Diagnostic and Statistical Manual-III (DSM-III). The measurement of laterality is another area that requires further reliability and validity research (Colbourn, 1979).

The critical research issue in the area of hemisphere asymmetry of function in affective illness is therefore the establishment of whether one of the cerebral hemispheres is differentially involved in affective illness and, if so, how. The proper strategy for answering this question should involve multiple measures of laterality in rigorously defined drug-free populations of affectively ill patients diagnosed by specific and reliable criteria.

ECT research can provide an excellent avenue for the study of hemispheric asymmetries in affective illness. ECT is an effective somatic treatment which is more easily quantifiable compared to pharmacological treatments. It also offers the distinct advantage and flexibility of being administered to either cerebral hemisphere or to both, whereas drugs are given systemically and therefore cannot be targeted to one part of the brain only. Thus, ECT offers a unique therapeutic and research strategy for the investigation of hemispheric dysfunction in affective illness. Patients could be assessed prior to treatment for both psychopathology and neuropsychological deficit as well as for measures of laterality such as EEG, dichotic listening, tachistoscopy, skin conductance and motoric preference. Repeat evaluation after unilateral ECT treatment to one hemisphere would then provide valuable data as to any dysfunction in either hemisphere, and to the concomitant laterality changes (if any) with therapeutic response.

References

Abrams, R., and DeVito, R.A. Clinical efficacy of unilateral ECT. *Dis. Nerv. Syst.*, 30:262-268, 1969.

Abrams, R., and Taylor, M.A. Differential EEG patterns in affective disorder and schizophrenia. *Arch. Gen. Psychiatry*, 36:1355-1358, 1979.

Alema, G., Rosadini, G., and Rossi, G.F. Psychic reactions associated with intracarotid amytol injection and relation to brain damage. *Excerpta Medica*, 37:154-155, 1961.

Babinski, M.J. Contributions a l'etude des troubles mentaux dans l'hemiplegie organique cerebrale (anosognosie). [Contributions to the study of mental problems in organic cerebral hemiphegia (visual inattention)]. *Rev. Neurol.*, 37:845-848, 1914.

Bakan, P. The eyes have it. *Psychology Today*, 4:64-67, 1971.

Bear, D.M., and Fedio, P. Quantitative analysis of interictal behavior in temporal lobe epilepsy. *Arch. Neurol.*, 34:454-467, 1977.

Bruder, G.E., and Yozawitz, A. Central auditory processing and lateralization in psychiatric patients. In: Gruzelier, J., and Flor-Henry, P. (eds.), *Hemisphere Asymmetries of Function in Psychopathology*, New York: Elsevier/North Holland Biomedical Press, 1979, pp. 561-580.

Buchsbaum, M.S., Ingvar, D.H., Kessler, R., et al. Cerebral glucography with positron tomography. Use in normal subjects and in patients with schizophrenia. *Arch. Gen. Psychiatry*, 39:251-259, 1982.

Caudrey, D.J., and Kirk, K. The perception of speech in schizophrenia and affective disorders. In: Gruzelier, J., and Flor-Henry, P. (eds.), *Hemisphere Asymmetries of Function in Psychopathology*. New York: Elsevier/North Holland Biomedical Press, 1979, pp. 581-601.

Chandler, B.C., and Parson, O.A. Altered hemispheric functioning under alcohol. *J. Stud. Alcohol*, 38:381-391, 1977.

Cohen, H.D., Rosen, R.C., and Goldstein, L. Electroencephalographic laterality changes during human sexual orgasm. *Arch. Sex. Behav.*, 5:189-199, 1976.

Colbourn, C.J. Laterality measurement and theory. In: Gruzelier, J., and Flor-Henry, P. *Hemisphere Asymmetries of Function in Psychopathology*. New York: Elsevier/North Holland Biomedical Press, 1979, pp. 65-76.

Costello, C.G., Belton, G.P., Abra, J.E., and Dunn, B.E. The amnesic and therapeutic effects of bilateral and unilateral ECT. *Br. J. Psychiatry*, 116:69-78, 1970.

Cronin, E., Bodley, P., Potts, L., et al. Unilateral and bilateral ECT: A study of memory disturbance and relief from depression. *J. Neurol. Neurosurg. Psychiatry*, 3:705-713, 1970.

Deglin, V.L., and Nikolaenko, N.N. Role of the dominant hemisphere in regulation of emotional states. *Hum. Physiol.*, 1:394-402, 1975.

Dvirskii, A.E. Functional asymmetry of the cerebral hemispheres in clinical types of schizophrenia. *Neurosci. Behav. Physiol.*, 7:236-239, 1976.

Farkas, T. Biochemical imaging of the brain. Paper read at the 35th Annual Meeting of the Society for Biological Psychiatry, Boston, Mass., September 1980.

Fleminger, J.J., Dalton, R., and Standage, K.F. Handedness in psychiatric patients. *Br. J. Psychiatry*, 131:448-452, 1977.

Flor-Henry, P. Psychosis and temporal lobe epilepsy: A controlled investigation. *Epilepsia*, 10:363-395, 1969.

Flor-Henry, P. Lateralized temporal-limbic dysfunction and psychopathology. *Ann. NY Acad. Sci.*, 280:777-797, 1976.

Flor-Henry, P. Laterality shifts of cerebral dominance, sinistrality, and psychosis. In: Gruzelier, J., and Flor-Henry, P. (eds.) *Hemisphere Asymmetries of Function in Psychopathology*. New York: Elsevier/North Holland Biomedical Press, 1979, pp. 3-20.

Frumkin, L.R., Ripley, H.S., and Cox, G.B. Changes in cerebral hemispheric lateralization with hypnosis. *Biol. Psychiatry*, 13:741-750, 1978.

Gainotti, G. Emotional behaviour and hemispheric side of the lesion. *Cortex*, 8:41-49, 1972.

Gazzaniga, M.S. *The Bisected Brain*. New York: Appleton-Century-Crofts, 1970.

Goldstein, K. *The Organism: A Holistic Approach to Biology, Derived from Pathological Data in Man*. New York: American Books, 1939.

Goldstein, L., Stoltz, N.W., and Gardocki, J.F. Changes in interhemispheric amplitude relationships in the EEG during sleep. *Physiol. Behav.*, 8:811-815, 1972.

Goldstein, L., and Stoltzfus, N.W. Psychoactive drug-induced changes of interhemispheric EEG amplitude relationships. *Agents and Actions,* 3:124-132, 1973.

Gruzelier, J., and Flor-Henry, P. (eds.) *Hemisphere Asymmetries of Function in Psychopathology.* New York: Elsevier/North Holland Biomedical Press, 1979.

Gruzelier, J.H., and Venables, P.H. Bimodality and lateral asymmetry of skin conductance orienting activity in schizophrenics: Replication and evidence of lateral asymmetry in patients with depression and disorders of personality. *Biol. Psychiatry,* 8:55-73, 1974.

Gur, R.E. Motoric laterality imbalance in schizophrenia. *Arch. Gen. Psychiatry,* 34:33-37, 1977.

Halliday, A.M., Davison, K., Brown, M.W., and Kreeger, L.C. Comparison of effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and non-dominant hemisphere. *Br. J. Psychiatry,* 114:997-1012, 1968.

Hommes, O.R., and Panhuysen, L.H.H.M. Depression and cerebral dominance. *Psychiatr. Neurol. Neurochir.,* 74: 259-270, 1971.

Kimura, D. Functional Asymmetry of the brain indichotic listening. *Cortex,* 3:163-178, 1967.

Kinsbourne, M. Eye and head turning indicates cerebral lateralization. *Science,* 176:539-541, 1972.

Kronfol, Z., Hamsher, K., Digre, K., and Waziri, R. Depression and hemispheric functions: Changes asociated with unilateral ECT. *Br. J. Psychiatry,* 132:560-567, 1978.

LeDoux, J.E., Wilson, D.H., and Gazzaniga, M.S. A divided mind: Observations on the conscious properties of the separated hemispheres. *Ann. Neurol.,* 2:417-421, 1977.

Lishman, W.A., and McMeekan, E.R.L. Hand preference in psychiatric patients. *Br. J. Psychiatry,* 129:158-166, 1976.

Milner, B. Discussion of the subject: Experimental analysis of cerebral dominance in man. In: Millikan, C.H., and Darley, F.L. (eds.), *Brain Mechanisms Underlying Speech and Language.* New York: Grune & Stratton, 1967.

Myers, R.E., and Sperry, R.W. Interocular transfer of a visual form discrimination habit in casts after section of the optic chiasm and corpus callosum. *Anat. Record,* 115:351-354, 1953.

Myslobodsky, M.S., and Horesh, N. Bilateral electrodermal activity in depressive patients. *Biol. Psychiatry,* 6:111-120, 1978.

Nasrallah, H.A. Laterality and hemispheric dysfunction in schizophrenia. In: Henn, F.A., and Nasrallah, H.A. (eds.), *Schizophrenia as a Brain Disease.* New York: Oxford University Press. (In press)

Nasrallah, H.A., Bigelow, L.B., Rauscher, F.P., and Wyatt, R.J. Corpus callosum thickness in schizophrenia. New Research Abstracts. American Psychiatric Association 132nd Annual Convention, Chicago, IL., May 1979.

Nasrallah, H.A., Kuperman, S., McCalley-Whitters, M., and Keelor, K. Laterality in paranoid and non-paranoid schizophrenia. New Research Abstracts. American Psychiatric Association 134th Annual Meeting, New Orleans, LA., May 1981.

Nasrallah, H.A., and McCalley-Whitters, M. Motoric lateralization in manic males. *Br. J. Psychiatry.,* (In press)

Nasrallah, H.A., McCalley-Whitters, M., and Keelor, K. Effect of ECT on sensory-motor lateralization. (Submitted, 1982.

Nasrallah, H.A., McCalley-Whitters, M., Rauscher, F.P., and Bigelow, L.B. Histopathology of the corpus callosum in early and late onset schizophrenia. Proceedings of the Annual Meeting of the American Association for the Advancement of Science, Washington, DC, January 1982.

Nasrallah, H.A., and McChesney, C.M. Psychopathology of corpus callosum tumours. *Biol. Psychiatry,* 16:661-667, 1981.

Nasrallah, H.A., Schroeder, C., Keeler, K., and McCalley-Whitters, M. Motoric lateralization in schizophrenic males. *Am. J. Psychiatry,* 138:1114-1115, 1981.

Newlin, D.B., Carpenter, B., and Golden, C.J. Hemisphere asymmetries in schizophrenia. *Biol. Psychiatry,* 16:561-582, 1981.

Puccetti, R. Brain bisection and personal identity. *Br. J. Philo. Sci.,* 24:339-355, 1973.

Rosenthal, R., and Bigelow, L.B. Quantitative brain measurements in chronic schizophrenia. *Br. J. Psychiatry,* 121:259-264, 1972.

Rossi, G.E., and Rosadini, G. Experimental analysis of cerebral dominance in man. In: Millikan, C.H., and Darley, F.L. (eds.), *Brain Mechanisms Underlying Speech and Language.* New York: Grune & Stratton, 1967.

Satz, P. Pathological left-handedness: An explanation. *Cortex,* 8:121-125, 1972.

Schwartz, G.E., Davidson, R.S., and Maer, F. Right hemisphere lateralization for emotion in the human brain. Interactions with cognition. *Science,* 190:286-288, 1975.

Schweitzer, L. Differences of cerebral lateralization among schizophrenic and depressed patients. *Biol. Psychiatry,* 14:721-733, 1979.

Serafetinides, E.A. Laterality and voltage in the EEG of psychiatric patients. *Dis. Nerv. Syst.,* 32:622-623, 1972.

Sourek, K. *The Nervous Control of Skin Potentials in Man.* Nakladatelstvi Ceskoslovensa Akademic Ved., Prague, 1965.

Sperry, R.W. Cerebral organization and behaviour. *Science,* 133:1749-1757, 1961.

Sperry, R.W. Hemisphere deconnection and unity in conscious awareness. *Am. Psychol.,* 23:723-733, 1968.

Sperry, R.W. Forebrain commissourotomy and conscious awareness. *J. Med. Philosophy,* 2:101-126, 1977.

Sperry, R.W., Stamm, J., and Miner, N. Relearning tests for interocular transfer following division of optic chiasma and corpus callosum in cats. *J. Comp. Physiol. Psychol.,* 49:529-533, 1956.

Terzian, H., and Ceccotto, C. Su un nuovo metodo per la determinazione e lo studio della dominanza emis erica. *Giorn. Psichiat. Neuropath.,* 87:889-924, 1959.

Tucker, D.M., Roth, R.S., Arneson, B.A., and Buckingham, V. Right hemisphere activation during stress. *Neuropsychologia,* 15:697-700, 1977.

Urstad, H. Hemisphere dominance: A temporal lobe shift in psychotic behaviour. *J. Oslo City Hosps.,* 1979.

Wexler, B.E., and Heninger, G.R. Alterations in cerebral laterality during acute psychotic illness. *Arch. Gen. Psychiatry,* 36:278-284, 1979.

Yozawitz, A., Bruder, G., Sutton, S., et al. Dichotic perception: Evidence for right hemisphere dysfunction in affective psychosis. *Br. J. Psychiatry,* 135:224-237, 1979.

The Relative Efficacy of Unilateral Nondominant and Bilateral Stimulation

Charles A. Welch, M.D.[1]

Unilateral nondominant electrode placement offers a marked reduction in adverse cognitive effects when compared to bilateral placement. In spite of this clear finding, bilateral placement remains the standard technique in the United States, and the 1976 APA Task Force on electroconvulsive therapy (ECT) found that 75% of survey respondents used bilateral electrode placement exclusively, presumably in the belief that it is more effective than the unilateral technique. The same is true in the United Kingdom. Over 35 different studies have compared the efficacy of unilateral and bilateral placement, but the results have been contradictory. Most investigators find equal efficacy for the two methods, and a few studies show one or the other to be superior. This disparity in findings has persisted to the present in spite of increasingly rigorous research designs. Because of the reduced morbidity associated with unilateral nondominant placement, it remains a pressing research priority to ascertain whether unilateral nondominant and bilateral placement are equally effective.

In a major review of this literature, d'Elia and Raotma (1975) examined 29 studies of this question published from 1962 to 1973. They divided the studies into five groups according to methodological criteria (random assignment, blind comparison, simultaneous controls, homogenous diagnostic groups, and open number of ECT treatments). They observed that the more rigorous the methodology, the more equivalent the efficacy of unilateral nondominant and bilateral ECT appear to be, and that of the five followup studies from 1 to 12 months, all found equal efficacy. They concluded, "The review of studies performed under adequate methodological conditions shows that nondominant ECT has the same antidepressive effect as bilateral ECT. This is in agreement with our knowledge that the antidepressive factor of ECT is bound to the seizure. Nondominant ECT has the advantage of a much lower frequency and intensity of side effects. In endogenous depression nondominant ECT should be the treatment of choice."

They speculated that one reason for the frequent finding of less efficacy with unilateral nondominant treatment may have been more frequent missed seizures with this technique than with bilateral placement.

Since this review, there have been five published comparison studies, and there are two in press. They have yeilded differing results.

Abrams and Taylor (1976) compared bilateral and simultaneous unilateral dominant and unilateral nondominant stimulation. They used random assignment, and a blind rater assessed improvement with the Hamilton Depression Scale 5 hours after the sixth treatment. Sine-wave stimulation was used throughout and there was no seizure monitoring. Bilateral ECT was found to be significantly more effective than simultaneous unilateral dominant—unilateral nondominant. The authors concluded, "The therapeutic differences we observed between our two treatment methods might therefore be explained by the different degree of diencephalic stimulation, the degree of frontal lobe stimulation, or both."

Although scientifically very interesting, this study is not a direct comparison of unilateral nondominant and bilateral ECT, and does not specifically address the question at hand.

Reichert, Benjamin, Keegan, and Marjerrison (1976) compared bilateral and unilateral nondominant ECT in a study of 50 patients. They employed a sinusoidal wave form but no seizure monitoring, although they stated that "All patients exhibited full tonic-clonic seizures." Blind raters assessed patients with the 17-scale Brief Psychiatric Rating Scale (BPRS) prior to treatment and 1 and 3 weeks after the last ECT. In addition, patients completed the Hildreth Mood and Attitude Scale, a subjective rating instrument, prior to treatment and 1 day after the third, fourth, fifth, sixth, and last treatments, and at 1 and 3 weeks after the last treatment. An open number of ECT were given based on clinical judgment. The authors found that there was no significant difference between the two groups on the BPRS ratings at 1 or 3 weeks. However, the bilateral group was significantly more improved subjectively at all points in time except the final

---

[1] Somatic Therapies Consultation Service, Massachusetts General Hospital, Boston, MA 02114.

rating at 3 weeks posttreatment, at which time there was no difference between the groups. They also found a 26% 1-month relapse rate with the unilateral group but only a 3% 1-month relapse rate with the bilateral group.

Heshe, Roder, and Theilgaard (1978), in a study of 51 patients, used random assignment and double-blind design in a comparison of bilateral and unilateral nondominant ECT. A sine-wave stimulus was used without seizure monitoring. The Hamilton Depression Scale was given pre-ECT and then 1 week and 3 months after the last treatment. The bilateral group was found to be slightly but significantly more improved at 1 week after treatment, but the difference disappeared at 3 months followup.

Weeks, Freeman, and Kendell (1980) studied 102 patients, comparing bitemporal with unilateral nondominant ECT. Sine-wave stimulus was used but there was no seizure monitoring. The number of ECT was open with a mean of 7.4 in the unilateral group and 7.2 in the bilateral group. Assignment was nonrandom, but blind raters assessed efficacy with the Hamilton Depression Scale pre-ECT and then at 1 week, 4 months, and 7 months after the last ECT. There were no significant differences in the degree of improvement at any of the assessment points. The authors performed extensive cognitive testing which confirmed prior findings that unilateral nondominant ECT causes very little cognitive impairment even short term, and markedly less impairment than bilateral ECT.

Fraser and Glass (1980), in a study of 29 elderly depressed patients with a mean age of 73, compared bitemporal and unilateral nondominant ECT. A unidirectional chopped sine-wave stimulus was used without seizure monitoring. Patients were randomly assigned and blind raters assessed improvement with the Hamilton Depression Scale pre-ECT, 24 hours after the fifth treatment, and 3 weeks after the last treatment. The number of treatments was free with a mean of 6.1 in the unilateral groups and 6.9 in the bilateral groups. The mean pre-ECT Hamilton score was 46 for both cells. No significant differences were found on Hamilton Depression Scales at either of the post-ECT test intervals. Assessment of cognitive side effects showed no correlation between severity of side effects and outcome.

Abrams, Taylor, Faber, et al. (in press), in a randomly assigned, double-blind study of 51 patients, compared bitemporal and unilateral nondominant ECT. Stimulation was delivered by sine-wave apparatus, and seizures were monitored with an oscilloscope. Improvement was assessed by the Hamilton Depression Scale after the sixth treatment. The total number of treatments was free, with a mean of 6.3 in the bilateral group and 9.1 in the unilateral group. The bilateral group showed 81.1% improvement on the Hamilton Depression Scale after six ECTs, while the unilateral group showed only a 55.5% improvement ($p = .004$), a finding which was independent of age, sex, pretreatment severity of illness, or sedative drug administration. After 10 treatments, the primary clinician, who was a blind rater, was free to switch to the alternate electrode placement if the series was felt to be ineffective. Seven unilateral patients were switched to bilateral, while none of the bilateral group was switched to unilateral ($p = .008$). Finally, no patient in the bilateral group received more than nine ECTs, compared with 10 patients in the unilateral group ($p = .0007$).

Welch, Weiner, Weir, et al. (1982) randomly assigned 59 patients to one of four modalities: unilateral nondominant sine, unilateral nondominant brief pulse, bilateral sine, and bilateral brief pulse. Stimulation was delivered by either a bidirectional sine-wave apparatus or a bidirectional brief-pulse apparatus, both at threshold levels of current. Seizures were monitored with either EEG or occlusion of ipsilateral upper extremity circulation. Improvement was measured by the difference between blindly obtained Hamilton Depression Scale ratings pre-ECT and 48 hours after the last ECT. The total number of treatments given was determined by a nonblind clinician and was 8.1 for the unilateral group and 7.3 for the bilateral group, a nonsignificant difference. The mean reduction in Hamilton Depression Scale was 35.1 for the unilateral group and 25.1 for the bilateral group ($p = .03$). No significant effect of waveform, age, sex, or number of treatments could be found. The authors speculated that the bilateral group may have appeared more depressed at 48 hours after the last treatment because of greater side effects associated with that treatment, and that the treatments were in fact probably equally efficacious.

Conclusion

The disparity between the findings of various investigators is difficult to explain. The most likely source of the difference in results rests in the failure of most investigators to use fastidious seizure monitoring. It has been suggested by Ottosson (1960) and asserted by subsequent investigators that the grand mal seizure itself is the therapeutic component of the treatment, and that the method of induction appears unrelated to efficacy as long as a generalized grand mal seizure is elicited. It is also established that unilateral or incomplete seizures are ineffective (Ulett, Gleser, Caldwell, & Smith, 1954; Fink, Kahn, & Green, 1958; Chatrian & Petersen, 1960) perhaps because they fail to recruit diencephalic centers. However, such incomplete seizures occur more frequently with unilateral than with bilateral stimulation (Lancaster, Steinert, & Front, 1958; Halliday, Davison, Browne, & Kreeger, 1968). In the absence of seizure monitoring, these ineffective seizures cannot be reliably identified and may be the cause of the frequent feeling that unilateral stimulation is less effective.

Another source of bias may be the different patient populations involved in these trials. For instance, the most recent work by Abrams et al. (in press) was done in a mostly male veterans' hospital population, while the population studied by Welch et al. (in press) was a mixture of general hospital and veterans' hospital patients.

The only firm conclusion that can be drawn is that further research is indicated to resolve the question of relative efficacy of unilateral nondominant and bilateral electrode placement. At this point it would appear that the only way to resolve it would be a large multicenter, randomly assigned, double-blind comparison, which simultaneously controls for side effects. Both short- and long-term assessment of severity of depression would be indicated.

Most important, however, is the monitoring of the seizure. Seizure monitoring should be done simultaneously by occlusion of arterial flow in the ipsilateral arm, with a blood pressure cuff, but also by a two-lead electroencephalograph (EEG) monitor. The EEG provides an accurate measure of seizure length, but occasionally fails to distinguish between partial and complete seizures, which are identical in appearance on a two-lead tracing. The occlusion of ipsilateral circulation provides a reliable check against this error, since partial seizures do not generally produce convulsive activity in the ipsilateral arm.

Although the research design outlined above is time consuming and cumbersome, the well-documented morbidity associated with the use of bilateral ECT warrants such a fastidiously controlled study to ascertain whether it is indeed more effective than unilateral nondominant ECT and, if so, in which patients.

References

Abrams, R., and Taylor, M.A. Diencephalic stimulation and the effects of ECT in endogenous depression. *Br. J. Psychiatry,* 129:482-485, 1976.

Abrams, R., Taylor, M.A., Faber, R., et al. Bilateral vs. unilateral ECT: Efficacy in melancholia. *Am. J. Psychiatry.* (In press)

Chatrian, G.E., and Petersen, M.C. The convulsive patterns provoked by Indoklon, Metrazol, and electroshock: Some depth electrographic observations in human patients. *Electroencephalogr. Clin. Neurophysiol.,* 12:715-725, 1960.

d'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? *Br. J. Psychiatry,* 126:83-89, 1975.

Fink, M., Kahn, R.L., and Green, M. Experimental studies of the electroshock process. *Dis. Nerv. Syst.,* 19:113-118, 1958.

Fraser, R.M., and Glass, I.B. Unilateral and bilateral ECT in elderly patients. *Acta Psychiatr. Scand.,* 62:13-21, 1980.

Halliday, A.M., Davison, K., Browne, M.W., and Kreeger, L.C. A comparison of the effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and nondominant hemispheres. *Br. J. Psychiatry,* 114:997-1012, 1968.

Heshe, J., Roder, E., and Theilgaard, A. Unilateral and bilateral ECT. *Acta Psychiatr. Scand. (Suppl.),* 275, 1978.

Lancaster, N.P., Steinert, R.R., and Frost, I. Unilateral electroconvulsive therapy. *J. Ment. Sci,* 104:221-227, 1958.

Ottosson, J.O. Experimental studies of the mode of action of electroconvulsive therapy. *Acta Psychiatr. Neurol. Scand. (Suppl. 145),* 35:1-141, 1960.

Reichert, H., Benjamin, J., Keegan, D., and Marjerrison, G. Bilateral and nondominant unilateral ECT, Parts I and II. *Can. J. Psychiatry,* 21:69-86, 1976.

Ulett, G.A., Gleser, G.C., Caldwell, B.W., and Smith, K. The use of matched groups in the evaluation of convulsive and subconvulsive photoshock. *Bull. Menninger Clin.,* 18:138-146, 1954.

Weeks, D., Freeman, C., and Kendell, R. ECT. III: Enduring cognitive deficits? *Br. J. Psychiatry,* 137:26-37, 1980.

Welch, C.A., Weiner, R.D., Weir, D., et al. Efficacy of ECT in the treatment of depression: Wave form and electrode placement considerations. *Psychopharmacol. Bull.,* 18(1):31-35, 1982.

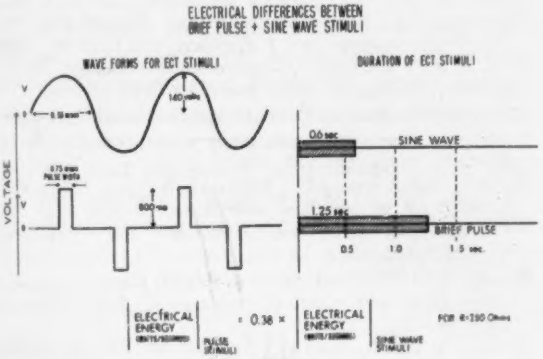
The Role of Stimulus Waveform in Therapeutic and Adverse Effects of ECT

Richard D. Weiner, M.D., Ph.D.[1]

Introduction

In electroconvulsive therapy (ECT), a seizure is produced by the application of a train of stereotypic electrical stimuli known as "waveforms." Although diverse types of stimulus waveforms have been used over the years, this brief review will consider just two, the sine wave and the pulse. These are the major waveform types utilized at the present time in the U.S.A., and they are representative of both ends of the waveform spectrum.

The sine wave stimulus (*see* Figure) is an oscillating pattern which is repeated 60 times a second (60 Hz). It is the same type of waveform which comes out of the wall socket, and for this reason not only was it the first stimulus waveform to be used with ECT, but also it is the one which remains the most popular stimulus waveform in the U.S.A. Adjustable parameters for the sine wave stimulus include voltage or current, and duration. The Figure shows typical initial parameter values for the use of the Medcraft B-24 (Hittman Corp.) sine wave ECT device (140 volts rms, 0.6 seconds' duration). For a patient resistance of 250 ohms, this stimulus will deliver 47 joules of electrical energy.



FIGURE

The pulse stimulus (*see* Figure) was first used with ECT in the early 1940s (Liberson, 1948), to produce seizures with a smaller amount of electrical energy, and thereby hopefully less adverse central nervous system (CNS) effects. The range of potential parameters with pulse ECT consists of voltage or current, duration, pulse width, and pulses per second (which reflects pulse spacing). The Figure shows typical initial parameter values for the MECTA (MECTA Corp.) pulse ECT device (800 ma current, 1.25 seconds' duration, 0.75 msec pulse width, and 60 pulse pairs per second). Again for a patient impedance of 250 ohms, this stimulus will deliver 18 joules of electrical energy, 38% of that described above for the sine wave stimulus. It should be noted that the energy per phase is considerably lower with the pulse stimulus, and that a longer stimulus duration is therefore generally necessary in order to provide the extent of neuronal depolarization necessary to initiate the seizure.

Therapeutic Correlates of Stimulus Waveform

The initial claims for the efficacy of pulse vs. sine wave ECT were that the two were equivalent (e.g., Liberson, 1948), although the research methodology was far from adequate. More recently, two prospective studies have demonstrated no significant therapeutic difference between sine wave and pulse stimuli (Weaver, Ives, Williams, & Nies, 1977; Welch, Weiner, Weir, Cahill, Rogers, Davidson, & Mandel, 1982). Others have suggested that the particular combination of pulse unilateral ECT may be less effective than other combinations (Lambourne & Gill, 1978; Price, 1981). Although such a phenomenon was not observed by either Weaver et al. (1977) or Welch et al. (1982), it remains possible that there may be a relatively small subgroup of patients who do not respond as well to unilateral ECT, whether given by pulse or by sine wave. At the same time, however, it should be made clear that the technique of unilateral ECT is considerably more difficult than with bilateral ECT, and that studies which have controlled for this have found little therapeutic difference between the two types of electrode placement (Weiner, 1980).

---

[1] Durham Veterans' Administration Medical Center and the Department of Psychiatry, Duke University Medical Center, Durham, NC 27710.

The role of pulse width in the diminishing of energy per phase has already been alluded to above. While shortening pulse width allows for more efficient seizure induction, it appears that ultrabrief pulses (pulse width less than 0.5 msec) may be associated with less complete, and thereby less effective, seizures (e.g., Cronholm & Ottosson, 1963).

The Effects of Stimulus Waveform Upon Adverse Effects

Early studies which compared pulse and sine wave stimuli with respect to adverse effects reported that, with the former, patients woke up earlier and demonstrated less confusion and amnesia (e.g., Liberson, 1948). Despite these claims, however, the methodology of these studies was inadequate in a number of ways, particularly in the use of concurrent differences in electrode placement between treatment groups, such that the observed advantage for pulse stimuli could actually have been due to the use of unilateral electrode placement.

More recently, Valentine, Keddie, and Dunne (1968) found less amnestic changes with pulse stimuli, but measurements were only made during the immediate postictal period and are therefore not applicable to interictal, and particularly to persistent, effects. Goldstein, Filskov, Weaver, and Ives (1977), using a comprehensive neuropsychological assessment battery, found no such difference 1 day following a course of ECT. Finally, Weiner, Rogers, Davidson, and Miller (1982), in a preliminary report, have described similar findings 2 days following a course of ECT, using sensitive measures of memory assessment, although a nonsignificant trend ($p \cong 0.08$) favoring the pulse stimulus was present. Electroencephalographically, the less intense seizures produced by pulse stimuli do, however, appear associated with less slowing 2 days after a course of ECT, based again on preliminary data (Weiner et al., 1982).

Summary and Recommendations for Future Research Investigations

In summary, the relative efficacy and safety of pulse stimuli with respect to sine wave stimuli is an issue deserving further study. While the two stimulus waveforms do appear to be roughly equivalent in terms of efficacy and memory effects, present studies have not been sufficient to delineate possible small differences, and there is some indication that waveform may have an effect upon acute electrophysiologic morbidity. Specific research questions for the future include:

1) Are there some patients who are more likely to respond to sine wave than to pulse stimuli, particularly in the case of unilateral electrode placement?
2) What are the specific roles of amplitude, pulse width, pulse separation, and stimulus duration in the production of effective seizures with pulse stimuli?
3) To what degree are adverse CNS effects less with pulse stimuli?

Answers to these questions will help to more adequately delineate the role of both types of stimuli in the clinical practice of ECT.

References

Cronholm, B., and Ottosson, J.O. Ultrabrief stimulus technique in electroconvulsive therapy: I. Influence on retrograde amnesia of treatments with the Elther ES electroshock apparatus, Siemens Konvulsator III and of lidocaine-modified treatment. *J. Nerv. Ment. Dis.*, 137(2):117-123, 1963.

Goldstein, S.G., Filskov, S.B., Weaver, L.A., and Ives, J.O. Neuropsychological effects of electroconvulsive therapy. *J. Clin. Psychol.*, 33(3):798-806, 1977.

Lambourn, J., and Gill, D. A controlled comparison of simulated and real ECT. *Br. J. Psychiatry*, 133(12):514-519, 1978.

Liberson, W.T. Brief stimulus therapy: Physiological and clinical observations. *Am. J. Psychiatry*, 105(1):28-39, 1948.

Price, T.R.P. Unilateral electroconvulsive therapy for depression. *N. Engl. J. Med.*, 304(1):53, 1981.

Valentine, M., Keddie, K.M.G., and Dunne, D. A comparison of techniques in electroconvulsive therapy. *Br. J. Psychiatry*, 114(8):989-996, 1968.

Weaver, L.A., Ives, J.O., Williams, R., and Nies, A. A comparison of standard alternating current and low-energy brief pulse electrotherapy. *Biol. Psychiatry*, 12(4):525-543, 1977.

Weiner, R.D. ECT and seizure threshold: Effects of stimulus wave form and electrode placement. *Biol. Psychiatry*, 15(2):225-241, 1980.

Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. Evaluation of the central nervous system risks of ECT. *Psychopharmacol. Bull.*, 18(1):29-31,1982.

Welch, C.A., Weiner, R.D., Weir, D., et al. Efficacy of ECT in the treatment of depression: Waveform and electrode placement considerations. *Psychopharmacol. Bull.*, 18(1):31-34, 1982.

ECT and Tricyclic Antidepressants in the Treatment of Endogenous Depression

Richard Abrams, M.D.[1]

It is an axiom among psychopharmacologists that rigorous experimental methods are required to demonstrate the efficacy of a new drug or its advantages over an old one. A prospective design, random assignment to treatment groups, and blind assessment of outcome are prerequisites in such studies. Other requirements include specified diagnostic criteria, objective outcome measures, and appropriate statistical analysis of the outcome data. Nothing less can ever suffice to demonstrate the absolute or relative efficacy of any treatment, and electroconvulsive therapy (ECT) is no exception. Considering that ECT and tricyclic antidepressants (TCAs) have coexisted for almost a quarter-century, and that endogenous depression is the primary indication for each treatment, it would be reasonable to expect a substantial number of comparisons of the two methods in this target population, employing such rigorous methodology. Such is not the case. There are, in fact, very few data to support the oft-heard comment that ECT is superior to TCA in the treatment of endogenous depression. Only two studies satisfied the minimal design criteria specified above, and one of the studies is seriously flawed by inadequate sample size.

The first study is that of Wilson and associates (1963) who conducted a two-phase trial in a sample of women hospitalized for manic-depressive illness, depressed type, involutional depression, or depressive reaction. In the first phase, patients were randomly assigned to four treatment groups of which two (six patients each) were ECT + placebo and placebo + imipramine (mean dose = 180 mg/day, range = 150 to 220 mg/day). Hamilton Rating Scale Scores obtained by blind raters after 5 weeks showed a change (improvement) score of 22.3 ± 1.6 for the ECT group, compared with only 11.7 ± 4.5 for the imipramine group ($t = 5.44$, $p < .005$). Fourteen new patients were then added to the study, four to receive ECT and 10 to receive imipramine at a higher dose (mean = 258 mg/day, range = 215 to 270 mg/day). This time, the improvement score after 5 weeks for the imipramine group was 25.1 ± 1.8, significantly greater than that of 22.5 ± 1.6 for the total of 10 ECT patients ($t = 3.41$, $p < .005$). (The authors erroneously concluded that the two treatments in this phase are "identical," but fortunately provide means and standard deviations for the inquisitive reader.) A major problem with this study is its very small sample size.

The second study is that reported to the Medical Research Council of Great Britain by its Clinical Psychiatry Committee (1965) Two-hundred sixty-nine patients with endogenous depression were randomly assigned to four different treatment groups. One group received four to eight ECT treatments ($N=65$) and another received imipramine ($N=63$) at a dose of 100 to 200 mg/day (mean = 193 mg/day). Fifty-eight patients in each group completed the first 4 weeks of treatment, at which time blind assessments on a 15-item depression rating form showed 71% of the ECT group recovered or markedly improved, compared with 52% of the imipramine group ($X = 4.99$, $p < .05$).

Thus, of two methodologically adequate studies, one shows a clear advantage for ECT over moderate-dose imipramine, and one shows a slight advantage for high-dose imipramine over ECT. The remainder of the ECT vs. TCA studies reviewed (Alexander, 1972; Angst, Varga, & Shepherd, 1967; Avery & Winokur, 1976; Bratfos & Haug, 1965; Bruce, Crone, Fitzpatrick, et al., 1960; Coryell, 1978; Fahy, Imlah, & Harrington, 1963; Greenblatt, Grosser, & Wechsler, 1962; Hutchinson & Smedberg, 1963; Kristiansen, 1961; McDonald, Perkins, Marjerrison, & Podilsky, 1966; Ravn, 1966; Robin & Harris, 1962; Wittenborn, Plante, Burgess, & Maurer, 1962) have the methodological problems detailed in the Table.

The study by Greenblatt et al. (1962) exemplifies the problem presented by well-known studies which must nonetheless be rejected as methodologically inadequate. The study employed random assignment, blind evaluations, and adequate drug dosages. It also correctly concluded that ECT was superior to imipramine in the total sample of 281 patients. Unfortunately, the sample was diagnostically heterogeneous and

---

[1] Department of Psychiatry, University of Health Sciences/The Chicago Medical School, North Chicago, IL 60064.

Table

Methodological Problems of ECT vs. TCA Studies

Study	Retrospective, Chart Review	Faulty Data Analysis	Non-Blind Evaluation	Non-Endogenous Depressives	Unstated Drug Dosage	Unstated Number of ECT	Unstated Outcome Criteria or Method
Bruce et al., 1960			+				+
Kristiansen, 1961	+						
Wittenborn et al., 1962				+	+	+	
Robin and Harris, 1962		+			+	+	
Hutchinson and Smedberg, 1962		+					
Fahy et al., 1963			+				
Greenblatt et al., 1964		+					
Bratfos and Haug, 1965	+						
McDonald et al., 1966			+				
Ravn, 1966	+						
Angst et al., 1967	+						
Alexander et al., 1972	+						
Avery and Winokur, 1977	+						
Coryell, 1978	+						

included 51 psychoneurotic depressives, 60 schizophrenics with depression, and 44 patients diagnosed only as "other." Thus, more than half the sample was nonendogenous, and cannot be combined for analysis. They do present a table displaying global improvement rates separately for each diagnostic subgroup, including the two presumably endogenous categories of manic-depressive, depressed ($N=76$), and involutional psychosis ($N=50$), but no statistical analyses or significance levels are described and the table is presented in such a peculiar fashion that the reader is unable to conduct his own analysis. An unsupported statement appears in the text that (among 28 other comparisons) ECT was no better than imipramine in the manic-depressives but was more effective than imipramine in the involutionals. In view of the multiple significance tests performed, the latter conclusion is unwarranted.

There is an additional problem with the ECT vs. TCA literature. Recent data suggest that optimal TCA therapy requires plasma-level monitoring, and several investigators have reported a significant relationship between TCA plasma levels and clinical outcome (Glassman & Perel, 1978). The largest study is that of Glassman, Perel, Shostak, et al. (1977), who treated 42 nondelusional endogenous depressives with a fixed (mg/kg) dose of imipramine and related plasma levels of this drug to clinical response as measured by changes in depression rating scale scores. The proportion of imipramine-responders increased in a stepwise fashion and was 29% in the group with plasma levels <150 ng/ml, 64% at 150-225 ng/ml, and 93% in the patients with levels exceeding 225 ng/ml, a figure quite comparable to improvement rates obtained with ECT in other studies. This study is marred by the fact that the authors do not specify their precise criteria for defining "responders" and "nonresponders."

Nonetheless, the results of the Glassman et al. (1977) study suggest that a valid comparison of the effects of ECT and TCA requires plasma-level monitoring in order to provide optimal TCA therapy. The need for such a study is obvious and should take first priority in future assessments of the efficacy of ECT.

References

Alexander, L., Berkeley, A.W., and Cohen, S.L. Which antidepressant for which patient? *Psychosomatics*, 13:49-56, 1972.

Angst, J., Varga, E., and Shepherd, M. Preliminary report of a retrospective study of the treatments of depression. In: Brill, H., Cole, J.O., Deniker, P., et al. (eds.), *Neuropsychopharmacology*. International Congress Series No. 129, Excerpta Medica Foundation, 1967, pp. 993-997.

Avery, D, and Winokur, G. Mortality in depressed patients treated with electroconvulsive therapy and antidepressants. *Arch. Gen. Psychiatry*, 33:1029-1037, 1976.

Bratfos, O., and Haug, J.O. Electroconvulsive therapy and antidepressant drugs in manic depressive disease. Treatment results at discharge and 3 months later. *Acta Psychiatr. Scand.*, 41:588-596, 1965.

Bruce, E.M., Crone, N., Fitzpatrick, G., et al. A comparative trial of ECT and Tofranil, *Am. J. Psychiatry*, 117:76, 1960.

Coryell, W. Intrapatient responses to ECT and tricyclic antidepressants. *Am. J. Psychiatry*, 135:1108-1110, 1978.

Fahy, P., Imlah, N.I., and Harrington, J. A controlled comparison of electroconvulsive therapy, imipramine, and thiopentone sleep in depression. *J. Neuropsychiatry*, 4:310-314, 1963.

Glassman, A.H., and Perel, J.M. Tricyclic blood levels and clinical outcome: A review of the art. In: Lipton, M., DiMascio, A., and Killam, K. (eds.), *Psychopharmacology: A Generation of Progress*. New York: Raven Press, 1978, pp. 917-922.

Glassman, A.H., Perel, J.M., Shostak, J., et al. Clinical implications of imipramine plasma levels for depressive illness. *Arch. Gen. Psychiatry*, 34:197-204, 1977.

Greenblatt, M., Grosser, G.H., and Wechsler, H. A comparative study of selected antidepressant medications and EST. *Am. J. Psychiatry*, 119:144-153, 1962.

Hutchinson, J.T., and Smedberg, D. Treatment of depression: A comparative study of ECT and six drugs. *Br. J. Psychiatry*, 109:536-538, 1963.

Kristiansen, E.S. A comparison of treatment of endogenous depression with electroshock and imipramine. *Acta Psychiatr. Scand. (Suppl.)*, 162:179-188, 1961.

McDonald, I.M., Perkins, M., Marjerrison, G., and Podilsky, M. A controlled comparison of amitriptyline and electroconvulsive therapy in the treatment of depression. *Am. J. Psychiatry*, 122:1427-1431, 1966.

Medical Research Council. Clinical trial of the treatment of depressive illness. *Br. Med. J.*, 5439:881-886, 1965.

Ravn, J. A comparison of past and present treatments of endogenous depression. *Br. J. Psychiatry*, 122:501-504, 1966.

Robin, A.A., and Harris, J.A. A controlled comparison of imipramine and electroplexy. *J. Ment. Sci.*, 108:217-219, 1962.

Wilson, I.C., Vernon, J.T., Guin, T., and Sandifer, M.G. A controlled study of treatment of depression. *J. Neuropsychiatry*, 4:331-337, 1963.

Wittenborn, J., Plante, M., Burgess, F., and Maurer, H. A comparison of imipramine, electroconvulsive therapy, and placebo in the treatment of depression. *J. Nerv. Ment. Dis.*, 135:131-137, 1962.

Factors Affecting Outcome After Successful Electroconvulsive Therapy

Roger F. Haskett, M.B.B.S.[1]

Electroconvulsive therapy (ECT) is accepted as an effective treatment for certain acute psychiatric syndromes, particularly the major affective disorders. Unfortunately, a significant number of patients relapse within a few months of a successful course of ECT. When examining this observation, it is important to consider the natural history of these illnesses and some popular assumptions about the long-term effects of treatment. Major affective disorders are commonly episodic and have a high spontaneous remission rate. It is usually impossible, however, to predict the duration of an untreated episode or the length of time that would elapse before the appearance of another episode. Pharmacotherapy of major affective disorder appears to assume that treatment reverses the pathogenetic process responsible for the clinical syndrome, but that the unidentified primary pathology persists. Antidepressant medication is continued for 6-12 months after clinical remission to prevent reappearance of the episode. Although there is no objective criterion for determining the appropriate time to withdraw medication, clinicians frequently deal with the uncertainty by extending the duration of treatment. By comparison, a course of ECT cannot be prolonged without definite indications. The number of treatments given to an individual must be limited because of concerns that excessive ECT produces serious side effects on cognitive functioning. In addition, outpatient ECT has many practical difficulties. The combination of the need to use ECT sparingly, and the lack of criteria for determining the spontaneous endpoint of an episode, have led to great variation in the long-term management of patients with ECT.

In the absence of objective markers for the therapeutic effects of ECT, clinicians have adopted various arbitrary guidelines to determine the "optimal dosage" of ECT. The twofold aim is to produce a full remission of the acute psychopathology and a low relapse rate. These guidelines are usually empirical and in most cases

---

[1] Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109.

inadequately tested by appropriately designed clinical studies. An inflexible number of treatments or duration of the course of ECT is sometimes prescribed without consideration for the clinical response of the patient. A frequently recommended practice consists of giving an additional two treatments after full remission of symptoms. Most commonly, clinicians are advised to treat until the psychopathology has resolved with the proviso that a certain minimum and maximum number of treatments are advised (American Psychiatric Association Task Force Report #14, 1978).

Clinical indications for followup treatment are more confusing than those dealing with treatment of the acute disorders. There appears to be little consensus on the risks of giving no continuation treatment, or the efficacy of specific medications or maintenance ECT in preventing relapse. Some clinicians believe that the characteristics of the original course of ECT significantly influence the relapse rate, whereas others suggest that outcome depends upon the use of prophylactic treatment and the natural history of the disorder.

A review of the literature does not provide the date to resolve these uncertainties. Interpretation of many reports is hindered by the use of different diagnostic systems and limitations in study design. Despite these constraints, there are several studies which provide some information on the outcome of successfully treated patients who have differing post-ECT interventions.

There are two reports which compare maintenance ECT with no treatment after recovery from the acute illness. Maintenance ECT was given on a varying schedule but no more than one treatment per month. The control or untreated groups consisted of patients who refused the offer of maintenance therapy. Geoghegan and Stevenson (1949) reported that 100% (13/13) of patients receiving maintenance ECT were well after 3 years and only 15% (2/13) relapsed in the subsequent 2 years (Stevenson & Geoghegan, 1951). By comparison, 100% (11/11) of patients who refused continuing treatment had relapsed within 3 years. All subjects had suffered two episodes in the 5 years prior to the study and "most" suffered from manic depressive illness. Karliner and Wehrheim (1965) offered a similar choice to 210 patients who had suffered a psychotic episode in the previous year which was successfully treated with ECT. After 6 years, only 12% of the patients treated with maintenance ECT had relapsed in contrast to 79% of the patients who had refused further ECT.

Although both studies showed a prophylactic effect for maintenance ECT, these results may not be replicated with randomly assigned patients recovering from their first psychiatric episode. The studies do demonstrate the difficulty in differentiating a relapse of the same episode of depression from the appearance of a new episode. The first study consisted of patients who already had evidence of frequently recurring episodes. The second study probably included many patients who had relapsed into the same episode after a temporary remission. The likelihood that these patients would suffer another episode within the followup period would depend upon the natural history of each patient's illness as well as the nature of the acute treatment. The effect of the patient's past history on his or her acceptance of maintenance therapy is also unlikely to be randomly distributed. The ability of maintenance ECT to sustain a remission during a single episode of illness, or prevent the occurrence of new episodes cannot be determined from these studies.

Thomas (1954) provided one of the earliest retrospective surveys of the long-term outcome of ECT. He examined the records of 307 patients and noted that 69% recovered or were much improved and another 28% were improved by a course of ECT. This author defined a "relapse" as a need for ECT within 4 weeks of original course of treatment. A "recurrence" occurred more than 4 weeks after treatment. Thomas found that 26% (81/307) of the patients "relapsed" and 91% (74/81) of these occurred by the 16th day post—treatment. Two hundred nineteen patients were followed for a further 12 months while receiving no somatic or pharmacological therapy. Fifty patients (23%) required readmission, further ECT, or committed suicide. Examination of the "recurrence" rates for these 219 patients revealed an interesting association. Sixteen percent (26/160) of the patients with an uneventful initial recovery had a "recurrence" during the subsequent year, whereas "recurrence" occurred in 41% (24/59) of the patients who "relapsed" during the initial course of treatment.

In one of the early attempts to find an objective marker for an adequate course of ECT, Roth, Kay, Shaw, and Green (1956) studied pentothal-induced delta wave EEG activity. They reported that 29% (12/41) of patients in their study suffered a relapse during the first 12 weeks after treatment. Eleven of these relapsing patients had failed to meet their criterion of EEG change with ECT. Further development of this potential marker for an unfavorable prognosis following ECT does not appear to have occurred. Strain, Brunschwig, Duffy, Agle, Rosenbaum, and Bidder (1968) compared the outcome of depressed patients treated with unilateral or bilateral ECT. Thirty-seven percent (17/45) of patients receiving bilateral ECT and 34% (17/50) receiving unilateral ECT relapsed during the 12 months after treatment. These two reports are notable, since they were prospective studies and provide information on the relapse/recurrence rates in depressed patients given no further treatment after successful ECT.

There is one study (Barton, Melta, & Snaith, 1973) which examined the effect on relapse rate of an additional two ECT after symptomatic relief. Fifty patients completed a course of ECT with random assignment to one of two groups. The groups whose ECT ended as soon as depressive symptoms disappeared had a 50% (13/26) relapse rate during the subsequent 3 months. The group receiving two additional ECT had a 42% (10/24) relapse rate for a similar period. These rates were not significantly different. They did find, like Thomas (1954), that most of the relapses occurred within 2 weeks after treatment was completed.

There are three reports of the relapse rates in depressed patients assigned randomly to maintenance medication at the time of beginning ECT. Each study followed its patients for at least 6 months. Seager and Bird (1962) compared imipramine, 75 mg/day, with placebo. Seventeen percent (2/12) of the patients taking imipramine relapsed in the 6 months after ECT compared with 69% (11/16) of those taking placebo. A similar study (Imlah, Ryan, & Harrington, 1965) compared the efficacy of phenelzine, imipramine, and placebo. Placebo was discontinued at the time of discharge from hospital. Patients maintained on imipramine, 75 mg/day, or phenelzine, 45 mg/day, had a relapse rate of 22%, whereas those on no medication had a relapse rate of 51% during the 6-month period. The third study (Kay, Fahy, & Garside, 1970) compared the effects of diazepam, 4-12 mg/day, with amitriptyline, 50-150 mg/day. Forty-seven percent (24/51) of the former group relapsed, including three suicides, whereas only 24% (8/34) of those taking amitriptyline relapsed. These studies showed a high relapse rate for patients continued on a minor tranquilizer, placebo, or no medication and a much lower relapse rate if maintenance antidepressants were prescribed. The actual relapse rates for patients taking antidepressants may have been influenced by the fact that many individuals were taking lower dosages than are considered therapeutic today. The relapse rate for patients continued on lithium was also compared with patients taking tricyclics in a retrospective chart review (Perry & Tsuang, 1979). Both groups of patients had similar relapse rates of 20 and 21%, respectively. The three prospective medication studies were also designed to examine the belief that concurrent medication shortened the duration of, or decreased the number of treatments in, an acute course of ECT. In all cases, there was no significant difference in the course of ECT treatment when antidepressant medication was also given.

In a recent study, Coppen, Abou-Saleh, Milln, Bailey, Metcalfe, Burns, & Armond (1981) compared the efficacy of continuation therapy with lithium against placebo. The outcome measure used in this report was the mean number of weeks spent in a relapse during the followup period. During the first 6 months after ECT there was no significant difference between the group taking lithium and the group taking placebo. The group taking lithium, however, showed much less evidence of relapse during the second 6-month period (mean time in relapse of 0.2 weeks) compared with the patients taking placebo (5.6 weeks).

In conclusion, there is ample evidence that the relapse rate after a course of ECT is unacceptably high unless some form of maintenance antidepressant therapy is administered. There has been little progress in the identification of specific treatment practices, or objective markers of therapeutic effect, which can identify those patients with a good prognosis after ECT. The endpoint of a course of treatment remains arbitrary and there is no reliably demonstrated method for determining which patients require prophylactic treatment to prevent relapse or recurrence.

It is possible that the characteristics of a course of ECT are no more able to influence the subsequent relapse rate than the initial treatment of melancholia with antidepressant medication. The tendency to relapse may be a function of the natural history, or subsequent duration of the episode, and may respond only to some form of continuation therapy. Studies which examine these questions must attempt to match patient groups for number of previous episodes, duration of current episode, and known recurrence rate. The development of biological markers which reflect the pathophysiology of the disorders and which can be used to monitor the therapeutic effect of ECT may enable the clinician to develop more objective guidelines for the administration of ECT. These markers may be neurophysiological or neurochemical, but perhaps the most hopeful developments have occurred with the use of neuroendocrine strategies. These are discussed in another section of this series.

References

American Psychiatric Association Task Force Report #14, Electroconvulsive Therapy, pp. 169, 1978.

Barton, J. L., Mehta, S., and Snaith, R. P. The prophylactic value of extra ECT in depressive illness. *Acta Psychiatr. Scand.*, 49:386-392, 1973.

Coppen, A., Abou-Saleh, M. T., Milln, P., et al. Lithium continuation therapy following electroconvulsive therapy. *Brit. J. Psychiatry,* 139:284-287, 1981.

Geoghegan, J. J., and Stevenson, G. H. Prophylactic electro-shock *Am. J. Psychiatry,* 105:494-495, 1949.

Imlah, N.W., Ryan, E., and Harrington, J.A. The influence of antidepressant drugs on the response to electroconvulsive therapy and on subsequent relapse rates. *Neuropsychopharmacology,* 4:438-442, 1965.

Karliner, W., and Wehrheim, H.K. Maintenance convulsive treatments. *Am. J. Psychiatry,* 212:1113-1115, 1965.

Kay, D. W. K., Fahy, T., and Garside, R. F. A seven-month double-blind trial of amitriptyline and diazepam in ECT-treated depressed patients. *Br. J. Psychiatry,* 117:667-671, 1970.

Perry, P., and Tsuang, M. T. Treatment of unipolar depression following electroconvulsive therapy. *J. Affect. Dis.,* 1:123-129, 1979.

Roth, M., Kay, D. W. K., Shaw, J., and Green, J. Prognosis and pentothal induced electroencephalographic changes in electro-convulsive treatment. *EEG Clin. Neurophys.*, 9:225-237, 1957.

Seager, C. P., and Bird, R. L. Imipramine with electrical treatment in depression—A controlled trial. *J. Ment. Sci.*, 108:704-707, 1962.

Stevenson, G. H., and Geoghegan, J. J. Prophylactic electroshock: A five year study. *Am. J. Psychiatry,* 107:743-748, 1951.

Strain, J. J., Brunschwig, L., Duffy, J. P., et al. Comparison of therapeutic effects and memory changes with bilateral and unilateral ECT. *Am. J. Psychiatry,* 125:294-304, 1968.

Thomas, D. L. C. Prognosis of depression with electrical treatment. *Br. Med. J.*, 950-954, 1954.

Electroencephalographic Correlates of ECT

Richard D. Weiner, M.D., Ph.D.[1]

Introduction

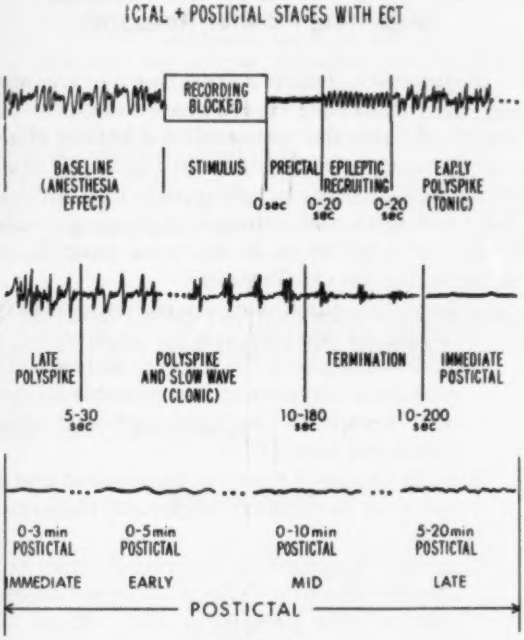
Electroconvulsive therapy (ECT) has a variety of effects upon the cerebral physiology, some of which may be correlated with therapeutic and adverse behavioral changes. From the early days of ECT, a routine test of cerebral function, the electroencephalogram (EEG), has proved to be a valuable means to observe and analyze the electrophysiologic correlates of these effects (Fleming, Golla, & Walter, 1939; Small, Small, & Milstein, 1978). The types of EEG changes seen with ECT can be subdivided chronologically into ictal, immediate postictal, interictal, and persistent categories.

The Ictal EEG

The prime function of the electrical stimulus used with ECT is to produce a generalized, major-motor type seizure. As such, the ictal EEG activity seen with ECT is strikingly similar to that observed with spontaneously occurring grand mal seizures. Electrically induced seizures may last anywhere from a few seconds to, rarely, many minutes, with typical mean seizure durations ranging from 45 to 60 seconds. The ictal EEG can itself be subdivided, again on a temporal basis, into 5 phases: preictal, epileptic recruiting activity, polyspike activity, polyspike and slow wave activity, and termination, as shown in A and B of the Figure.

---

[1] Durham Veteran's Administration Medical Center and the Department of Psychiatry, Duke University Medical Center, Durham, NC 27710.



FIGURE

The preictal phase of the impending seizure is not commonly seen with ECT, since seizure onset is generally immediate, or is at least underway by the time EEG amplifiers have begun to unblock. When seen, this phase typically presents as a period of relative suppression (*see* A of the Figure).

The earliest ictal phase generally seen in the EEG is rhythmic 18-22 Hz beta activity, typically occurring in a bilaterally synchronous fashion and lasting from a fraction of a second to no more than a few seconds (*see* A of the Figure). This activity can be called the epileptic recruiting rhythm, in deference to the use of this term in epileptology. For unknown reasons, this phase often appears absent.

The recruiting rhythm gives way to a chaotic mixture of high amplitude polyspikes which mark the tonic and early clonic convulsive movements accompanying the seizure (*see* A and B of the Figure). This phase lasts from a few seconds to tens of seconds, with approximately 10-20 seconds being most common.

Often in a piecewise fashion, the polyspike activity begins to break up into a regular pattern of polyspike and slow wave discharges, which begin at a frequency of 4-6 Hz, eventually slowing to 1-2 Hz (*see* B of the Figure). This phase, which generally makes up the bulk of the seizure duration, may not always be as well formed as described above, however, and may present as a mixed polyspike and polyspike/slow-wave pattern. The clonic convulsive movements always end before, or at least concurrent with, the end of this phase.

The termination phase of the seizure may be quite varied, ranging from an abrupt dissipation, termed by Blachly and Gowing (1966) as the "fit switch," to a breaking up of the polyspike/slow-wave activity into an irregular mixture of polyspikes and slow waves of steadily diminishing amplitude which may last for up to 30 seconds or, rarely, more. A typical termination phase is shown schematically in B of the Figure.

As far as one can tell electroencephalographically, the seizure onset is generalized, suggesting an early diencephalic activation of corticoreticular pathways, yet there is some suggestive evidence for a local onset within the hemisphere of stimulation with unilateral ECT (Staton, Hass, & Brumback, 1981). In addition, there have been a number of reports of unilateral seizures with unilateral ECT, presumably in response to barely threshold stimuli. Another reported difference between unilateral and bilateral ECT is with respect to the magnitude of ictal activity, with both EEG amplitude and the intensity of clonic convulsive movements being asymmetric with unilateral ECT (Kriss, Halliday, Halliday, & Pratt, 1978). Although ictal EEG differences between sine wave and pulse stimulation have not been investigated, there have been reports that clonic movements may be less intense with the latter (Marshall & Dobbs, 1959). In general, seizure duration appears to be independent of electrode placement and stimulus waveform, except that with small interelectrode distances, seizures produced by sine wave unilateral stimulation may be somewhat abbreviated (Weiner, 1980a).

The Postictal EEG

Immediately postictally, there is some degree of suppression of EEG activity, much as there is following spontaneous grand mal seizures. The degree of suppression is quite variable, and is more prominant with longer seizures and with bilateral stimulation. With unilateral stimulation, the suppression is typically greater over the stimulated hemisphere, as one would expect given the higher amplitude of ipsilateral ictal EEG activity. In observing the postictal EEG in cases where little suppression occurs, one must take into account the fact that some degree of high amplitude mixed slow and fast activity may be present due to the effects of the barbiturate anesthesia and that this should not be confused with continuing ictal activity. By 10 to 15 minutes postictally, the EEG gradually returns to its baseline state, with an initial appearance of very slow delta activity followed by theta, alpha, and beta rhythms (*see* C of the Figure). This shift toward higher and more normal-appearing frequencies is most easily observed in records showing the greatest degree of suppression.

The Interical EEG

Interictally, the most prominent type of EEG finding is the presence of generalized slowing in the theta and delta ranges. This slowing may be either regular or irregular in morphology, is frequently accentuated by drowsiness and by hyperventilation, and is greater for both bilateral stimulation and with the use of sine wave stimuli (Weiner, Rogers, Davidson, & Miller, 1981). Though most often bilaterally synchronous, the slowing may occasionally be greater over the stimulated hemisphere with unilateral ECT. The degree of slowing varies quite a bit among individuals, but clearly increases with the number of treatments.

The Persistence of EEG Effects

The persistence of EEG changes, chiefly slowing following ECT, also appears to be quite variable. A recent review of this literature indicates that in most cases slowing disappears within the first month, and only rarely is it present past 3 months (Weiner, 1980b). The role of electrode placement and stimulus waveform in the persistence of EEG abnormalities is presently unclear.

Summary and Recommendations Regarding Further Research

In summary, despite a great deal of variability, the EEG correlates of ECT are relatively well described, and though occasional severe abnormalities may exist on an acute basis, the risk of permanent adverse changes appears low. Although much is known about these correlates, a number of pertinent questions in this area await further investigation for clarification:

1) In what fashion does the electrical stimulus induce the seizure?
2) To what degree is the seizure, and each of its structural components, responsible for both the therapeutic and the adverse effects associated with ECT?
3) Is the degree of postictal suppression and the speed of its recovery important therapeutically?
4) Is there a difference, in terms of either therapeutic or adverse effects, between patients who develop prominent EEG effects and those who do not?
5) What is the true incidence of long-lasting EEG abnormalities with ECT?
6) What roles do electrode placement, stimulus waveform, and stimulus intensity have in these EEG correlates, particularly in the persistence of EEG changes?

In attempting to answer these questions, we may arrive at a better understanding not only of how ECT works, but also in how it should be optimally used.

References

Fleming, G.W.T.H., Golla, F.L., and Walter, W.G. ECT of schizophrenia. *Lancet,* 2(12):1353-1355, 1939.

Kriss, A., Halliday, A.M., Halliday, E., et al. EEG immediately after unilateral ECT. *Acta Psychiatr. Scand.*, 58(9):231-244, 1978.

Marshall, T.J., and Dobbs, D. Treatment technique and apnea in electroshock. *Dis. Nerv. Syst.*, 20(12):582-583, 1959.

Small, J.G., Small, I.F., and Milstein, V. Electrophysiology of EST. In: Lipton, M.A., DiMascio, A., Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress.* New York:Raven Press, 1978, pp. 759-769.

Staton, R.D., Hass, P.J., and Brumback, R.A. Electroencephalographic recording during bitemporal and unilateral nondominant hemisphere (Lancaster position) electroconvulsive therapy. *J. Clin. Psychiatry,* 42(7):264-269, 1981.

Weiner, R.D. ECT and seizure threshold: Effects of stimulus wave form and electrode placement. *Biol. Psychiatry,* 15(2):225-241, 1980a.

Weiner, R.D. The persistence of electroconvulsive therapy-induced changes in the electroencephalogram. *J. Nerv. Ment. Dis.,* 168(4):224-228, 1980b.

Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. Evaluation of the central nervous system risks of ECT. *Psychopharmacol. Bull.* 18(1):29-31, 1982.

Short- and Long-Term Cognitive Effects of ECT: Part I—Effects on Memory

Trevor R.P. Price, M.D.[1]

Introduction

In this article and the one that follows, the effects of electroconvulsive therapy (ECT) on various cognitive functions, both short- and long-term, will be reviewed. In the interest of simplification and clarity, they will be discussed in two separate sections: one dealing with the effects of ECT on memory function and the other with the effects of ECT on nonmemory-associated cognitive function. Obviously this is a heuristically useful though somewhat artificial distinction, since memory capacity is an important underlying component of at least some so-called nonmemory-associated cognitive functions.

In attempting to understand the effects of ECT on neuropsychological and cognitive functions, it is crucial to bear in mind that the diseases for which it is most frequently used, i.e., major depressive disorder and schizophrenia, may themselves cause significant changes in these functions. It is therefore important, but at the same time often difficult, in patients receiving ECT to separate out the extent to which observed cognitive changes are due to the treatment as opposed to the underlying disease. The article by Nasrallah in this series speaks to this issue in greater detail.

Memory Dysfunction Associated with Depression

Patients with depression may have impaired concentrating ability and experience difficulty in focusing attention (Wexler, 1980). Depression may also cause impaired memory function (Sternberg & Jarvik, 1976) of a particular type. It has been shown that short-term memory, which is dependent on registration, is impaired, while long-term memory, which is dependent on retention and recall, is not (Cronholm & Ottosson, 1961). Further, it is thought that impaired registration is a result of concentration and attention deficits, so-called "prograde effects" (Reichert, Benjamin, Neufeldt, & Marjerrison, 1976). It has been shown that when patients are treated, improvement in depression and short-term memory function are highly correlated and tend to be proportional in magnitude. In general, as will be detailed below, the memory impairments resulting from ECT tend to be just the reverse of those associated with depression. There may be uncertainty in some cases as to whether observed memory problems are due to depression or to the effects of ECT. Squire, Wetzel, and Slater (1979) have developed a self-rating instrument which may allow for differentiation between them. Using this scale, they showed that the patterns of memory complaints 1 week and 6 months post-bilateral ECT were qualitatively similar to each other, though quantitatively different, with the memory impairment at 1 week, as expected, being greater. In comparison to the pattern obtained before treatment, however, the two post-treatment scores differed both qualitatively and quantitatively, allowing for clear differentiation between them.

Methodological and Technical Issues

In reading the literature on the cognitive effects of ECT, one must be aware that much of the work

---

[1] Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755.

done in the past on the effects of ECT on memory and cognition has suffered from inadequate research methodology. There has been a great need evident in earlier studies, which has only in recent years begun to be met, for more standardized and sophisticated assessments of memory function (Harper & Wiens, 1975).

One must also bear in mind that conclusions regarding ECT's effect on memory depend to a great extent on how one measures memory function (Squire & Miller, 1974) and what one is measuring. Thus the experimental methodology employed; the sensory modality that is mediating memory, be it auditory, visual, or tactile; the content of the material administered, whether verbal or nonverbal; and whether one is measuring recognition, recall, relearning, or forgetting (the differences between immediate and delayed reproduction scores) are all important in interpreting and comparing the results of studies of the effects of ECT on memory function.

One should also be aware that while much is now known with a reasonably high degree of certainty about the effects of differential electrode placement on certain cognitive and memory functions, so-called laterality effects, their relationship to the type of stimulus waveform, and the frequency and intensity of stimuli and seizures have not thus far been adequately investigated.

The Effects of ECT on Memory Function

Memory impairment is a frequent and distressing, though for the most part, reversible, consequence of ECT. It occurs in a variety of forms which will be discussed below, and its nature and severity depend to an important degree on where and how the electric stimulus is delivered. While over the years this has been a subject of considerable debate, there is now widespread agreement that memory deficits are neither correlated with nor necessary for clinical improvement with ECT (Korin, Fink, & Kwalwasser, 1956; Fink, 1974; Squire, 1977; Dornbush & Williams, 1974). They are thus considered undesirable and often largely avoidable side effects of ECT.

General Aspects of ECT-Induced Memory Dysfunction

ECT can induce both retrograde and anterograde amnesia and has deleterious, though generally variable and transient, effects on immediate, intermediate, and remote memory (Fink, 1977). It has relatively little effect on short-term memory; its major impact is therefore on long-term memory (Dornbush & Williams, 1974; McGaugh & Williams, 1974).

Bilateral ECT seems to accelerate the process of normal forgetting (Squire, Wetzel, & Slater, 1978). Immediately following each treatment it induces a global anterograde amnesia which by 30 to 45 minutes later has become a well-circumscribed deficit characterized by good immediate memory, rapid forgetting, and temporally graded retrograde amnesia occurring in the absence of confusion or intellectual impairment (Squire et al., 1978; Squire, 1977). After ECT, memory performance is best on recognition testing and worst on recall testing, with relearning intermediate but tending to be more similar to recall than recognition (Dornbush & Williams, 1974). Evaluation of the ability to retain information following ECT is most sensitivity accomplished by the use of recall or relearning rather than recognition testing paradigms. While the ability to recall information is generally more important to patients than simple recognition, it is also considerably more difficult to test.

With ECT there is amnesia (of variable duration) for the seizure itself as well as for immediate pre- and posttreatment periods (Fink, 1977). While memory impairment is typically seen immediately after a treatment is over, its onset may occasionally be delayed for up to 24 hours (Hargreaves, Fischer, Elashoff, & Blacker, 1972). In general terms, Ottosson (1968) has described ECT as transforming the memory disturbance associated with depression from one characterized by poor learning with normal retention to one characterized by normal learning with poor retention.

It is believed that the severity and duration of ECT-induced memory impairments are positively correlated with the number, frequency (Squire & Miller, 1974; Korin et al., 1956; Dornbush, Abrams, & Fink, 1971; Fromholt, Christensen, & Stromgren, 1973), and intensity (Fink, Kahn, & Green, 1958; Ottosson, 1960; McGaugh &

Alpern, 1966) of the electrical stimuli given as well as of the seizures experienced (Laurell, 1970; Ottosson, 1960; Small & Small, 1972).

While increased frequency of treatments may have important implications with bilateral ECT, this may not be the case with unilateral nondominant ECT. Thus, Stromgren, Christensen, and Fromholt (1976) found that four unilateral nondominant treatments per week, as opposed to two, resulted in greater improvement in memory due presumably to more rapid improvement in the underlying depression. Likewise, Abrams (1967) found no greater memory impairment when unilateral nondominant ECT was given on a daily basis as opposed to three times a week.

While early studies suggested that alternating current sine wave stimuli caused more severe cognitive effects than other types of stimulus waveforms (Lieberson, 1953; Valentine, Keddie, & Dunne, 1968), more recent work has indicated that differences between brief pulse and sinusoidal waveform are not likely to be major factors in determining the degree of memory dysfunction associated with ECT (Weaver, Ives, Williams, & Nies, 1977; Weiner, Rogers, Davidson, & Miller, 1981; Spanis & Squire, 1981).

Some work with multiple monitored ECT has reported that it causes both anterograde and retrograde memory disturbances no greater in extent and severity than those seen after a single conventional treatment of the same type and of lesser proportions than if the same number of seizures had been induced individually on an alternate day schedule (Abrams & Fink, 1972).

Giving ECT via unilateral as opposed to standard bilateral administration substantially decreases the extent of memory impairment. Treating unilaterally over the nondominant or dominant hemispheres will also result in major differences in the kinds of memory impairment that occur. These differences will be discussed in detail in a later part of this review.

Administering ECT via anterior bifrontal (Inglis, 1970; Abrams & Taylor, 1973) as opposed to standard bitemporal electrode placement has been reported to lead to a reduction in memory dysfunction while achieving therapeutic efficacy intermediate between unilateral and bilateral ECT.

Stimulating unilaterally over various combinations of anatomic areas seems to have relatively little effect on memory dysfunction. Thus, there is no difference in the impact on memory between nondominant unilateral fronto-parietal and temporo-parietal lead placements (d'Elia & Widepalm, 1974). The findings are somewhat more complex in regard to comparison between fronto-frontal and temporo-parietal lead placements. While two earlier studies reported no difference in anterograde memory function between them both for verbal as well as nonverbal material (d'Elia, 1976; d'Elia, Frederiksen, Raotma, & Widepalm, 1977), a later study reported less retrograde amnesia with fronto-frontal as compared to temporo-parietal stimulation (d'Elia, 1981).

One study has indicated that the degree of immediate memory dysfunction following ECT is highly correlated with the rise in systolic blood pressure that occurs during treatment (Hamilton, Stocker, & Spencer, 1979).

Memory research in animals has shown that material ordinarily not affected by ECT may be forgotten if a reminder of it is presented just before a treatment is given (Schneider & Sherman, 1968; Misanin, Miller, & Lewis, 1968; Lewis, Bregman, & Mahan, 1972). This is known as the "reinstatement phenomenon." The evidence available (Squire, Slater, & Chace, 1976) suggests that this phenomenon does not occur in humans given ECT.

ECT-Induced Anterograde Amnesia

Both bilateral and unilateral ECT can cause anterograde amnesia which is the inability to incorporate material newly learned after ECT into long-term memory storage (Squire & Miller, 1974; Squire et al., 1976; Fleminger, Horne, Nair, & Nott, 1970a; d'Elia, 1974; Halliday, Davison, Browne, & Kreeger, 1968). Adequate investigation of ECT-induced anterograde amnesia requires the use of both immediate and delayed recall assessment devices. This is because tests of delayed reproduction which predominantly reflect retention are generally more sensitive to the deleterious effects of ECT than are tests of immediate reproduction which predominantly reflect new learning ability (Squire & Miller, 1974). Over the course of several treatments new learning ability may actually be improved. Subtracting delayed from immediate reproduction scores yields a highly useful direct measure of memory function, the so-called "forgetting score" (Harper & Wiens, 1975).

The severity of ECT-induced anterograde amnesia depends on the temporal distance from ECT of the new learning. Thus, in a study by Squire et al. (1976), recognition memory for material learned 3 hours after bilateral ECT was significantly better than for that learned 1 hour or less after ECT. Furthermore, the ability to retain material over a short (e.g., 30-minute) period recovers rapidly after ECT, being nearly normal by 3 hours after treatment. There is no cumulative impairment in this short-term measure over the first four treatments. However, the ability to retain new material over longer periods such as 24 hours appears to be much more vulnerable to the effects of ECT. Thus impairment in 24-hour retention was more severe than that seen with short-term retention given comparable amounts of ECT, and the effects of ECT were cumulative. Based on these observations, the theories that ECT causes anterograde amnesia by disrupting the ability to transfer material from short-term memory to long-term memory or to recall material from long-term memory have been advanced.

On the other hand, Squire et al. (1976) postulated that anterograde amnesia results from an ECT-induced impairment of acquisition and consolidation of new information, rather than an impairment of the ability to call upon and use information that has already been stored. Others (Cronholm & Ottosson, 1961, 1963) have suggested that ECT interferes with the memory function, retention, while concomitantly improving new learning, i.e., acquisition and consolidation, to the extent that it reverses the patient's depression. Thus, ECT may have a mixed effect on various aspects of memory function.

ECT-induced anterograde amnesia does not appear to depend on the presence of intellectual dysfunction, confusion, or disorientation following ECT. In general, it gradually recedes after each individual treatment but may be cumulative over a series of treatments (Squire & Miller, 1974).

In 1958, Lancaster, Steinert, and Frost first reported that memory and cognitive impairment due to ECT could be reduced without a major diminution in therapeutic efficacy by using unilateral rather than bilateral stimulation. Subsequently, a variety of studies clearly documented that bilateral ECT produced greater amounts of anterograde amnesia than did either unilateral nondominant (Halliday et al., 1968; Fleminger et al., 1970a; d'Elia, 1970, 1974) or unilateral dominant ECT (Jackson, 1968).

In the mid- to late sixties evidence began to accumulate that there was a differential effect of unilateral dominant and nondominant ECT on verbal and nonverbal visuospatial anterograde memory. This was based on ECT studies that employed assessment batteries which specifically tapped verbal and nonverbal memory function.

Zamora and Kaelbling (1965), using Form One of the Wechsler Memory Scale, found that unilateral dominant ECT caused deterioration in verbal memory performance whereas unilateral nondominant ECT enhanced it, an effect they attributed to ECT-induced improvement in depression in the patients they studied. However, since the instrument they used did not include delayed reproduction subtests, it is more likely that they were measuring differences in new verbal learning ability rather than true verbal memory function.

Subsequently, a study by Jackson (1968) comparing verbal and nonverbal memory effects of right and left unilateral as well as bilateral ECT showed that patients treated with right unilateral ECT had the least verbal memory impairment; those treated with left unilateral, the least nonverbal visuospatial impairment; and those treated with bilateral the greatest degree of both. Similar findings were also reported by Halliday et al. (1968), Cohen, Noblin, Silverman, and Penick (1968); and Zinkin and Birtchnell (1968).
chnell (1968).

Kozma and Galbraith (1968) reported similar results in that they noted improvement in memory with unilateral nondominant ECT, some deterioration with unilateral dominant, and marked deterioration with bilateral ECT.

Sutherland, Oliver, and Knight (1969), in a double-blind study comparing the effects of unilateral dominant, unilateral nondominant, and bilateral ECT on memory function, found that all three types of treatment improved it, and attributed this to the indirect beneficial effect of improvement in depression on cognitive and memory function. They, like others, found that the greatest degree of improvement occurred with unilateral nondominant ECT.

Two years later Cronin, Bodley, Potts, et al. (1970) showed that impairment of anterograde verbal memory as assessed by word learning and the Wechsler Memory Scale was less marked with unilateral nondominant than with either unilateral dominant or bilateral ECT. Also in 1970, Fleminger, Horne, and Nott, (1970b) reported anterograde verbal memory to be more impaired after left unilateral than right unilateral ECT.

Two more recent well-designed and executed studies (Squire & Slater, 1978; Robertson & Inglis, 1978) have provided further confirmation of the differential effects of various types of ECT on verbal and nonverbal memory. The first study, using a before and after five-treatment design, showed that right unilateral ECT impaired delayed retention of nonverbal material in the form of faces, designs, and spatial relations, without affecting delayed retention of verbal material in the form of a paragraph. In this study, as in earlier ones, bilateral ECT caused greater impairment of both verbal and nonverbal memory than right unilateral ECT. The second study, using more sophisticated dimensions of symbolism and imagery in addition to the usual verbal and nonverbal dimensions in memory testing, further confirmed the differential effects of unilateral nondominant and bilateral ECT on verbal and nonverbal memory function. Unlike earlier studies, neither of these studies directly assessed the effects of unilateral dominant ECT on verbal and nonverbal memory.

Several of the studies that showed clear-cut differential effects of various forms of ECT on memory function reported virtually identical degrees of therapeutic efficacy (Fleminger et al., 1970a; d'Elia, 1974; Halliday et al., 1968; d'Elia & Raotma, 1975). Other studies have disputed the notion that unilateral and bilateral ECT are equipotent (Abrams, Fink, Dornbush, et al., 1972; Abrams, Taylor, Faber, et al., 1981; Price, 1980). Thus, whether or not the risk-benefit ratio (Fink, 1978, 1979) with respect to potential memory effects clearly favors unilateral nondominant over bilateral ECT in all cases is at present unclear and is an issue the APA Task Force on ECT felt should be left up to the clinical judgment of individual practitioners (APA Task Force Report on ECT, 1978).

Relatively few studies have attempted to establish the duration of ECT-induced anterograde amnesia. Halliday et al. (1968) reported that verbal memory impairment persisted over at least a 3-month period after unilateral dominant ECT. This study also indicated that nonverbal memory impairment persists longer after bilateral than unilateral nondominant ECT. Bidder, Strain, and Brunschwig (1970) found verbal memory as assessed by a paired-associate learning test to have returned to baseline within 30 days of the end of courses of both unilateral and bilateral ECT. At the followup assessment, memory was better than it had been before treatment in both groups. Finally, Cronin et al. (1970) showed that differences in anterograde verbal memory resulting from unilateral dominant, unilateral nondominant, or bilateral ECT persisted for 4 to 6 weeks following a course of eight treatments.

ECT-Induced Retrograde Amnesia

As mentioned previously, retrograde amnesia, which is a lack of ability to recall events occurring prior to ECT, also occurs as a result of both bilateral and unilateral ECT though to a significantly lesser extent with the latter (Cohen et al., 1968). It is more severe with increased number and frequency of bilateral ECTs and is thought by some to increase in severity with increasing patient age (Squire, 1974; Fink, 1977), though not all researchers agree on this (Fink, 1979). It often occurs in association with confusion, disorientation, or impairment on the verbal portion of the Wechsler Adult Intelligence Scale (WAIS) (Squire, 1974), but can also be present as an isolated defect.

ECT-induced retrograde amnesia occurs for both public and autobiographical events both temporally close in occurrence to (Harper & Wiens, 1975; Dornbush & Williams, 1974; and Dornbush, 1972), as well as many years (even up to 20) prior to treatment (Squire, 1977; Squire et al., 1975; Squire, 1975; Squire, Chace, and Slater, 1976; Brody, 1944; Squire, 1974; Janis, 1950). In the past the standard explanation for retrograde amnesia due to ECT had been the "consolidation hypothesis," which held that ECT somehow disrupted neural mechanisms and processes underlying the consolidation of memory traces (Zinkin & Birtchnell, 1968; McGaugh & Williams, 1974). Current theories, however, focus more on ECT-induced interference with the "retrieval process" as the underlying mechanism (Patterson, Lawler, & Rochester, 1978).

There is a temporal gradient in retrograde amnesia induced by ECT (Squire, 1975; Squire, 1976). Thus it was shown that following five bilateral ECTs, television programs broadcasted 1 to 3 years before ECT were forgotten, whereas those broadcasted 4 to 17 years before ECT were not.

Long-term memory for temporal order, which depends on recall not just recognition, appears to be more sensitive to bilateral ECT than other aspects of memory and is, like other forms of retrograde amnesia, associated with a temporal gradient of impairment (Squire et al., 1976). Thus temporal sequencing of events occurring from 4 to 7 years before ECT was impaired, whereas it was not impaired for events 8 to 16 years before. This temporal sequencing impairment persisted unchanged for 1 to 3 weeks after the end of treatment.

d'Elia (1970) reported that unilateral nondominent ECT caused less retrograde amnesia than bilateral ECT with unilateral dominant intermediate between them.

Cohen et al. (1968) showed that five unilateral dominant ECTs selectively impaired retrograde verbal memory, while five unilateral nondominant ECTs selectively impaired retrograde nonverbal, visuospatial memory. They also showed that both verbal and nonverbal memory were more profoundly impaired by five bilateral ECTs than with a comparable number of administrations of either form of unilateral treatment.

Berent, Cohen, and Silverman (1975) replicated the findings of Cohen et al. (1968) after one unilateral nondominant, unilateral dominant, or bilateral ECT, using words or visual forms learned 24-48 hours before and tested 5 hours after ECT. Based on their observation that verbal memory impairment after five unilateral dominant ECTs was much greater than after one, whereas visuospatial memory impairment was nearly identical after both five and one unilateral nondominant treatments, they suggested that the left hemisphere and verbal memory might be more susceptible to the cumulative effects of a series of ECTs than the right hemisphere and visuospatial memory.

Clearing of retrograde amnesia following ECT occurs as a result of spontaneous recovery not via relearning or "prompting" (though this may indeed help). As would be expected from Ribot's Law of Regression (Ribot, 1885), there is greater recovery of more remote events, months to years before ECT, than of very recent events, within days of treatment, for which loss of memory may be permanent (APA Task Force Report on ECT, 1978). Ease of restitution of retrograde memory loss is directly related to the patient's motivation to remember forgotten material, the degree of personal importance and hence presumably the amount of attention paid to it, the amount of affect associated with it, the degree of familiarity with it, and the ease with which it was originally assimilated into memory storage (Williams, 1975).

Recovery from ECT-induced retrograde amnesia occurs over a variable and, thus far, not definitely determined period of time. Various studies have demonstrated persistence of retrograde amnesia over periods ranging from 24 hours (Squire, 1975) to 10 to 14 weeks (Janis, 1950), to as much as 1 year or more following ECT (Brody, 1944). The last was an early study which was uncontrolled, and assessed memory function with respect to familiar, long-known names of persons and places as well as habits of work. Several more recent studies have indicated that the recovery of memory for remote events may be substantially complete in as little as 1 to 2 weeks (Squire, 1975, 1976) or as much as 6 to 9 months post-ECT (Squire & Chace, 1975; APA Task Force Report on ECT, 1978; Squire, 1980; Squire et al., 1980). The latter two studies indicated that memory impairment for events occurring more than 2 years before ECT, as well as new learning capacity, return to normal by 6 months post-ECT. While impaired memory for events occurring during the 1- to 2-year period before ECT substantially improves over the 6 months following ECT, there may be permanent loss of memory for some of them. Most of these permanent memory "gaps" are irritating but not functionally incapacitating to the patient (Freeman, Weeks, & Kendell, 1980).

Followup Studies of Long-Term Effects of ECT on Memory

Assessing the long-term effects of ECT on memory function is difficult because, as was first described nearly 20 years ago (Cronholm & Ottosson, 1963), and more recently confirmed (Squire & Chace, 1975), patients' subjective experience of their memory function is often at odds with the results of objective testing. In general, a patient's subjective assessment of the adequacy of his or her memory function post-ECT is directly related to verbal but not visuospatial performance, the degree of affective improvement from ECT, and the adequacy of immediate reproduction capacity, i.e., learning, more than delayed reproduction capacity, i.e., retention (Cronholm & Ottosson, 1963). Given the numerous and potentially complex interactions that may occur between these variables, it is not surprising that subjective and objective assessments of memory are often at variance with each other.

Squire and Chace (1975) found no objective difference in new learning, retention memory scores, remote memory, or self-rating of memory function 6 to 9 months after unilateral nondominant or bilateral ECT or inpatient psychiatric treatment without ECT. Despite the lack of objective differences, 63% of prior bilateral ECT patients felt their memory was not as good as it had been before treatment, while only 30% of unilateral ECT patients and 17% of non-ECT-treated patients felt similarly.

Squire et al. (1979), using a self-report memory assessment scale, found that subjective complaints of memory impairment persist in a gradually diminishing fashion for up to 6 months after ECT. The complaints present 6 months after ECT differ qualitatively from the depression-associated complaints present prior to ECT and are similar to, but less marked than, those present 1 week following ECT. Thus, while their etiology is unclear, the authors suggested that they are unlikely to be due to such commonly advanced explanations as persistent low self-esteem, a general tendency to complain about memory capacity, or recurrent depression-associated memory dysfunction.

Freeman, Weeks, and Kendel, (1980) retrospectively studied patients who had had ECT (mainly bilateral) from 2.6 to 12.8 years (mean = 10 years) previously and who complained of permanent unwanted effects secondary to the ECT. They found these patients to be more depressed and anxious and to be taking more psychotropic medications than the noncomplainers. Nonetheless, even after partialling out the effects of these factors, they still found more impairment in the patients than in volunteer, nonpatient controls on 3 out of 19 wide-ranging cognitive and memory tests. In fact, a few of the patients scored in the organically-impaired range on some of the tests. The authors concluded that: ECT may induce permanent memory impairment in a very small proportion of patients who receive it; this memory loss is, for the most part, irritating but not incapacitating; and that ECT does not normally produce persistent memory defects in most patients.

In a related study, Weeks, Freeman, and Kendell (1980) studied unilateral nondominant and bilateral ECT patients as well as normal and non-ECT-treated patient controls with a battery of tests that assessed both memory and nonmemory associated cognitive function. These tests assessed recall, relearning, and recognition functions in auditory, verbal, and visuospatial modes. They also tested immediate and delayed retrieval, short and long-term memory, as well as remote (long-term) memory for both personal and impersonal material. They found that unilateral nondominant ECT patients scored close to normal controls on many of the tests after 1 week of treatment; whereas, bilateral ECT patients showed significantly greater impairment after 1 week. At 3-month followup, however, unilateral nondominant and bilateral ECT patient performances were identical. At 4- and 7-month followups both ECT patients and non-ECT patient controls showed deficits on some tests when compared to the normal controls. They also complained subjectively of memory deficits which were attributed to the effects of residual depression, medication, and/or persistent ECT-induced memory impairment.

While there have been several anecdotal reports of patients who have received very large numbers of ECT with no apparent cognitive or memory impairment, such as that of Perlson's (1945) male patient who had received 248 bilateral ECTs, other reports (Templer, Ruff, & Armstrong, 1973; Goldman, Gomer, & Templer, 1972; Teuber, Corkin, & Twitchell, submitted) have raised the possibility that large numbers of bilateral ECT (more than 50 treatments per patient) may be associated with impairment on a variety of memory tests not present in controls on followup testing many years later. The conclusion of these studies that ECT is responsible for the observed persistent impairment must be viewed with caution since, given their design and retrospective nature, the effects of underlying chronic schizophrenia, depression, and/or associated organic lesions such as cingulotomy cannot be separated from the effects of ECT.

Summary

From this review a variety of reasonably firm conclusions about the effects of ECT on memory can be drawn. These include:

1. ECT causes both retrograde and anterograde amnesia.
2. Bilateral ECT causes greater anterograde amnesia than unilateral nondominant or dominant ECT, both for nonverbal and verbal memory.
3. Anterograde amnesia severity depends on the temporal distance from ECT of the new learning in question.
4. Anterograde amnesia recedes gradually after each individual treatment, but is cumulative over a series of treatments.
5. The early time course of recovery of anterograde amnesia due to ECT is not clear but is substantially complete by at least 6-9 months post-ECT.
6. Bilateral ECT causes greater retrograde amnesia than unilateral dominant and nondominant ECT, both for verbal and nonverbal memory.
7. Retrograde amnesia is characterized by a temporal gradient, and recall of when events occurred intime is more sensitive to impairment than other aspects of retrograde memory.
8. Unilateral nondominant ECT selectively impairs nonverbal retrograde memory, while unilateral dominant ECT selectively impairs verbal retrograde memory.
9. Recovery from retrograde amnesia following ECT is substantially complete by 6-9 months; however, some events during the 1-2 years before ECT and events during the course of treatment may be lost permanently.
10. ECT-induced memory dysfunction appears to be qualitatively different than depression-related memory dysfunction, at least as assessed by self-report scales.
11. Despite lack of objective evidence of memory dysfunction several months post-ECT, patients will often complain of subjective memory impairment following treatment. These complaints are more frequent following bilateral than unilateral ECT.
12. ECT, in a small number of patients, may cause permanent memory impairment; the functional significance of this memory loss is unclear at present.
13. ECT does not normally cause enduring memory deficits, and with unilateral nondominant ECT there is generally relatively little clinically apparent memory disturbance even immediately following ECT.

Areas for Future Research

Despite the extensive investigation of the effects of ECT on memory function over the past two decades and despite the fact that, as this review indicates, much is known about this area with a reasonable degree of certainty, many questions remain, and these indicate important directions for future research.

For example, what is the true incidence of permanent memory dysfunction from bilateral ECT? Does it ever occur in patients treated with unilateral ECT? If so, how often, and is the type of dysfunction different than that seen with bilateral ECT? Is it possible to identify, prior to treatment, through biological markers or clinical profiles, that small but finite number of patients who will be prone to experience permanent ECT-induced memory impairment? Can the nature and functional significance of such deficits be better characterized, especially with respect to the kinds of impact they have on the patient's life and work?

How long do subjective memory deficits persist post-ECT and what relationship do they bear to permanent memory impairments on objective memory tests?

How do ECT, particularly unilateral nondominant ECT, and various commonly used drug treatments for depression compare in regard to causing cognitive or memory disturbances in the short-run, but even more importantly over extended followup periods after acute treatment?

Does ECT have differential effects on memory function in different diagnostic groups, for example, in patients with schizophrenia as opposed to patients with major depressive disorders? Some early studies suggested that there might be such differences but this issue has not been adequately examined with studies using rigorous experimental designs in patient populations carefully defined by current research diagnostic criteria.

Studies of the latter type, as well as rigorously designed, prospective controlled studies with long-term followups involving large enough numbers of patients so that solid statistical inferences, regarding observed differences can be drawn, are badly needed. Multicenter, collaborative studies, despite their obvious drawbacks, lend themselves uniquely well to the need to collect large numbers of experimental subjects. Carefully done, large-scale, longitudinal, studies of the incidence, nature, and natural history of various types of ECT-induced memory dysfunction are also sorely needed. Additional rigorously designed and executed studies of the relationship between ECT-induced memory changes and the electrical characteristics (waveform, intensity, duration, frequency, etc.) of the stimulus; the number, frequency, and duration of induced seizures; and various ECT-induced neurophysiological and neuroendocrinological changes would also be important additions to the literature.

Research aimed at developing means of further attenuating, or even preventing altogether, ECT-induced memory loss via additional technical modifications of ECT or pharmacological interventions with, for example, peptide hormone fragments, should also have a high priority. Efforts aimed at identifying the basic mechanisms underlying ECT's therapeutic effects should be encouraged, as these may make it possible to develop an alternate form of treatment that will have comparable therapeutic efficacy without memory impairment.

References

Abrams, R. Daily administration of unilateral ECT. *Am. J. Psychiatry*, 124:384-386, 1967.

Abrams, R., and Fink, M. Clinical experience with multiple electroconvulsive treatments. *Compr. Psychiatry*, 13:115-121, 1972.

Abrams, R., Fink, M., Dornbush, R.L., et al. Unilateral and bilateral electroconvulsive therapy. *Arch. Gen. Psychiatry*, 27:88-91, 1972.

Abrams, R., and Taylor, M. Anterior bifrontal ECT: A clinical trial. *Br. J. Psychiatry*, 122:587-590, 1973.

Abrams, R., Taylor, M., Faber, R., et al. Bilateral vs. unilateral ECT: Efficacy in melancholia. *Am. J. Psychiatry*. (In press)

American Psychiatric Association Task Force Report on Electroconvulsive Therapy, Washington, D.C., 1978.

Berent, S., Cohen, B.D., and Silverman, A.J. Changes in verbal and nonverbal learning following a single left or right unilateral electroconvulsive treatment. *Biol. Psychiatry*, 10:95-100, 1975.

Bidder, T.G., Strain, J.J., and Brunschwig, L. Bilateral and unilateral ECT: Followup study and critique. *Am. J. Psychiatry*, 127:737-745, 1970.

Brody, M.B. Prolonged memory defects following electrotherapy. *J. Ment. Sci.*, 90:777-779, 1944.

Cohen, B.D., Noblin, C.D., Silverman, A.J., and Penick, S.B. Functional asymmetry of the human brain. *Science*, 162:475-476, 1968.

Cronholm, B., and Ottosson, J.O. Memory functions in endogenous depression: Before and after electroconvulsive therapy. *Arch. Gen. Psychiatry*, 5:193-199, 1961.

Cronholm, B., and Ottosson, J.O. The experience of memory function after electroconvulsive therapy. *Br. J. Psychiatry*, 109:251-258, 1963.

Cronin, D., Bodley, P., Potts, L., et al. Unilateral and bilateral ECT: A study of memory disturbance and relief from depression. *J. Neurol. Neurosurg. Psychiatry*, 33:705-713, 1970.

d'Elia, G. Unilateral ECT. *Acta Psychiatr. Scand. (Suppl.)*, 215:5-98, 1970.

d'Elia, G. Unilateral electroconvulsive therapy. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy*. Washington, D.C.: V.H. Winston and Sons, 1974, pp. 21-34.

d'Elia, G. Memory changes after unilateral electroconvulsive therapy with different electrode positions. *Cortex*, 7:280-289, 1976.

d'Elia, G. The effect of fronto-frontal and temporo-parietal unilateral ECT on retrograde memory. *Biol. Psychiatry*, 16:55-59, 1981.

d'Elia, G., Fredericksen, S.-O., Raotma, H., and Widepalm, K. Comparison of fronto-frontal and temporo-parietal unilateral ECT. *Acta Psychiatr. Scand.*, 56:233-239, 1977.

d'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? *Br. J. Psychiatry*, 126:83-89, 1975.

d'Elia, G., and Widepalm, K. Comparison of fronto-parietal and temporo-parietal unilateral ECT. *Acta Psychiatr. Scand.*, 50:225-232, 1974.

Dornbush, R. Memory and induced ECT convulsions. *Semin. Psychiatry,* 4:47-54, 1972.

Dornbush, R.L., Abrams, R., and Fink, M. Memory changes after unilateral and bilateral convulsive therapy. *Br. J. Psychiatry,* 119:75-78, 1971.

Dornbush, R.L., and Williams, M. Memory and ECT. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 199-207.

Fink, M. Induced seizures and human behavior. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 1-171.

Fink, M. CNS sequelae of electroseizure therapy: Risks of therapy and their prophylaxis. In: Shagass, C., Gershon, S., and Friedhoff, A.J. (eds.), *Psychopathology and Brain Dysfunction.* New York: Raven Press, 1977, pp. 223-240.

Fink, M. Convulsive therapy: A risk-benefit analysis. Abstracted from *Convulsive Therapy: Theory and Practice.* New York: Raven Press, 1979, p. 304, and presented, in part, at the ECT: Efficacy and Impact Conference, New Orleans, LA, February 1978.

Fink, M., Kahn, R.L., and Green, M. Experimental studies of the electroshock process. *Dis. Nerv. Syst.,* 19:113-118, 1958.

Fleminger, J.J., Horne, D.J. deL., Mair, N.P.V., and Nott, P.N. Differential effect of unilateral and bilateral ECT. *Am. J. Psychiatry,* 127:430-436, 1970a.

Fleminger, J.J., Horne, D.J. deL., and Nott, P.N. Unilateral electroconvulsive therapy and cerebral dominance: Effect of right and left-sided electrode placement on verbal memory. *J. Neurol. Neurosurg. Psychiatry,* 33:408-411, 1970b.

Freeman, C.P.L., Weeks, D., and Kendell, R.E. ECT: II: Patients who complain. *Br. J. Psychiatry,* 137:17-25, 1980.

Fromholt, T.P., Christensen, A., and Stromgren, L.S. The effects of unilateral and bilateral electroconvulsive therapy on memory. *Acta Psychiatr. Scand.,* 49:466-478, 1973.

Goldman, H., Gomer, F.E., and Templer, D.I. Long-term effects of electroconvulsive therapy upon memory and perceptual motor performance. *J. Clin. Psychol.,* 28:32-34, 1972.

Halliday, A.M., Davison, K., Browne, M.W., and Kreeger, I.L. A comparison of the effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and nondominant hemispheres. *Br. J. Psychiatry,* 114:997-1012, 1968.

Hamilton, M., Stocker, M.J., and Spencer, C.M. Post-ECT cognitive defect and elevation of blood pressure. *Br. J. Psychiatry,* 135:77-78, 1979.

Hargreaves, W.A, Fischer, A., Elashoff, R.M., and Blacker, K.H. Delayed onset of impairment following electrically induced convulsions. *Acta Psychiatr. Scand.,* 48:69-77, 1972.

Harper, R.G., and Wiens, A.N. Electroconvulsive therapy and memory. *J. Nerv. Ment. Dis.,* 161:245-254, 1975.

Inglis, J. Shock, surgery, and cerebral asymmetry. *Br. J. Psychiatry,* 117:143-148, 1970.

Jackson, B. The effects of unilateral and bilateral ECT on verbal and visual spatial memory. *J. Clin. Psychol.,* 34:4-13, 1978.

Janis, I.L. Psychologic effects of electric convulsive treatments. *J. Nerv. Ment. Dis.,* 3:359-382, 1950.

Korin, H., Fink, M., and Kwalwasser, S. Relation of changes in memory and learning to improvement in electroshock. *Confin. Neurol.,* 16:88-96, 1956.

Kozma, A., and Galbraith, D. The effects of unilateral dominant and non-dominant and bilateral ECT on changes in depression and memory. Paper read at Canadian Psychological Association meeting, Calgary, Alberta, June 1968.

Lancaster, N.P., Steinert, R.R., and Frost, I. Unilateral electroconvulsive therapy. *J. Ment. Sci.,* 104:221-227, 1958.

Laurell, B. Fluothyl convulsive therapy. *Acta Psychiatr. Scand. (Suppl.),* 213:5-79, 1970.

Lewis, J., Bregman, N.J., and Mahan, J.J. Cue dependent amnesia in the K-maze. *J. Comp. Physiol. Psychol.,* 81:243-247, 1972.

Lieberson, W.T. Current evaluation of electric convulsive therapies. In: *Psychiatric Treatment.* Baltimore, MD: Williams and Wilkins, 1953, pp. 199-231.

McGaugh, J.L., and Alpern, H.P. Effects of electroshock on memory: Amnesia without convulsions. *Science,* 152:665-666, 1966.

McGaugh, J.L., and Williams, T.A. Neurophysiological and behavioral effects of convulsive phenomena. In: Fink, M., Kety, S., McGaugh, J.L., and Williams, T.A. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 279-283.

Misanin, J.R., Miller, R.E., and Lewis, D.J. Retrograde amnesia produced by electroconvulsive shock after reactivation of a consolidated memory trace. *Science,* 160:554-555, 1968.

Ottosson, J.O. Experimental studies of memory impairment after electroconvulsive therapy. *Acta Psychiatr. Scand. (Suppl.),* 145(35):103-127, 1960.

Ottosson, J.O. Psychological or physiological theories of ECT. *Int. J. Psychiatry,* 5:170-174, 1968.

Patterson, K.E., Lawler, E., and Rochester, S.R. Retrograde amnesia from electroconvulsive therapy. *Neuropsychologia,* 16:91-97, 1978.

Perlson, J. Psychologic studies on a patient who received two hundred and forty-eight shock treatments. *Arch. Neurol. Psychiatr.,* 54:409-411, 1945.

Price, T.R.P. Unilateral electroconvulsive therapy for depression. *N. Engl. J. Med.,* 304:53, 1980.

Reichert, H., Benjamin, J., Neufeldt, A.H., and Marjerrison, G. Bilateral and non-dominant unilateral ECT: Part II: Development of prograde effects. *Can Psychiatr. Assoc. J.,* 21:79-86, 1976.

Ribot, T. (ed.). *Diseases of Memory.* London: Kegan Paul, 1885.

Robertson, A.D., and Inglis, J. Memory deficits after electroconvulsive therapy: Cerebral asymmetry and dual-encoding. *Neuropsychologia,* 16:179-187, 1978.

Schneider, A.M., and Sherman, W. Amnesia: A function of the temporal relation of footshock to electroconvulsive shock. *Science,* 159:219-221, 1968.

Small, J.G., and Small, I.F. Clinical results: Indoklon versus ECT. *Semin. Psychiatry,* 4:13-16, 1972.

Spanis, C.W., and Squire, L.R. Memory and convulsive stimulation: Effects of stimulus waveform. *Am. J. Psychiatry,* 138:1177-1181, 1981.

Squire, L.R. Amnesia for remote events following electroconvulsive therapy. *Behav. Biol.,* 12:119-125, 1974.

Squire, L.R. A stable impairment in remote memory following electroconvulsive therapy. *Neuropsychologia,* 13:51-58, 1975.

Squire, L.R. ECT and memory loss. *Am. J. Psychiatry,* 134: 997-1001, 1977.

Squire, L.R. Memory dysfunction and memory complaint: Long-term followup studies. In: Autry, J., Squire, L.R., Shagass, C., and Cole, J.O. (eds.), *ECT; Impact and Efficacy.* New York: Grune & Stratton, 1980.

Squire, L.R., and Chace, P.M. Memory functions six to nine months after electroconvulsive therapy. *Arch. Gen. Psychiatry,* 32:1557-1564, 1975.

Squire, L.R., Chace, P.M., and Slater, P.C. Retrograde amnesia following electroconvulsive therapy. *Nature,* 260: 775-777, 1976.

Squire, L.R., and Miller, P.L. Diminution of anterograde amnesia following electroconvulsive therapy. *Br. J. Psychiatry,* 125:490-495, 1974.

Squire, L.R., and Slater, P.C. Bilateral and unilateral ECT: Effects on verbal and nonverbal memory. *Am. J. Psychiatry,* 135:1316-1320, 1978.

Squire, L.R., Slater, P.C., and Chace, P.M. Retrograde amnesia: Temporal gradient in very long-term memory following electroconvulsive therapy. *Science,* 187:77-79, 1975.

Squire, L.R., Slater, P.C., and Chace, P.M. Anterograde amnesia following electroconvulsive therapy: No evidence for state-dependent learning. *Behav. Biol.,* 17:31-41, 1976a.

Squire, L.R., Slater, P.C., and Chace, P.M. Reactivation of recent or remote memory before electroconvulsive therapy does not produce retrograde amnesia. *Behav. Biol.,* 18:333-343, 1976b.

Squire, L.R., Slater, P.C., and Miller, P.L. Retrograde amnesia and bilateral electroconvulsive therapy: Long-term followup. *Arch. Gen. Psychiatry,* 38:89-95, 1980.

Squire, L.R., Wetzel, C.D., and Slater, P.C. Anterograde amnesia following ECT: An analysis of the beneficial effects of partial information. *Neuropsychologia,* 16:339-348, 1978.

Squire, L.R., Wetzel, C.D., and Slater, P.C. Memory complaint after electroconvulsive therapy: Assessment with a new self-rating instrument. *Biol. Psychiatry,* 14:791-801, 1979.

Sternberg, D.E., and Jarvik, M.E. Memory function in depression. *Arch. Gen. Psychiatry,* 33:219-224, 1976.

Stromgren, L.S., Christensen, A.L., and Fromholt, P. The effects of unilateral brief-interval ECT on memory. *Acta Psychiatr. Scand.,* 54:336-346, 1976.

Sutherland, E.M., Oliver, J.E., and Knight, D.R. EEG, memory, and confusion in dominant, non-dominant, and bi-temporal ECT. *Br. J. Psychiatry,* 115:1059-1064, 1969.

Templer, D.I., Ruff, C.F., and Armstrong, G. Cognitive functioning and degree of psychosis in schizophrenics given many electroconvulsive treatments. *Br. J. Psychiatry,* 123:441-443, 1973.

Teuber, H.L., Corkin, S., and Twitchell, T.E. A study of cingulotomy in man. Report submitted to the National Committee for the Protection of Human Subjects of Biomedical and Behavioral Research.

Valentine, M., Keddie, K.M.G., and Dunne, D. A comparison of techniques in electroconvulsive therapy. *Br. J. Psychiatry,* 114:989-996, 1968.

Weaver, L.A., Ives, J.O., Williams, R., and Nies, A. A comparison on standard alternating current and low energy brief-pulse electrotherapy. *Biol. Psychiatry,* 12:525-543, 1977.

Weeks, D., Freeman, C.P.L., and Kendell, R.E. ECT: III. Enduring cognitive deficits. *Br. J. Psychiatry,* 137:26-37, 1980.

Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. Evaluation of the central nervous system risks of ECT. *Psychopharmacol. Bull.,* 18(1):29-31, 1982.

Wexler, B.E. Cerebral laterality and psychiatry: A review of the literature. *Am. J. Psychiatry,* 137:279-291, 1980.

Williams, M. Retrograde amnesia. In: Kennedy, A., and Wilkes, A. (eds.), *Studies in Long-Term Memory.* London: John Wiley & Sons, 1975, pp.323-326.

Zamora, E.N., and Kaelbling, R. Memory and electroconvulsive therapy. *Am. J. Psychiatry,* 122:546-554, 1965.

Zinkin, S., and Birtchnell, J. Unilateral electroconvulsive therapy: Its effect on memory and its therapeutic efficacy. *Br. J. Psychiatry,* 114:973-998, 1968.

Short- and Long-Term Cognitive Effects of ECT: Part II—Effects On Nonmemory Associated Cognitive Functions.

Trevor R.P. Price, M.D.[1]

In addition to the multiple effects that electroconvulsive therapy (ECT) has on memory function, which were reviewed in the preceding article (Price, 1982), it likewise has a variety of effects on cognitive functions which are largely independent of memory. The range of cognitive domains affected include, for example, perceptual function, psychomotor speed, visuomotor ability, simple and complex sensory capacity, complex discrimination ability, and synthesizing and abstracting ability (Fink, 1979). This article will review these effects of ECT.

To understand ECT's effects on memory function or nonmemory-associated cognitive and neuropsychological function, it is important to

---

[1] Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755.

keep in mind that the diseases for which ECT finds its principal use, i.e., major depressive disorder and schizophrenia, may themselves be responsible for significant deviations from the norm in these functions. Thus the problem of how much of an observed cognitive impairment is due to the treatment as opposed to the underlying disease again confronts the clinician. For a more detailed discussion of this issue, the reader is referred to the discussion by Nasrallah in this series.

Nonmemory Cognitive Impairments Associated with Depression

Depression may be associated with nonmemory-associated cognitive dysfunctions, ranging from impaired concentration and attention (Wohlberg & Kornetsky, 1973) to a state-dependent delirium with mild to moderate, diffuse, generalized impairment on the Halstead-Reitan battery (Donnelly, Dent, & Murphy, 1972; Goldstein, Filskov, Weaver, & Ives, 1977) to the clinical picture of a profound pseudodementia with gross cognitive impairment and marked general function disability (Wells, 1979; Cavenar, Maltbie, & Austin, 1979). Unfortunately, the research literature in this area is inconsistent and at times even somewhat contradictory. For example, Small, Small, Milstein, and Moore (1972) reported no evidence of diffuse of localized neuropsychological dysfunction on Halstead-Reitan testing in a cohort of psychotically depressed patients but, subsequently, in a followup study of the same patients, reported improvement in some right hemispheric functions with ECT, suggesting the likely presence of an unrecognized asymmetric abnormality prior to treatment (Small, Small, Milstein, & Sharpley, 1973). Several other workers have also reported right hemispheric, particularly frontal, abnormalities (Tucker, Stenslie, Roth, & Shearer, 1981; Kronfol, Hamsher, Digre, & Waziri, 1978; Goldstein et al., 1977), as well as atypical patterns of hemispheric activation (Moscovitch, Strauss, & Olds, 1981) and impaired ability to learn new material (Campbell, 1957), to note just a few of the many different types of cognitive dysfunction that may be associated with depression.

Despite these interesting and provocative preliminary findings, thus far no characteristic patterns of cerebral dysfunction of hemispheric asymmetry occurring in association with depression have been clearly established (Marin & Tucker, 1981).

Cognitive Impairment Associated with Schizophrenia

In patients with schizophrenia, a variety of nonmemory-associated cognitive impairments have been found. As with depression, impaired attention and concentrating ability are common (Wohlberg & Kornetsky, 1973), as is diffuse cognitive dysfunction as assessed by the Halstead-Reitan battery as well as other tests of neuropsychological function (DeWolfe, Barrell, Becker, & Spaner, 1971; Watson, 1971). Wexler (1980) described specific left hemispheric dysfunction in schizophrenia in his review of the literature on cerebral laterality and psychiatric illness. Others (Taylor, Greenspan, & Abrams, 1979; Newlin, Carpenter, & Golden, 1981) have reported similar findings. However, Marin and Tucker (1981) and Merrin (1981) note that while some studies seem to support the notion of specific left hemispheric dysfunctions in schizophrenia, a variety of others do not. They also point out the existence of a variety of methodologic shortcomings in many of the studies that have been done in this area.

Methodological and Technical Issues

In view of the foregoing, it is clear that any research on the nonmemory-associated cognitive effects of ECT must be designed and executed so as to carefully control for and, as much as possible, eliminate the following confounding factors.

First, one must anticipate finding impaired attention and concentration as well as diffuse cognitive dysfunction in both depressives and schizophrenics. Next, presumed lateralized ECT-induced cognitive changes must be interpreted in the light of the evidence that suggests there may be differential right hemispheric dysfunction in depression and left hemispheric dysfunction in schizophrenia. One must attempt to control for patient age, treatment with psychotropic medication, intelligence quotient (IQ), education, and severity of illness, given the potentially important impact each of these may have on various cognitive functions. It is thus important that studies of the effects of ECT on cognition include age- and IQ-matched, comparably ill, medication-free, patient controls as well as normal controls.

It is also crucial to design cognitive test batteries with the practice effect in mind. Finally, in this type of research it is important to determine accurately hemispheric dominance, since just giving right unilateral ECT to all patients can result in stimulation over the dominant hemisphere in as many as 10% of cases even among strong right-handers (Clyma, 1975). Testing for dysphasia after ECT (Warrington & Pratt, 1973; Pratt & Warrington, 1972) and using the handwriting test (Levy & Reid, 1976), in addition to administering standard handedness questionnaires, can significantly increase the accuracy of determining cerebral dominance.

General Principals Regarding the Effects of ECT on Nonmemory-Associated Cognitive Function

In general, the literature during the 1940s and 1950s on nonmemory-associated cognitive effects of ECT was somewhat more extensive than that regarding the effects of ECT on memory. However, interest in this area waned in the 1960s and 1970s, though in very recent years there appears to have been a resurgence of research interest in this area in conjunction with the growth of interest in topics such as the laterality of cerebral functions, the neuropsychological abnormalities associated with various types of psychopathology, and the differential effects of dominant and nondominant unilateral ECT.

Fink (1979) reported that ECT-induced impairments in certain neuropsychological functions, e.g., perceptual acuity and psychomotor speed, are proportional to the number and frequency of seizures induced. As is the case with memory dysfunction, ECT-induced cognitive dysfunction may be delayed in its onset for up to 24 hours (Hargreaves, Fischer, Elashoff, & Blacker, 1972). Further, it has been reported that the impairments in nonmemory-associated cognitive functions are maximal at the time of the seizure and rapidly revert to pretreatment levels or better during the 14 days following the last seizure. Some evidence suggests that there is a cumulative effect on certain cognitive measures, such as the verbal Wechsler Adult Intelligence Scale (WAIS). Thus, Squire (1975) reported that the verbal WAIS had returned to normal within 40 minutes of the first bilateral ECT in a series, but took up to 48 hours to return to normal after the sixth. Three other studies suggested that with unilateral ECT, performance on a variety of psychological tests deteriorates progressively up to the fifth treatment, then improves despite continued treatment (Small & Small, 1971; Scanlon & Mathas, 1967; Fink, Kahn, Kapp, et al., 1961). Not surprisingly, simple cognitive and neuropsychological functions tend to be less severely disrupted and to return to baseline more rapidly than do complex ones.

In addition to the general changes in neuropsychological function already mentioned, ECT can cause topographical disorganization and disorientation (A Practicing Psychiatrist, 1965). Another interesting but as yet unexplained finding is that the number of errors on the Benton Visual Retention Test correlates highly with the degree of rise in blood pressure that occurs during ECT (Hamilton, Stocker, & Spencer, 1979). Furthermore, analogous to its effects on memory, unilateral dominant ECT has been reported to have greater effects on verbalization than is the case with unilateral nondominant ECT (Pratt & Warrington, 1972). Curiously, patients who have had unilateral dominant or bilateral ECT have been found to have greater difficulty with picture recognition than those who received unilateral nondominant ECT (Halliday, Davison, Browne, & Kreeger, 1968). This is thought to be due to the important influence verbal functions play in encoding visual stimuli (Williams, 1973), a role perhaps even more important than that of visual perceptual factors.

Unlike memory functions, there has been a relative paucity of investigation of the relationship between nonmemory-associated cognitive functions and stimulus intensity and waveform, the location (laterality) of stimulation, and the interaction between the cognitive effects of ECT and patient age, IQ, and sex. In fact, it has only very recently become apparent that the last-mentioned of these variables may be important in relation to general cognitive functioning (Miller, Small, Milstein, et al., 1981; Inglis & Lawson, 1981).

The Clinical Spectrum of ECT-Induced Nonmemory-Associated Cognitive Dysfunctions

Post-ECT cognitive dysfunctions span a broad spectrum of clinical presentations ranging from no apparent dysfunction to mild delirium with confusion all the way to gross delirium with flagrant organic psychotic features.

Post-ECT Confusion

Since post-ECT confusion is so frequently seen, it has, not surprisingly, been studied by a number of researchers over the years. Unfortunately, many of the articles dealing with it have failed to provide adequate operational definitions of "confusion" and have not established objective criteria for quantitative measurement of it. Despite these shortcomings, there seems to be a general consensus in these studies that bilateral ECT causes a greater degree of confusion and confusional behavior than unilateral ECT (Lancaster, Steinert, & Frost, 1958; Cannicott, 1962; Impastato & Karliner, 1966). Impastato and Karliner (1966) further reported that the degree of confusion occurring after unilateral nondominant ECT was less than that observed after unilateral dominant ECT. Consistent with this finding was that of Abrams (1967), who reported that neither confusion nor confusional behavior occurred after unilateral nondominant ECT, even when it was given on a daily basis for a large number of treatments.

Some researchers seeking to quantify the somewhat nebulous notion of confusion have employed as an objective measure the amount of time necessary after ECT for patients to regain full orientation to person, place, and time. Using this operational definition, several workers including Valentine, Keddie, and Dunne (1968); Halliday et al. (1968); Sutherland, Oliver, and Knight (1969); and d'Elia (1970) have replicated and confirmed the qualitative findings of earlier studies that unilateral ECT is followed by more rapid reorientation, and therefore less confusion, than is bilateral ECT. Fraser and Glass (1978, 1980) using a quantitative index of recovery after ECT that included, among other measures, orientation time, found that recovery was more rapid after unilateral nondominant than after bilateral ECT. Furthermore, they found that the recovery time after bilateral but not unilateral nondominant ECT increased as the course of treatment progressed, especially if the interval between treatments was shorter, e.g., 1 day, as opposed to 2 or 3 days. They also found that recovery times were longer in elderly as opposed to young patients with both unilateral and bilateral treatment modes. The differences were five times greater with unilateral and nine times greater with bilateral ECT.

Several other related studies have confirmed the fact that reorientation occurs considerably more rapidly after unilateral nondominant than unilateral dominant or bilateral ECT (Halliday et al., 1968; Sutherland et al., 1969; Wilson & Gottlieb, 1967; Cronin, Bodley, Mather, et al., 1970; d'Elia, 1970).

As is true with memory dysfunction following ECT, post-ECT confusion does not have prognostic implications as far as treatment outcome is concerned, nor is it a necessary concomitant of affective improvement. Thus, Wilcox (1953) found that there was no relationship between prolonged confusion after the first ECT, nor the degree of cumulative confusion after the tenth ECT in a series, and the results of a full course of ECT, either in respect to affective or cognitive outcome.

Acute Organic Mental Syndromes

ECT-induced acute organic mental syndrome, as it is currently known, is a clinical syndrome characterized by variable symptomatology ranging from mild confusion and bewilderment to grossly psychotic signs and symptoms in association with global cognitive impairment. It was first described in 1945 by Kalinowsky and has since been reported in a number of studies (Gallinek, 1952; Ottosson, 1968; Elmore & Sugerman, 1975; Arnot, 1975; Summers, Robins, & Reich, 1979; Fink, 1979; Marshall, Kalin, & Tariot, 1980).

This syndrome may be characterized by any or all of the following: difficulty concentrating, gross disorientation and confusion, a sense of perplexity and bewilderment, perseveration and circumstantiality, aphasic and apraxic symptoms, facial and body dysgnosias, and hallucinations and delusions (Kalinowsky, 1945). Typically such episodes clear suddenly and, according to Kalinowsky (1945), they frequently clear within 7 to 10 days of their onset.

In a recent series (Summers et al., 1979), 40% of patients receiving bilateral ECT developed acute organic mental syndromes. These varied in severity, developed after a mean of 5.5 bilateral ECTs, had a mean duration of 20.1 days, and were seen more frequently in patients with a history of major medical illness or in patients who were on psychotropic drugs, especially drugs having anticholinergic effects. The last finding, of course, is consistent with the widespread clinical experience that ECT and anticholinergic agents may have additive deliriogenic effects. Similarly, a number of recent reports (Ayd, 1981; Mandel, Madsen, Miller, & Baldessarini, 1980; Small, Kellams, Milstein, & Small, 1980; Weiner, Whanger, Erwin, & Wilson, 1980) indicate that ECT and lithium in combination may have a particular propensity in some, but not all, patients to cause reversible acute organic mental dysfunction.

Fink (1974) has reported an increased frequency of acute organic mental syndromes with increased numbers and frequency of bilateral ECTs. Abrams and Fink (1972) also reported, in a preliminary fashion, that the incidence of prolonged organic confusional states seemed to be greater with multiple monitored than with comparable conventional ECT.

A variety of other related post-ECT phenomena have also been reported. Gottlieb and Wilson (1965) reported dysphasia in the form of mumbling and jargon speech especially after unilateral dominant ECT. Clyma (1975) reported finding similar dysphasis in his patients which typically resolved within 30 minutes of ECT. Annett, Hudson, and Turner (1974) also reported that dysphasia, as reflected in a naming task, was more pronounced after left than right unilateral ECT. In this same study, however, no difference between the modes of stimulation could be found in their effects on visual discrimination tasks.

There have been reports of transient neurological signs and symptoms occurring immediately after ECT (Kane, 1963; Kriss, Blumhardt, Halliday, & Pratt, 1978; Impastato & Karliner, 1966). These neurological findings have been mainly contralateral to the side of stimulation, transient with resolution within 20 minutes of treatment, and include decreased contralateral sensory discrimination, transient flaccid hemiparesis and even paralysis, asymmetric deep tendon reflexes, tactile and visual inattention (agnosognosia), and homonymous hemianopsia.

Early Psychometric Studies of Nonmemory-Associated Cognitive Effects of ECT

In the 1940s, in response to fears as to the potential for ECT to cause significant and perhaps even permanent brain damage, Perlson (1945) published a report of a male patient who had received 248 bilateral ECTs over a 2-year time span. When assessed with an extensive battery of tests following this 2-year period, he was found by the author to be of superior ability in comparison to the general population, to have "intellectual ability slightly better than expected for college level performance," and to have experienced no greater change in intellectual functioning than would have normally occurred as a consequence of 2 years of aging.

Stone (1947) reported generalized cognitive dysfunction, of which amnesia was only a part, occurring in association with from 4 to 20 ECTs. He noted that it progressively increased in severity with ECT from prior to the first treatment to from 24 to 30 hours after the last ECT and subsequently gradually diminished over the next 2 weeks. The kinds of post-ECT cognitive impairment he found included: decreased calculating ability, decreased auditory and reading comprehension, decreased ability to think abstractly and perceive interrelationships, decreased ability to make choices and clarify issues, and diminished ability to arrange words or objects according to a specified plan.

Luborsky (1948) found the effects of ECT on cognitive function to differ in schizophrenics and depressives. He gave each patient group a diverse battery of psychometric tests before ECT, after the 10th or 11th treatment, and 5 or 6 days after a completed series of 12 treatments. In the schizophrenics, he found impaired organizational-synthetic, visuomotor, and fluency of association functions after the 10th or 11th treatment in comparison to baseline, which he felt suggested the presence of organic brain dysfunction, but he could find little or no evidence of impairment 5 to 6 days after the last ECT. His depressed patients showed a different pattern, with progressive improvement from baseline to posttreatment testing, without the initial impairment.

Huston and Strother (1948) administered the Babcock and Shipley-Hartford test batteries to depressed patients prior to ECT and 11 days and 6 months after the last treatment. The former battery includes 31 items that assess memory, attention, and psychomotor speed; the latter taps vocabulary and abstract thinking. At 11 days post-ECT, the results on the Babcock were slightly improved. At the 6-month posttreatment followup, statistically significant improvement had occurred with both.

Fisher (1949) demonstrated improvement in a variety of cognitive functions in depressed patients who had improved clinically with bilateral ECT, when pretreatment performance was compared with performance 14 days after treatment. He found significant changes in synthesizing ability, abstracting ability, speed of ideation, visuomotor ability, and estimation of self-performance.

Stone (1950) reported two patients who had received 14 and 20 ECTs, respectively, who manifested neither objective nor subjective diminution in performance on a battery of cognitive and intelligence tests from before to after ECT.

Pascal and Zeaman (1951) reported four patients in whom serial testing was done before, during, and after ECT with four different cognitive tests. These tests were: a noun-naming test, a color-naming test, the Bender-Gestalt, and a serial subtraction test. They found improvement in the tests early in the course of ECT followed by worsening as the course of treatment progressed with return to pretreatment baseline levels or better within several days of the last treatment.

Although their findings appear to be somewhat at variance with other reports in the the literature, Shapiro, Campbell, Harris, and Dewsberry (1958) reported that ECT did not cause an increase and, in fact, probably caused a relative decrease in psychomotor speed. Nor did it reduce the so-called "distraction effect" in which depressed patients doing a paper and pencil maze task speed up their performance when asked to count aloud at the same time.

More Recent Psychometric Studies of Nonmemory-Associated Cognitive Effects of ECT

McAndrew, Berkley, and Matthews (1967), on the basis of a battery of neuropsychological tests sensitive to specific right and left lateralized hemispheric functions as well as some sensitive to diffuse organic impairment without lateralization, given before and after six right or left unilateral or bilateral ECTs, found no statistically significant differences between or within groups. They did find an interesting trend for right unilateral ECT to lead to more frequent improvement on right than left hemisphere tests, for left unilateral to do just the reverse, and for bilateral to lead to identical percentages of improvement on both right and left hemisphere tests. The Halstead categories test, which is sensitive to diffuse cerebral dysfunction, showed identical percentages of improvement (75%) and worsening (25%) among the three treatment groups. In all three groups, after the sixth treatment there was evidence of some transient cerebral dysfunction. These findings suggest that, on the whole, ECT improves nonmemory cognitive function, though it may in some cases and at certain points in the treatment course induce variable degrees of transient diffuse cerebral dysfunction.

Small et al. (1972) tested ECT patients who had been randomly assigned to unilateral nondominant or unilateral dominant ECT with a battery of neuropsychological tests, modified from the Halstead-Reitan and Wechsler test batteries, before ECT, after five treatments, and 60 to 90 days after the last treatment. They found that after five unilateral nondominant treatments several Halstead-Reitan subtests (mainly right-sided) were improved. Five unilateral dominant ECTs did not result in Halstead-Reitan subtest improvement but did result in impaired Story Memory A performance. At followup 60 to 90 days later, the unilateral nondominant group showed sustained improvement, while the unilateral dominant group now had comparable improvement with clearing of the impairment in Story Memory A.

In a related study (Small et al., 1973), it was found that unilateral dominant, unilateral nondominant, and bilateral ECT were all associated with improvement in nonverbal, visuospatial, nonmemory-related performance tasks and with temporary deterioration on tests requiring intact verbal function. Halstead-Reitan subtests that did change in this study were predominantly in the direction of improvement and were equally distributed among test items reflecting dominant, nondominant, and bilateral hemispheric function.

Reichert, Benjamin, Neufeldt, and Marjerrison (1976) reported that bilateral but not unilateral nondominant ECT produced impairments in "prograde effects" as reflected by decreased performance on the Quick Test, a test of general verbal cognitive processes and performance. These "prograde effects" included motivational, attentional, perceptual, and performance dimensions and therefore play an important role in facilitating information acquisition and storage, but not in mediating recall functions.

Kronfol et al. (1978) studied 18 depressed patients before and during ECT with a battery of neuropsychological tests capable of differentially assessing verbal and nonverbal cognitive functions. Prior to ECT, they found that 5 of the verbal and 13 of the nonverbal subtests were within the impaired range, and interpreted these findings as indicating that depression interferes with both verbal and nonverbal cognitive function but more so with respect to the latter. The posttreatment cognitive testing results, though actually involving relatively small and, for the most part, not statistically significant changes, was interpreted by the authors as indicating that left hemisphere functions declined following left-sided ECT while right hemispheric functions tended to improve after right-sided ECT. They noted disruption of both verbal and nonverbal cognitive tests after one unilateral dominant or nondominant ECT with the degree of verbal impairment being more significant. They interpreted the results obtained after the eighth ECT as reflecting the interaction of two factors, the disruptive effect of ECT in conjunction with the enhancing effect of relief from depression on cognitive processes. Their general conclusion was that ECT did not impair brain functioning but rather brought about significant improvement in nonmemory-related cognitive function as well as in depression.

Consistent with this is the finding of Miller et al. (1981) that the Halstead-Reitan impairment index and verbal, performance, and full-scale IQ scores obtained 2 weeks after a course of ECT are improved when they are compared to those obtained beforehand. As might be expected, the degree of improvement was greater with unilateral than bilateral ECT.

MacKenzie, Price, Tucker, and Culver (1982) compared the daily performance of patients receiving bilateral sinusoidal ECT with that of psychiatric inpatient controls not treated with ECT on a battery of four neuropsychological tests over the first 8 to 12 days of a course of bilateral ECT during which time a mean of 3.1 ECTs had been administered. Both groups improved on all the tests given, but the rate of improvement in the ECT patients was significantly less after three treatments had been given than that in the controls for the Letter Cancellation Test, though not for the others. On the basis of their findings, the authors suggested that some of the earliest effects of bifrontotemporal ECT may be impairment in attentional processes and the capacity to make appropriate shifts in behavioral set, functions thought to be mediated primarily by the frontal lobes (Mattes, 1980; Silverstein, Morrison, & Weinberg, 1980).

Goldstein et al. (1977) found on Halstead-Reitan testing in a small group of psychotically depressed patients evidence of diffuse, generalized, as well as localized right hemispheric dysfunction which was more prominent in patients with a prior history of ECT. There was neither systematic improvment nor worsening in the Halstead-Reitan battery after a course of either brief-pulse or sinusoidal ECT (it is unclear from the study whether the ECT was unilateral or bilateral). However, evidence of right hemisphere dysfunction had increased immediately after treatment and was even more pronounced at 3-month followup. The evidence of generalized, diffuse dysfunction was still present but decreased at 3 months post-ECT. A somewhat similar study done previously by Kendall, Mills, and Thale (1956) had also found no difference between pulse and sine wave stimulation in their effects on cognitive functions.

Horan, Ashton, and Minto (1980) studied depressed patients after three right unilateral ECTs with a battery of tests which tapped four general areas of cerebral functioning including verbal, memory, visuospatial, and visuomotor. The main findings were that the Knox Cube Imitation Test performance was improved, whereas other tests in the battery were not. The authors interpreted this finding as suggesting that the left hemisphere is specialized for processing sequential, time-dependent information. Further, they pointed out that unilateral ECT may be a powerful tool for investigating differential hemisphere functioning in cognitive areas other than memory, a research area that has been relatively little explored thus far.

Short- and Long-Term Followup Studies of the Effect of ECT on Nonmemory-Associated Cognitive Function

While relatively few studies have examined the long-term natural history of ECT-induced cognitive dysfunction, a variety of studies, some of which have been previously discussed, have examined the evolution of cognitive dysfunction over relatively short periods of time, i.e., 2 to 3 weeks at most, following ECT. The following are a few selected longer-term followup studies.

Goldman, Gomer, and Templer (1972) compared the results of Bender-Gestalt and Benton tests in 20 male schizophrenics who had received more than 50 ECT (50-219 with a median of 69.5) between 10 and 15 years previously, with matched schizophrenic controls without a history of ECT. They found a higher error rate in the ECT-treated patients and interpreted this as indicating organicity or permanent brain damage secondary to ECT. In view of the lack of control for severity of illness and the use of uncertain diagnostic criteria in this study, this conclusion must be viewed with caution.

Templer, Ruff, and Armstrong (1973) replicated the preceding study controlling for degree of psychosis and found that schizophrenics who had received more than 50 (median 58.5) ECTs at least 7 years before did not differ in WAIS and Benton scores but did have lower Bender-Gestalt scores than schizophrenic controls without a history of treatment with ECT. They interpreted their finding as being consistent with permanent brain dysfunction due to ECT.

Weeks, Freeman, and Kendell (1980) compared the results of a battery of 19 different memory and nonmemory tests administered to depressed patients before, 1 week, 4 months, and 7 months after unilateral nondominant or bilateral ECT to results obtained from non-ECT patient controls as well as normal controls. At 1 week posttreatment, ECT-treated patients did not perform worse on any of the cognitive tests and, in fact, improved significantly on several of them. At 4-month followup, the scores on cognitive tests in the ECT and non-ECT patient groups were virtually identical. At 7-month followup, the same was true except that there was a tendency for both patient groups to have slightly more impaired scores than the normal control groups. When the unilateral and bilateral ECT patients were compared, it was found that the former were significantly less impaired on cognitive testing than the latter at 1 week post-ECT and, in fact, were scoring close to the normal controls on many of the tests. However, at 4 months post-ECT there was no difference between the two ECT groups. The authors conclude that, in general, ECT does not cause lasting cognitive impairment and that with unilateral nondominant ECT there is very little impairment even in the short-term.

Freeman, Weeks, and Kendell (1980) reported that patients who had had ECT in the past, a mean of 10 years previously, and who still complained of cognitive dysfunction secondary to ECT, performed for the most part as well as normal controls on a variety of nonmemory cognitive tests. On the basis of these results, the authors concluded that ECT usually does not produce enduring ill effects on nonmemory-dependent cognitive function.

Summary

Based on this review, several conclusions emerge.

1. ECT causes immediate posttreatment confusion, which may be cumulative over a course of treatment; this posttreatment confusion is considerably less severe with unilateral than with bilateral treatment.
2. ECT does not cause lasting or permanent dysfunction in nonmemory-associated cognitive functions; though there may be initially or at some other point during the course of treatment, transient, reversible evidence of impairment.
3. If such transient impairments do occur, most studies suggest they will have cleared completely by between 2 and 8

weeks after the treatment course is completed.

4. A few studies raise the question of whether or not bilateral ECT may cause some long-lasting cognitive impairments in schizophrenic patients.
5. Overall, ECT improves nonmemory-associated cognitive functions compared to pretreatment baseline scores.
6. In general, effective treatment with ECT seems to improve nonmemory-associated cognitive dysfunctions associated with depression.
7. Unilateral nondominant ECT appears to improve specific right-sided neuropsychological dysfunction associated with depression, whereas unilateral dominant ECT may impair some left-sided neuropsychological funtion.
8. Acute organic mental syndromes are known to occur in up to 40-50% of patients receiving bilateral ECT; whether or not, and how frequently these may occur with unilateral nondominant treatment is not clear.
9. Certain drugs such as lithium and highly anticholinergic psychotropes such as amitriptyline or benztropine may, when given concurrently with ECT, increase the incidence of acute organic mental syndromes associated with it.

Questions for Future Research

Since the whole area of the effects of ECT on nonmemory-associated cognitive function is virtually in its infancy, a broad array of important research questions for the future exists. For example, will the fascinating early findings in regard to specific lateralized cognitive effects of right and left unilateral ECT hold up in future, well-controlled, prospective replicative studies? In this vein, will ECT turn out, as some suspect it may, to be a useful research tool in investigating the lateralization of cerebral hemispheric functions?

Could careful investigation of the relationship between stimulus and seizure variables and ECT-induced cognitive impairment allow for the development of treatment protocols which in terms of stimulus parameters and treatment schedules could optimize treatment efficacy while further minimizing the occurrence, however transient, of cognitive disturbances? Specifically, if, as seems possible, changes in attentional function are among the earliest to occur after bilateral ECT and if, as also seems possible, they occur early on a continuum with more diffuse and flagrant later organic mental symptoms, might it be possible by monitoring them to identify patients at high risk of developing acute organic mental syndrome and, on the basis of these findings, appropriately adjust the number, type, and/or frequency of treatments given.

Will careful future investigation of the beneficial effects of ECT on certain specific cognitive dysfunctions in depression perhaps shed further light on their etiology or perhaps on the basis for some of the therapeutic effects of ECT?

Other important questions include the following. How frequently do acute organic mental syndromes occur after unilateral nondominant ECT and how might their clinical manifestations differ from those that occur after bilateral ECT? If interference with frontal-lobe attentional mechanisms is the basis for at least some portion of the post-ECT acute organic mental syndrome, might there perhaps be some pharmacological means of preventing this, such as with Ritalin or Pemoline?

References

A Practicing Psychiatrist, Experience of ECT. *Br. J. Psychiatry,* 111:365-367, 1965.

Abrams, R. Daily administration of unilateral ECT. *Am. J. Psychiatry,* 124:384-386, 1967.

Abrams, R., and Fink, M. Clinical experience with multiple electroconvulsive treatments. *Comp. Psychiatry,* 13:115-121, 1972.

Annett, M., Hudson, P.T.W., and Turner, A. Effects of right and left unilateral ECT on naming and visual discrimination analyzed in relation to handedness *Br. J. Psychiatry,* 124:260-264, 1974.

Arnot, R.E. Observations on the effects of electric convulsive treatment in man—psychological. *Dis. Nerv. Syst.,* 36:499-502, 1975.

Ayd, F. Lithium-ECT induced cerebral toxicity. *Int. Drug Ther. Newsl.,* 16:21-23, 1981.

Campbell, D. A study of some sensorimotor functions in psychiatric patients. Thesis, University of London, 1957.

Cannicott, S.M. Unilateral electroconvulsive therapy. *Postgrad. Med.,* 38:451-459, 1962.

Cavenar, J-O., Maltbie, A.A., and Austin, L. Depression simulating organic brain disease. *Am. J. Psychiatry,* 136:521-523, 1979.

Clyma, E.A. Unilateral convulsive therapy: How to determine which hemisphere is dominant. *Br. J. Psychiatry,*

126:372-379, 1975.

Cronin, D., Bodley, P., Potts, L., et al. Unilateral and bilateral ECT: A study of memory disturbance and relief from depression. *J. Neurol. Neurosurg. Psychiatry,* 33:705-713, 1970.

d'Elia, G. Unilateral ECT. *Acta Psychiatr. Scand. (Suppl.),*215: 5-98, 1970.

DeWolfe, A.S., Barrell, R.P., Becker, B.C., and Spaner, F.C. Intellectual deficit in chronic schizophrenia and brain damage. *J. Consult. Clin. Psychol.,* 36:197-204, 1971.

Donnelly, E., Dent, K., and Murphy, D. Comparison of temporal lobe epileptics and affective disorders on the Halstead-Reitan test battery. *J. Clin. Psychol.,* 28:61-62, 1972.

Elmore, J.L., and Sugerman, A.A. Precipitation of psychosis during electroshock therapy. *Dis. Nerv. Syst.,* 36:115-117, 1975.

Fink, M. Clinical progress in convulsive therapies. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 271-277.

Fink, M. (ed.) *Convulsive Therapy: Theory and Practice.* New York: Raven Press, 1979.

Fink, M., Kahn, R.L., Kapp, E., et al. Inhalant-induced convulsions. *Arch. Gen. Psychiatry,* 4:259-266, 1961.

Fisher, K.A. Changes in test performance of ambulatory depressed patients undergoing electroshock therapy. *J. Clin. Psychol.,* 41:195-232, 1949.

Fraser, R.M., and Glass, I.B. Recovery from ECT in elderly patients. *Br. J. Psychiatry.* 133:524-528, 1978.

Fraser, R.M., and Glass, I.B. Unilateral and bilateral ECT in elderly patients. *Acta Psychiatr. Scand.,* 62:13-31, 1980.

Freeman, C.P.L., Weeks, D., and Kendell, R.E. ECT: II. Patients who complain. *Br. J. Psychiatry,* 137:17-25, 1980.

Gallinek, A. Organic sequelae of electric convulsive therapy including facial and body dysgnosias. *J. Nerv. Ment. Dis.,* 115:377-393, 1952.

Goldman, H., Gomer, F.E., and Templer, D.I. Long-term effects of electroconvulsive therapy upon memory and perceptual motor performance. *J. Clin. Psychol.,* 28:32-34, 1972.

Goldstein, S.G., Filskov, S.B., Weaver, L.A., and Ives, J.O. Neuropsychological effects of electroconvulsive therapy. *J. Clin. Psychol.,* 33:798-806, 1977.

Gottlieb, G., and Wilson, I. Cerebral dominance: Temporary disruption of verbal memory by unilateral electroconvulsive shock treatment. *J. Comp. Physiol. Psychol.,* 60:368-372, 1965.

Halliday, A.M., Davison, K., Browne, M.W., and Kreeger, I.C. A comparison of the effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and non-dominant hemispheres. *Br. J. Psychiatry,* 114:997-1012, 1968.

Hamilton, M., Stocker, M.J., and Spencer, C.M. Post-ECT cognitive defect and elevation of blood pressure. *Br. J. Psychiatry,* 135:77-78, 1979.

Hargreaves, W.A., Fischer, A., Elashoff, R.M., and Blacker, K.H. Delayed onset of impairment following electrically induced convulsions. *Acta Psychiatr. Scand.,* 48:69-77, 1972.

Horan, M., Ashton, R., and Minto, J. Using ECT to study hemispheric specialization for sequential processes. *Br. J. Psychiatry,* 137:119-125, 1980.

Huston, P.E., and Strother, C.R. The effect of electric shock on mental efficiency. *Am. J. Psychiatry,* 104:707-712, 1948.

Impastato, D.M., and Karliner, W. Control of memory impairment in EST by unilateral stimulation of the nondominant hemisphere. *Dis. Nerv. Syst.,* 27:182-188, 1966.

Inglis, J., and Lawson, J.S. Sex differences in the effects of unilateral brain damage on intelligence. *Science,* 212:693-695, 1981.

Kalinowsky, L. Organic psychotic syndromes occurring during electric convulsive therapy. *Arch. Neurol. Psychol.,*53:269-273, 1945.

Kane, F.J. Transient neurological symptoms accompanying ECT. *Am. J. Psychiatry,* 119:786-787, 1963.

Kendall, B.S., Mills, W.B., and Thale, T. Comparison of two methods of electroshock in their effect on cognitive functions. *J. Consult. Psychol.,* 20:423-429, 1956.

Kriss, A., Blumhardt, L.D., Halliday, A.M., and Pratt, R.T.C. Neurological asymmetries immediately after unilateral ECT. *J. Neurol. Neurosurg. Psychiatry,* 41:1135-1144, 1978.

Kronfol, Z., Hamsher, K. deS., Digre, K., and Waziri, R. Depression and hemispheric functions: Changes associated with unilateral ECT. *Br. J. Psychiatry,* 132:560-567, 1978.

Lancaster, N.P., Steinert, R.R., and Frost, I. Unilateral electroconvulsive therapy. *J. Ment. Sci.,* 104:221-227, 1958.

Levy, J., and Reid, M. Variations in writing posture and cerebral organization. *Science,* 191:337-339, 1976.

Luborsky, L.B. Psychometric changes during electric shock treatment. *J. Nerv. Ment. Dis.,* 107:531-536, 1948.

MacKenzie, T.B., Price, T.R.P., Tucker, G.J., and Culver, C.M. An early change in cognitive performance accompanying ECT. (Submitted, 1982)

Mandel, M.R., Madsen, J., Miller, A.L., and Baldessarini, R.J. Intoxication associated with lithium and ECT. *Am. J. Psychiatry,* 137:1107-1109, 1980.

Marin, R.S., and Tucker, G.J. Psychopathology and hemispheric dysfunction: A review. *J. Nerv. Ment. Dis.,* 169:546-557, 1981.

Marshall, J.R., Kalin, N.G., and Tariot, A.M. An organic psychosis associated with electroconvulsive therapy. *Psychiatr. Opin.,* 17:33-39, 1980.

Mattes, J.A. The role of frontal lobe dysfunction in childhood hyperkinesis. *Compr. Psychiatry.,* 21:358-364, 1980.

McAndrew, J., Berkley, B., and Matthews, L. The effects of dominant and nondominant unilateral ECT as compared to bilateral ECT. *Am. J. Psychiatry,* 124:483-490, 1967.

Merrin, E.L. Schizophrenia and brain asymmetry: An evaluation of evidence for dominant lobe dysfunction. *J. Nerv. Ment. Dis.,* 169:405-416, 1981.

Miller, M.J., Small, I.F., Milstein, V., et al. Electrode placement and cognitive change with ECT: Male and female response. *Am. J. Psychiatry,* 138:384-386, 1981.

Moscovitch, M., Strauss, E., and Olds, J. Handedness and dichotic listening performance in patients with unipolar endogenous depression who received ECT. *Am. J. Psychiatry,* 138:988-990, 1981.

Newlin, D.B., Carpenter, B., and Golden, C.J. Hemispheric asymmetries in schizophrenia. *Biol. Psychiatry,* 16:561-582, 1981.

Ottosson, J.O. Psychological or physiological theories of ECT. *Int. J. Psychiatry,* 5:170-174, 1968.

Pascal, G.R., and Zeaman, J.B. Measurement of some effects of electroconvulsive therapy on the individual patient. *J. Abnorm. Soc. Psychol.,* 46:104-115, 1951.

Perlson, J. Psychologic studies on a patient who received two hundred and forty-eight shock treatments. *Arch. Neurol. Psychiatry.,* 54:409-411, 1945.

Pratt, R.T.C., and Warrington, E.K. Cerebral dominance and unilateral ECT. *Br. J. Psychiatry,* 121:327-328, 1972.

Price, T.R.P. Short- and long-term cognitive effects of ECT. Part I: Effects on memory. *Psychopharmacol. Bull.,* 18(2): 81-91, 1982.

Reichert, H., Benjamin, J., Neufeldt, A.H., and Marjerrison, G. Bilateral and nondominant unilateral ECT. Part II: Development of prograde effects. *Can. Psychiatr. Assoc. J.,* 21:79-86, 1976.

Scanlon, W.G., and Mathas, J. Electroencephalographic and psychometric studies of Indoklon convulsive treatment and electroconvulsive treatment. *Int. J. Neuropsychiatry,* 3:276-281, 1967.

Shapiro, M.B., Campbell, D., Harris, A., and Dewsberry, B.M. Effects of ECT upon psychomotor speed and the distraction effect in depressed psychiatric patients. *J. Ment. Sci.,* 104:681-695, 1958.

Silverstein, M.L., Morrison, H.L., and Weinberg, J. Relevance of modern neuropsychology to psychiatry. *J. Nerv. Ment. Dis.,* 168:673-678, 1980.

Small, I.F., and Small, J.G. EEG, evoked potential, and DC responses with unilateral ECT. *J. Nerv. Ment Dis.,* 152:396-404, 1971.

Small, I.F., Small, J.G., Milstein, V., and Moore, J.E. Neuropsychological observations with psychosis and somatic treatment. *J. Nerv. Ment. Dis.,* 155:6-13, 1972.

Small, I.F., Small, J.G., Milstein, V., and Sharpley, P. Interhemispheric relationships with somatic therapy. *Dis. Nerv. Syst.,* 34:170-177, 1973.

Small, J.G., Kellams, J.J., Milstein, V., and Small, I.F. Complications with electroconvulsive treatment combined with lithium. *Biol. Psychiatry,* 15:103-112, 1980.

Squire, L.R. A stable impairment in remote memory following electroconvulsive therapy. *Neuropsychologia,* 13:51-58, 1975.

Stone, C.P. Losses and gains in cognitive functions as related to electroconvulsive shocks. *J. Abnorm. Soc. Psychol.,* 42:206-214, 1947.

Stone, C.P. Pre-illness records compared with performances during and after electroconvulsive shocks. *J. Abnorm. Soc. Psychol.,* 45:154-159, 1960.

Summers, W.K., Robins, E., and Reich, T. The natural history of acute organic mental syndrome after bilateral electroconvulsive therapy. *Biol. Psychiatry,* 14:905-912, 1979.

Sutherland, E.M., Oliver, J.E., and Knight, D.R. EEG, memory, and confusion in dominant, non-dominant, and bi-temporal ECT. *Br. J. Psychiatry,* 115:1059-1064, 1969.

Taylor, M.A., Greenspan, B., and Abrams, R. Lateralized neuropsychological dysfunction in affective disorder and schizophrenia. *Am. J. Psychiatry,* 136:1031-1034, 1979.

Templer, D.I., Ruff, C.F., and Armstrong, G. Cognitive functioning and degree of psychosis in schizophrenics given many electroconvulsive treatments. *Br. J. Psychiatry,* 123:441-443, 1973.

Tucker, D.M., Stenslie, C.E., Roth, R.S., and Shearer, S.L. Right frontal lobe activation and right hemispheric performance. *Arch. Gen. Psychiatry,* 38:169-174, 1981.

Valentine, M., Keddie, K.M.G., and Dunne, D. A comparison of techniques in electroconvulsive therapy. *Br. J. Psychiatry,* 114:989-996, 1968.

Warrington, E.K., and Pratt, R.T.C. Language laterality in left-handers assessed by ECT. *Neuropsychologia,* 11:423-428, 1973.

Watson, C.G. Separation of brain-damaged from schizophrenic patients by Reitan-Halstead pattern analysis: An unsuccessful replication. *Psychol. Rep.,* 29:1343-1346, 1971.

Weeks, D., Freeman, C.P.L., and Kendell, R.E. ECT. III: Enduring cognitive deficits. *Br. J. Psychiatry,* 137:26-37, 1980.

Weiner, R.D., Whanger, A.D., Erwin, C.W., and Wilson, W.P. Prolonged confusional state and EEG seizure activity following concurrent ECT and lithium use. *Am. J. Psychiatry,* 137:1452-1453, 1980.

Wells, C.E. Pseudodementia. *Am. J. Psychiatry,* 136:895-900, 1979.

Wexler, B.E. Cerebral laterality and psychiatry: A review of the literature. *Am. J. Psychiatry,* 137:279-291, 1980.

Wilcox, K.W. Confusion and therapy in electroconvulsive treatment. *Confin. Neurol.,* 13:318-327, 1953.

Williams, M. Errors in picture recognition after ECT. *Neuropsychologia,* 11:429-436, 1973.

Wilson, I., and Gottlieb, G. Unilateral electroconvulsive shock therapy. *Dis. Nerv. Syst.,* 28:541-545, 1967.

Wohlberg, G.W., and Kornetsky, C. Sustained attention in remitted schizophrenics. *Arch. Gen. Psychiatry,* 28:533-537, 1973.

Nonmemory Higher Cognitive Function and Electroconvulsive Treatment

Sheri A. Berenbaum, Ph.D.,[1] and
Michael Alan Taylor, M.D.[1]

The short-term effects of electroconvulsive therapy (ECT) upon mnestic function are well known. Bilateral ECT results in both retrograde and anterograde amnesia, with both verbal and nonverbal memory adversely affected. The effect is significantly smaller but not insubstantial following unilateral ECT. The degree of deficit is not correlated with clinical improvement of depression, and significant recovery of mnestic function occurs within 1 to 2 weeks after completion of treatment. By 6 months posttreatment, recovery is virtually complete, although some deficit remains for recall of events during the treatment period (Fink, 1979; Harper & Wiens, 1975; Fink, 1977; Squire, 1977; Squire & Chace, 1975). The effects of ECT upon other higher cortical and subcortical functions are less clearly understood, although results from early and more recent studies suggest little if any permanent disability.

---

[1] Departments of Psychology, and Psychiatry and Behavioral Sciences, University of Health Sciences/The Chicago Medical School, North Chicago, IL 60064.

Further study is essential, as careful evaluation of cognitive changes associated with ECT has practical and theoretical importance. Treatment decisions clearly necessitate consideration of potential side effects associated with ECT, and delineation of cognitive performance before and after ECT may help to explain possible mechanisms accounting for treatment efficacy, the nature of the dysfunction in depressive illness and, in general, may provide information on brain-behavior relationships. Realization of these goals, however, requires that studies be designed and evaluated with respect to several important issues.

Methodological and Theoretical Considerations

Subject Sample Characteristics

To properly evaluate the cognitive effects of ECT, patient selection must be precise, as there is evidence (Taylor, Redfield, & Abrams, 1981; Abrams, Redfield, & Taylor, 1981) that there are differing patterns of cognitive deficits between the major psychiatric disorders. Nevertheless, several studies use heterogeneous patient groups and include schizophrenics (Horan, Ashton, & Minto, 1980; Small, I.F., Small, J.G., Milstein, & Moore, 1972) who have significant cortical dysfunction (Abrams et al., 1981; Taylor et al., 1981). Diagnostic problems extend to difficulty in evaluating and controlling for severity of psychopathology: Matching groups by depression score alone is inappropriate and should include for comparison other symptoms that form the constellation of the depressive illness so that nonendogenous patients are separately evaluated or excluded from study (Taylor, 1982a). Subject demographic variables (e.g., age, sex, education) are usually controlled, but other important and confounding variables (e.g., medication, previous ECT) often are ignored (Horan, Ashton, & Minto, 1980; Kronofol, Hamsher, Digre, & Waziri, 1978; McAndrew, Berkley, & Matthews, 1967).

Further, evaluation of cognitive effects of ECT is confounded by patients' premorbid ability levels. Cognitive level has been examined only in the immediate pre-ECT period, when the nature of the psychiatric illness itself is likely to impair performance. Lack of change or improvement in cognitive performance after ECT could be due to either a lack of serious neuropsychological effects of ECT, or ECT-induced cognitive impairment associated with cortical dysfunction which is counteracted by improved performance resulting from elevated mood. Educational attainment can be evaluated as an approximate index of premorbid intelligence. Examination of earlier records and/or assessment of vocabulary are more exact.

Cognitive Testing

In evaluating cognitive effects of ECT, it is essential to specify the testing schedule, since effects appear to vary with the number of treatments and the time period between the ECT and the assessment, both for a given ECT and after a course of treatments.

In selecting tests to assess cognitive change, the following standard design features and psychometric criteria should be satisfied: a) acceptable reliability and validity; b) normative data available or easily collectable; c) appropriateness for use with psychiatric patients, as evidenced by previous use with younger subjects, neurological, or other psychiatric samples; d) standardized instructions and procedures to ensure uniformity of administration within and across centers; e) objective scoring procedures; f) reasonable time limits, to allow assessment of multiple abilities within one test session without compromising reliability; and g) appropriateness for repeated testing, so that practice and fatigue effects are minimized, and state-dependent learning factors do not confound the results.

Attempts to relate cognitive changes to neurological function or to etiological theories of depressive illness require that the tests used meet the following specific theoretical criteria: a) established or suggested sensitivity to neurological disruption, i.e., that there be data on changes with localized or lateralized damage; b) ability to tap "higher order" cognitive functions of the type reputed to be disrupted with ECT or drugs; c) minimal involvement of short-term memory, to minimize performance changes due to memory disruption and maximize ability to see true "cognitive" changes; and d) ability to examine constituent components of complex cognitive functions, i.e., to attribute cognitive changes to specific aspects of processing, or to statistically control the influence of simpler functions on performance on more complex tasks.

Ultimately, it is desirable to determine the nature of the cognitive disruption(s) or improvement(s), i.e., to what extent the processes affected are specifically attention/concentration, speed, perceptual-motor ability, reasoning, synthesis, planning, disorientation, or general cognitive deficit, and tests should be administered that provide such information.

Data Analysis

Studies evaluating effects on a number of correlated tasks with several groups each of small size are plagued by statistical difficulties of high Type I error, nonindependence of comparisons and low power. These problems can be attentuated by using matching procedures and associated statistics, and multivariate analysis (Timm, 1975). Difficulties with matching on pre-ECT cognitive level can be handled with analysis of covariance designs (Cohen & Cohen, 1975).

Some studies (e.g., Kronofol et al., 1978) contain implicit or explicit statements concerning the relationship between cognitive changes and clinical efficacy of ECT, i.e., cognitive improvement is directly associated with relief from depression. In no study has this been adequately tested by correlating cognitive performance with clinical course.

Review of Results Reported

The literature on the adverse effects of ECT most frequently reports transient neuropsychological deficits that occur during the first 30 minutes post-ECT. These include dysphasia after unilateral dominant ECT (Clyma, 1975), and tactile and visual inattentions (Kriss, Blumhardt, Halliday, & Pratt, 1978) and construction dyspraxia following unilateral nondominant ECT. Until recently, most studies have had serious methodological limitations and have examined neurological and perceptual functions, rather than higher order cognitive abilities.

The recent studies reporting more extensive testing of long-term cognitive function have better methodological controls than the older studies, but are still far from optimal. It is possible, however, to evaluate these recent reports in light of the complexities discussed above. The results are confusing and often contradictory, but some tentative findings emerge, along with testable explanations for the discrepancies. In general, the data suggest that little, if any, permanent disability occurs as a result of ECT, and that the treatment may actually improve at least some aspects of cognition, possibly as a result of relief of depression. These conclusions emerge from six relatively large studies attempting to provide methodological controls and using extensive neuropsychological testing. All of these studies, however, are limited by one or another difficulty cited above, including diagnostic problems, varying ECT course and testing schedule, pre-ECT cognitive deficits, small sample size, inadequate test battery, and incomplete data analysis.

McAndrew et al. (1967) compared cognitive consequences of courses of six unilateral right, unilateral left, or bilateral ECT treatments in a group of patients containing mostly depressives. Their results revealed no significant interaction effects, "indicating that pre- and post-ECT test score differences on measures shown to bear a relationship to right as opposed to left cerebral hemisphere dysfunction did not vary as a function of unilateral right, unilateral left, or bilateral electrode placement." The authors interpreted the trends, which were weak at best, as indicating that right ECT was associated more frequently with improvement and less frequently with decrement on right as compared with left hemisphere tasks, while left ECT was associated more frequently with improvement and less frequently with decrement on left vs. right hemisphere tasks. Post-ECT performance improved on several tests and declined on others, with no apparent pattern. Interestingly, performance on the Halstead Category Test, in part a measure of concept formation, improved post-ECT in all three groups, perhaps as a result of mood elevation. Surprisingly, there were no differences in cognitive change between unilateral and bilateral ECT groups.

Small et al. (1972, 1973) examined cognitive effects of different kinds of somatic treatment, including unilateral left and right and bilateral ECT. A heterogeneous group of patients was tested on a neuropsychological test battery immediately after a treatment of five ECTs, and then again 60-90 days later. Although important details of the methods and results are omitted from the reports, in general it appears that right ECT was associated with immediate unchanged or improved function, and left ECT was associated with impairment in story memory. Testing at 60-90 days revealed that improvements were sustained and the deficit in the left ECT group eliminated. Performance on the Rod and Frame Test of field dependence was assessed in some patients; mean number of errors was unchanged after ECT. However, analysis of responses with respect to direction of rod displacement indicated that the majority of errors occurred on the side contralateral to stimulation.

Kronofol et al. (1978) examined the effects of differing amounts of left and right unilateral ECT in depressed patients. Their data indicated that the small deficits seen after the first ECT were mostly eliminated by the eighth ECT, with the possible exception of verbal fluency, a left frontal function (Benton, 1968; Milner, 1967). The authors stated that, "Neuropsychological tests showed that the right hemispheric functions were more frequently abnormal as compared to left hemispheric (dominant) functions in the pre-ECT tests. ECTs delivered to either the right or left side improved right hemispheric functions when the depression was ameliorated . . . in depression right hemispheric functions are initally disturbed and ECT, instead of being deleterious to these functions, tends to improve them." These interpretations, however, are difficult to defend: only one (of eight) of the increases in right hemisphere performance was significant; normative data were not reported, so there is no way to assess the abnormality of right hemispheric functions pre-ECT; correlations between cognitive improvement and depression amelioration were not reported; depression was relieved with both left and right ECT, whereas no right hemisphere cognitive function was significantly improved with left ECT (and one left hemisphere ability was significantly impaired); differences between left and right ECT groups on some pre-ECT cognitive measures and depression score were not tested statistically; direct comparisons were not made between right and left unilateral ECT groups.

Horan et al. (1980) compared unilateral right and bilateral ECT in two heterogeneous patient samples; testing was conducted 6 to 8 hours after the last of a series of three ECTs. In both samples, performance on the Knox Cube Imitation Test (a sequential, presumably left hemisphere task) was significantly improved. In the one sample where other tests were administered, Vocabulary was impaired in the bilateral group and Form Assembly was impaired in both the unilateral and bilateral groups. The authors suggested that since improvement was specific to the sequencing test, it did not reflect change due to relief from depression, but rather the facilitation or enhancement of left hemisphere sequencing operations with the partial suppression of the right hemisphere accomplished with ECT. Although this explanation fits the data for both left and right hemisphere tasks, it is incompatible with data from their own and other studies showing unchanged or improved performance on some right hemisphere tasks (Kronofol et al., 1978; Small et al., 1972) or failing to show improvement on some sequencing tasks (Kronofol et al., 1978) after right ECT.

Weeks, Freeman, and Kendell (1980) examined prolonged effects (up to 6 months post-ECT) of nondominant unilateral and bilateral ECT in depressed patients. In general, the results indicated no deficits and some improvement with unilateral nondominant ECT at both 1 week post-ECT and later, and small immediate deficits with bilateral ECT that, with the possible exception of memory, cleared up by 6 months post-ECT. Details of these results are difficult to interpret, since pre-post ECT comparisons are made only for the 1-week assessment. At later assessments, both ECT groups are compared to non-ECT and normal controls. Examination of the data provided indicates that in the unilateral group, both psychomotor speed and cube analysis performance showed significant improvement at 1 week, and performance on a test of short-term attention and concentration was at normal levels by 4 months.

On scales of depression, both ECT and non-ECT groups improved significantly, suggesting that the similar cognitive performance of the groups was due in part to relief from depression. This finding is surprising, since there were no significant differences between groups in amount of medication taken at any stage, raising the possibility that the non-ECT group consisted of more reactive depressives who get well over time without treatment (Taylor, 1982b), an interpretation supported by the significantly greater impairment of the ECT group (as compared to the non-ECT group) on pretreatment cognitive performance.

In a related but less extensive study examining cognitive functioning and ECT, Cohen, Berent, and Silverman (1973) administered the Rod and Frame Test to a group of depressed patients pre-ECT and 5 hours after a single unilateral left, right, or no ECT. Performance was enhanced following right ECT and impaired following left ECT, with no change in the control group. These results led the authors to speculate about "two cognitive controls of attention deployment." The scanning control, related to extensiveness of sampling stimuli, was suggested to be mediated by structures of the right hemisphere. In contrast, the field articulation control—the sorting-out of elements of the field—was proposed to be related to left hemisphere structures.

The studies reviewed above differ in a number of methodological and theoretical variables, several of which could account for the differing conclusions. These include patient sample, sample size, number of ECT treatments, time between ECT and testing, pre-ECT cognitive performance, nature of control group, tests administered, analyses performed, and interpretation of results.

Time Course

The three studies examining the time course of ECT (Kronofol et al., 1978; Small et al., 1972; Weeks et al., 1980) address two separate issues: Effects of differing numbers of ECT, and effects of time since last ECT. The results of Kronofol et al. (1978) indicated that deficits which appear after a single ECT treatment may clear up after a course of eight ECTs. This suggests that the deficit seen by Cohen et al. (1973) on the Rod and Frame Test might disappear with continued ECT treatment, and that the changes seen by Horan et al. (1980) after three ECTs might not persist with additional treatment.

Two studies (Small et al., 1972; Weeks et al., 1980) examined changes in cognition as a function of time after last ECT. The results of Weeks et al. (1980) suggest that cognitive functioning improves with time from ECT, so that small deficits present at 1 week post-bilateral ECT are gone 6 months post-ECT, and improvements seen at 1 week post-unilateral nondominant ECT may actually increase later. Similar results are reported by Small et al. (1972) for testing done immediately following ECT and 60-90 days later. It is likely that there is an endpoint to this recovery and maintenance of cognitive function in at least some patients due to onset of another depressive episode with associated cognitive impairment. Except for the studies of Small and colleagues (1972, 1973), there are no investigations which separate out the changes due to relief of depression from effects specific to ECT. Small et al.'s (1972, 1973) studies are difficult to interpret, however, because of confounds between treatment and clinical variables, and unclear methodological procedures.

The period between ECT and test session is an important time course variable not studied. Of the studies reviewed, tests were administered either between 5 and 8 hours post-ECT (Horan et al., 1980; Kronofol et al., 1978), at 24 hours (Small et al., 1972; Small et al., 1973), "within 48 hours" (McAndrew et al., 1967), or at least a week after ECT (Weeks et al., 1980). Some studies of perceptual and cognitive functioning and neurological effects post-ECT report transient deficits that disappear after 30 minutes (Clyma, 1975; Kriss et al., 1978). It is possible, however, that the recovery curve differs for different functions, particularly higher-order cognitive abilities, and perhaps for the left vs. right cerebral hemispheres.

Electrode Placement

There is surprisingly little support for differential cognitive effects by site of electrode placement, except for a tendency for faster recovery (Small et al., 1972; Weeks et al., 1980) and perhaps improved performance (Cohen et al., 1973; Kronofol et al., 1978; Small et al., 1972) from unilateral nondominant ECT. Unfortunately, sample sizes are often too small to see even moderate effects, groups often differ on pretreatment variables, and direct comparisons between groups are rarely made.

In the only study (McAndrew et al., 1967) in which the effects of all three electrode placements were compared on right and left hemisphere tests, there were no significant interactions between pre-post task performance and electrode placement. Conclusions arguing against differential effects, however, need to be considered in light of the small sample size and insufficient power to see effects.

Pre-ECT Cognition

In those studies (McAndrew et al., 1967; Weeks et al., 1980) where abnormality of pre-ECT cognitive functioning can be assessed, scores are found to be low, consistent with reports of impaired cognition in untreated depressed patients (Goldstein, Filskov, Weaver, & Ives, 1977; Wexler, 1980). Additional difficulties in interpreting pre-post differences are due to pre-ECT cognitive differences between ECT groups (Kronofol et al., 1978; McAndrew et al., 1967) or between ECT groups and controls (Weeks et al., 1980). In order to attribute cognitive changes to ECT treatment, it is crucial to consider pre-ECT levels and to have appropriate control groups, which should consist of non-ECT treated depressed patients matched on demographic, illness, and cognitive variables.

Cognitive Tests

Most studies (Horan et al., 1980; Kronofol et al., 1978; McAndrew et al., 1967; Small et al., 1972) claim to use tests that measure right and left hemisphere function and/or general cerebral dysfunction. Unfortunately, the appropriate reliability and validity data are not always provided or even known. Thus, failure to find effects or unreliability of effects reported (including inability to replicate results) may be a function of the measuring instruments rather than ECT effects. For example, Kronofol et al.'s (1978) finding of post-ECT improvement on one right hemisphere test and no change on other putative right hemisphere tests may be due to test unreliability or to different aspects of hemisphere function measured by each test.

Furthermore, studies have rarely used tests which can identify the nature of the possible cognitive changes, or separate component processes of a task. It is possible, for example, that part of the cognitive impairment seen pre-ECT is due to inattention and/or psychomotor retardation associated with depression. If these deficits are eliminated when mood is elevated, then tasks requiring attention and/or speed would show greater improvement post-ECT. The influence of attention and speed would create further problems in interpreting pre-post ECT effects if right and left hemisphere tasks differentially required these abilities. Thus, complete analysis of the cognitive effects of ECT would include evaluation of attention and psychomotor speed, and statistical analysis of the influence of these variables on performance on other tasks.

One of the most problematic areas of neuropsychological assessment and an area rarely examined in ECT studies is frontal lobe function. The frontal lobes have been implicated in planning, organization, ability to categorize and shift mental set, concept formation, creativity and, in general, in higher order cognitive activities (Hecaen & Albert, 1978; Luria, 1973; Warren & Akert, 1964). It is crucial to assess the influence of ECT on these functions, since they are related to important everyday activities. Persistent patient complaints despite empirical failures to find ECT-induced impairment suggest that it is these higher order frontal lobe functions that may be adversely affected by ECT. Interestingly, one of the largest and most stable deficits resulting from ECT is verbal fluency (Kronofol et al., 1978), an ability shown to be subserved by the left frontal lobe (Benton, 1968; Milner, 1967).

Study Proposals

The inconclusive evidence of cognitive effects of ECT discussed above suggests that further studies be conducted that incorporate changes in study design to allow for more definitive results. Our analysis of the literature, and methodological and theoretical concerns, leads to the following suggested guidelines for designing such studies.

Subject Sample

To attribute pre-post ECT cognitive changes to the treatment, it is crucial to control for the effects of the depressive illness, preferably by matching the ECT group on demographic, illness, and cognitive variables to another group of depressive patients receiving alternative treatment or no treatment. Attempts should be made, where possible, to restrict the sample to endogenous depressives.

Testing Schedule

Since cognitive effects of ECT appear to vary with number of treatments (Kronofol et al., 1978) and time between treatment and assessment (Small et al., 1972; Weeks et al., 1980), it is desirable to test patients before ECT, after one ECT treatment, immediately after a course of six to eight treatments, and longitudinally (perhaps through a period of maintenance) for several months.

Test Battery

The suggested test battery takes approximately 3 hours to administer and is designed specifically to measure potential long-term adverse effects of ECT on higher cognitive function. The tests chosen satisfy the technical criteria specified earlier, and derive from extensive literature on ability testing in normal populations (e.g., Ekstrom, French, and Harman, 1976; Hakstian & Cattell, 1976; Wilson, DeFries, McClearn, & Vandenberg, 1975), and assessment of cognitive changes in clinical neurological populations (e.g., Benton, 1968; Hecaen & Albert, 1978; Jones-Gotman & Milner, 1977; Luria, 1973; Milner, 1963; Milner, 1967; Newcombe, 1969; Rosvold, Mirsky, Sarason, et al., 1956; Teuber & Weinstein, 1956; Warren & Akert, 1964; Warrington & James, 1967) and in drug-treated groups (Harshman, Crawford, & Hecht, 1976; Müller-Oërlinghausen, Bauer, Girke, Kanowski, Gonçalves, 1977). The battery also meets the theoretical concerns expressed earlier and has the capacity to provide closure on unresolved issues of ECT-induced cognitive effects. In particular, tests were selected to allow examination of the influence of attention and psychomotor speed on other cognitive functions, to see differential localization/lateralization effects, and to tap more extensively frontal lobe function.

The Table displays the individual tests recommended, and some relevant technical and theoretical information, including cognitive function measured, reliability and validity, and suggested neurological involvement or drug effect. Further details may be obtained in the references cited, or from the authors.

Conclusions

Although available data suggest that ECT does not result in long-term non-mnestic cognitive disruption, qualifications about possible adverse effects are necessary due to incomplete assessment and inadequate methodological and theoretical controls of past studies. Investigations designed according to guidelines suggested above should help delineate whatever effects may be present.

In particular, the following general set of questions may be answered: What is the nature and extent of the adverse non-mnestic cognitive effects of ECT, and are they prolonged, related to number of treatments, electrode placement, clinical course or the pathophysiology of depressive illness? Should adverse non-mnestic cognitive effects occur, what do these effects indicate about neurological correlates of cognitive functioning, and the mechanisms by which these functions may be affected by depressive illness and somatic therapy?

Table

Suggested Cognitive Battery

Test	Ability Measured	Reliability	Suggested Neurological or Drug Effects
Timed Sentence Writing	Motor speed		
Number Comparison Test	Perceptual speed	.70 - .82	↓ with lithium
Continuous Performance Test	Attention	.74 - .90	↓ with brain damage (various types)
Wisconsin Card Sorting Test	Abstract categorization and ability to change set		Frontal lobe
Analogies	New concept formation		
Logical Inference Test	Logical verbal reasoning	.57 - .78	Left hemisphere; ↓ with marijuana
Reading Comprehension Test	Reading comprehension		Left hemisphere; Some minimal ability in right hemisphere
Originality	Creativity	.74	Frontal lobe for fluency aspect
Word Beginnings and Endings Test	Word fluency	.68 - .71	Left hemisphere especially left frontal
Thing Categories Test	Ideational fluency	.59 - .74	Left hemisphere; Interaction of left and right hemispheres
Design Fluency	Figural fluency		Right frontal, right frontocentral
Gollin Figures	Speed of closure		Right hemisphere temporal or parietal; ↑ with marijuana
Embedded Figures Test	Disembedding		Left and right hemisphere, especially left Similar test — ↓ with left ECT, ↑ with right ECT
Copying a Geometric Figure	Constructional ability		Right parietal
Finger Tapping	Fine motor regulation		Contralateral premotor frontal

References

Abrams, R., Redfield, J., and Taylor, M.A. Cognitive dysfunction compared in schizophrenia and affective disorder. *Br. J. Psychiatry*, 139:190-194, 1981.

Benton, A.L. Differential behavioral effects in frontal lobe disease. *Neuropsychologia*, 6:53-60, 1968.

Clyma, E.A. Unilateral electroconvulsive therapy: How to determine which hemisphere is dominant. *Br. J. Psychiatry*, 126:372-379, 1975.

Cohen, B.D., Berent, S., and Silverman, A.J. Field-dependence and lateralization of function in the human brain. *Arch. Gen. Psychiatry*, 28:165-167, 1973.

Cohen, J., and Cohen, P. *Multiple Regression/Correlation for the Behavioral Sciences*. New York: Wiley & Sons, 1975.

Ekstrom, R.B., French, J.W., and Harman, H.H. Kit of Factor-Referenced Cognitive Tests. Princeton, NJ: Educational Testing Service, 1976.

Fink, M. Myths of "shock therapy." *Am. J. Psychiatry*, 134: 991-996, 1977.

Fink, M. *Convulsive Therapy: Theory and Practice*. New York: Raven Press, 1979, pp. 107-129.

Goldstein, S.G., Filskov, S.B., Weaver, L.A., and Ives, J.O. Neuropsychological effects of electroconvulsive therapy. *J. Clin. Psychol.*, 33:798-806, 1977.

Hakstian, A.R., and Cattell, R.B. *Comprehensive Ability Battery*. Champaign, IL: Institute for Personality and Ability Testing, 1976.

Harper, R.G., and Wiens, A.N. Electroconvulsive therapy and memory. *J. Nerv. Ment. Dis.*, 161:245-254, 1975.

Harshman, R.A., Crawford, H.J., and Hecht, E. Marijuana, cognitive style, and lateralized hemispheric functions. In: Cohen, S., and Stillman, R.C. (eds.), *The Therapeutic Potential of Marijuana*. New York: Plenum Press, 1976.

Hecaen, H., and Albert, M.L. *Human Neuropsychology*. New York: John Wiley & Sons, 1978, pp. 354-378.

Horan, M., Ashton, R., and Minto, J. Using ECT to study hemispheric specialization for sequential processes. *Br. J. Psychiatry*, 137:119-125, 1980.

Jones-Gotman, M., and Milner, B. Design fluency: The invention of nonsense drawings after focal cortical lesions. *Neuropsychologia*, 15:653-674, 1977.

Kriss, A., Blumhardt, L.D., Halliday, A.M., and Pratt, R.T.C. Neurological asymmetries immediately after ECT. *J. Neurol. Neurosurg. Psychiatry*, 41:1135-1144, 1978.

Kronofol, Z., Hamsher, K. DeS., Digre, K, and Waziri, R. Depression and hemisphere functions: Changes associated with unilateral ECT. *Br. J. Psychiatry*, 132:560-567, 1978.

Luria, A.R. *The Working Brain: An Introduction to Neuropsychology*. New York: Basic Books, 1973, pp. 187-225.

McAndrew, J., Berkley, B., and Matthews, C. The effects of dominant and nondominant unilateral ECT as compared to bilateral ECT. *Am. J. Psychiatry*, 124:483-490, 1967.

Milner, B. Effects of different brain lesions on card sorting. *Arch. Neurol.*, 9:90-100, 1963.

Milner, B. Brain mechanisms suggested by studies of temporal lobes. In: Millikan, C.H., and Darley, F.L. (eds.), *Brain Mechanisms Underlying Speech and Language*. New York: Grune & Stratton, 1967.

Müller-Oërlinghausen, B., Bauer, H., Girke, W., Kanowski, S., and Gonçalves, N. Impairment of vigilance and performance under lithium treatment. *Pharmakopsychiatr-Neuropsychopharmakol.* 10:67-78, 1977.

Newcombe, F. *Missile Wounds of the Brain*. London: Oxford University Press, 1969.

Rosvold, H.E., Mirsky, A.F., Sarason, I., et al. A continuous performance test of brain damage. *J. Consult. Psychol.*, 20:343-350, 1956.

Small, I.F., Small, J.G., Milstein, V., and Moore, J.E. Neuropsychological observations with psychosis and somatic treatment. *J. Nerv. Ment. Dis.*, 155:6-13, 1972.

Small, I.F., Small, J.G., Milstein, V., and Sharpley, P. Interhemispheric relationships with somatic therapy. *Dis. Nerv. Syst.*, 34:170-177, 1973.

Squire, L.R. ECT and memory loss. *Am. J. Psychiatry*, 134: 997-1001, 1977.

Squire, L.R., and Chace, P.M. Memory functions six to nine months after electroconvulsive therapy. *Arch. Gen. Psychiatry*, 32:1557-1564, 1975.

Taylor, M.A. The importance of diagnostic criteria for depression in the study of ECT. *Psychopharmacol. Bull.*, 18(2): 44-48, 1982a.

Taylor, M.A. Indications for electroconvulsive treatment. In: Abrams, R., and Essman, W.B. (ed.), *Electroconvulsive Therapy: Theory and Practice*, New York: Spectrum Publications, 1982b.

Taylor, M.A., Redfield, J., and Abrams, R. Neuropsychological dysfunction compared in schizophrenia, affective disorder, and coarse brain disease. *Biol. Psychiatry*, 16:467-478, 1981.

Teuber, H.L., and Weinstein, S. Ability to discover hidden figures after cerebral lesions. *Arch. Neurol. Psychiatry*, 76:369-379, 1956.

Timm, N.H. *Multivariate Analysis with Applications in Education and Psychology*. Monterey, CA: Brooks/Cole, 1975.

Warren, J.M., and Akert, K. (eds.), *The Frontal Granular Cortex and Behavior*. New York:McGraw-Hill, 1964.

Warrington, E.K., and James, M. Disorders of visual perception in patients with localized cerebral lesions. *Neuropsychologia*, 5:253-266, 1967.

Weeks, D., Freeman, C.P.L., and Kendell, R.E. ECT. III. Enduring cognitive deficits? *Br. J. Psychiatry*, 137:26-37, 1980.

Wexler, B.E. Cerebral laterality and psychiatry: A review of the literature. *Am. J. Psychiatry*, 137:279-291, 1980.

Wilson, J.R., DeFries, J.C., McClearn, G.E., and Vandenberg, S.G. Cognitive abilities: Use of family data as a control to assess sex and age differences in two ethnic groups. *Int. J. Aging Hum. Dev.*, 6:261-276, 1975.

Convulsive Therapy: A Risk-Benefit Analysis

Max Fink, M.D.[1]

Since its development in 1934, convulsive therapy has been a center of controversy. It has been applied in many conditions, both in the mentally ill and in patients with physical disorders. The reports vary from anecdotal testimonials and acrimonious diatribes on the one hand, to cautious, well-controlled, independent assessments on the other. To the welter of data, two additional factors emerge to make an assessment difficult—the fluctuating history of enthusiasm and disparagement, and changes in the technique and instrumentation of the treatment. Much of the controversy is highlighted and extensively reviewed in recent publications (Kiloh, 1977; APA, 1978; Fink, 1979; Breggin, 1979; Palmer, 1981; Kendell, 1981).

While convulsive therapy has salutary effects in a variety of conditions, the effects in severe depression are the best documented and are the basis for its continued clinical use. In evaluating the treatment, one is inclined to use the data from the 50-year history of the therapy, despite an awareness that treatments administered in the first decades differed significantly from present practice. But present practice also varies, for as new developments are tested, they are accepted at a varying rate. The introduction of unilateral electrode placement about 1961 showed that complaints of amnesia could be sharply reduced, but doubts as to the efficacy of these modifications are the basis for the continuing controversy. The introduction of succinylcholine in 1953 soon became part of standard academic practice, but its use is still controversial among practitioners who administer the treatments in outpatient settings or patient's homes. The present assessment of efficacy and risks is based on the data of the past two decades, with an emphasis on the use of electroconvulsive therapy (ECT) in the treatment of melancholia, with due regard for the most widely accepted practice as to safety and a reduction of unpleasant sequellae.

This review assumes ideal conditions as to selection of cases, administration of treatments, monitoring of side effects, and the training of the therapists. The wide latitude in experience in ECT (and even in the alternate therapies) is surely a principal factor in the outcome of a therapeutic trial, particularly one as complex as convulsive therapy. From a practical point of view, this assessment may be idealized, and may be true only for those patients who are fortunate to be treated by therapists who maintain a sufficient interest in this therapy to maintain their skills for optimal performance.

Efficacy

Convulsive therapy rapidly and efficiently relieves the symptoms of melancholia, regardless of type or duration. It is as effective, and often more so, than pharmacotherapy, and is clearly superior to other therapies in these conditions. The reduction in mortality is a particularly compelling observation, making the risk of suicide an important indication for ECT (Kiloh, 1977; APA, 1978; Fink, 1978a, 1979; Avery & Lubrano, 1979; Kendell, 1981).

Many patients with endogenous depression fail to respond to tricyclic antidepressant drugs, even under the optimized conditions of blood level monitoring for adequacy of dosing. Yet, many of these respond rapidly to ECT. These patients are usually described as being depressed psychotic patients with delusions (Hordern, Holt, Burt, & Gordon, 1963; Glassman, Kantor, & Shostak, 1975; Avery & Winokur, 1977; Davidson, McLeod, Kurland, & White, 1977; Kantor & Glassman, 1977; Nelson & Bowers, 1978; Minter & Mandel, 1979 a,b; Kaskey, Nasr, & Meltzer, 1980; Charney & Nelson 1981). The diagnosis of psychotic depression provides a second compelling indication for the use of ECT.

Catatonia is a syndrome that is particularly responsive to ECT. While it is often classified as a subtype of schizophrenia, it is also a feature of severe infectious diseases and manic-depressive psychosis (Abrams & Taylor, 1976; Taylor & Abrams, 1977; Abrams, Taylor, & Stolurow, 1978). Catatonic patients may also exhibit dysregulation of cortisol metabolism in a fashion that is characteristic of some subtypes of depressive psychosis (Dysken et al., 1979; Greden & Carroll, 1979). With ECT, this dysregulation rapidly normalizes as the clinical condition improves, suggesting an intimate connection in pathophysiology betweeen the ECT responsive forms of depressive psychosis and catatonia (Fink, 1981).

---

[1] Department of Psychiatry and Behavioral Science, School of Medicine, State University of New York at Stony Brook, Long Island, NY 11794. Supported in part by USPHS Grant MH-35518 to the International Association for Psychiatric Research, Inc., St. James, NY 11780.

ECT was introduced as a treatment for schizophrenia, but the efficacy and ease of administration of the antipsychotic drugs, introduced in the 1950s, led to their preferential use. use. But doubts linger that perhaps ECT was discarded too soon. While recent reviews of the literature find little support for its use in such patients (Fink, 1978 a,b; Salzman, 1980), the published studies comparing ECT and antipsychotic drugs do not meet our present standards, so it is unclear whether there is a defined superiority for the antipsychotic drugs. And, as the reports of the incidence and severity of tardive dyskinesia with the use of psychotropic drugs increase, some clinicians are again asking whether there is a place for ECT in the treatment of schizophrenic patients.

Taylor and Fleminger (1980), in a double-blind trial of ECT in patients with paranoid schizophrenia, compared the results of seizures three times weekly (for 8 to 12 treatments) with those of sham seizures. After six treatments, patients in both the ECT and sham-ECT groups improved, with the change clearly greater in the ECT group. Four weeks later, the control group showed little further change, but the ECT group continued to improve. Only one patient in the ECT group still had a rating of illness, while 9 of 10 controls had scores in the pathological range, demonstrating an efficacy for ECT in paranoid schizophrenic patients who had not responded rapidly to medication. In another study, Ries et al. (1981) describe the successful treatment with ECT of nine schizoaffective patients who had not responded to pharmacologic treatment.

In the first years after the introduction of convulsive therapy, mania was reported to respond favorably, with the number of treatments necessary for recovery to be similar to those needed for depressive states. In succeeding years, the number of treatments needed for a favorable outcome increased until the numbers were equal to those used in the treatment of schizophrenia. The reasons for this change in experience are unclear, but may reflect, perhaps, the introduction of alternate treatments for responsive cases of mania, or a change in clinical typology. Since the introduction of lithium and antipsychotic drugs, the efficacy of ECT in mania has not been examined in a prospective study, although McCabe (1976) and McCabe and Norris (1977) make compelling observations of the efficacy of ECT in retrospective reviews. However, the combined use of lithium and ECT may increase the hazards of an organic mental syndrome (Hoenig & Chaulk, 1977; Remick, 1978; Mandel et al., 1980; Small et al., 1980).

In most other conditions in which ECT has been examined, its efficacy is low. This includes patients with drug addiction, alcoholism, psychopathy, and neuroses. Dotted through the ECT literature, however, there are anecdotal reports of patients with parkinsonism showing marked improvement not only in their symptoms of depression, but also in the motor symptoms (Lebensohn & Jenkins, 1975; Dysken et al., 1976; Asnis, 1977; Yudofsky, 1979; Ananth et al., 1980). Balldin et al. (1980) successfully used ECT in seven bedridden parkinson patients without symptoms of endogenous depression. The patients improved in their motor abilities, sufficient for some to return home. Another recent report finds ECT to lower blood sugar levels among diabetics of recent onset (Fakhri et al., 1980).

On efficacy criteria, ECT is clearly justified in the treatment of patients with endogenous depression, particularly those with delusions or suicidal intent, in those with catatonia, and in some cases of mania, and as a weak alternative in the management of the symptoms of acute schizophrenia.

Safety

The principal risks of convulsive therapy are fracture, organic mental syndrome, missed and tardive seizures, and death. These complications were significant features of the early treatments, particularly those that used pentylenetetrazol for induction. But modern treatment methods, which include anesthesia, oxygenation, and muscle relaxation, reduce the complication rate significantly. Anesthesia and monitoring of the seizures further reduce the incidence of missed and tardive seizures. Thus, for the present methods of induction, two complications remain —death and amnesia.

Under modern conditions of treatment, death may occur with an incidence of 4/100,000 treatments (Royal College of Psychiatrists, 1977; Fink, 1979). More deaths were reported in the early years, when treatment procedures were less well defined (Turek & Hanlon, 1977; Asnis, Fink & Saferstein, 1978; APA, 1978). A principal factor is the risk associated with anesthesia, although the death rate for ECT and its anesthesia is considerably less than that for anesthesia alone (Fink, 1979). A consequence of the relative safety of modern ECT is the paucity of pathologic material, leaving the issue of persistent brain damage unresolved (Fink, 1977, 1979).

The principal risk of modern ECT is amnesia. Every patient who experiences a grand mal convulsion exhibits amnesia for the event, as well as retrograde amnesia. The amnesia persists for varying lengths of time, depending on the age of the subject, location of the electrodes, intensity of the currents, and the number of prior seizures and their frequency (Harper & Wiens, 1975; Fink 1977, 1979; APA, 1978; Fraser & Glass, 1978, 1980; Summers, Robins, & Reich, 1979). But, performance on memory tasks recovers rapidly, so that within 2 weeks of the last treatment, patients perform as well or better than before the treatment (Dornbush & Williams, 1974; Squire, 1977). The principal objection to ECT is the persistence of this syndrome into the recovery period. In an analysis which the author undertook elsewhere, he suggested that the persistence of an organic mental syndrome was no greater than 1/200 cases and may be reduced further by good treatment practice (Fink, 1979).

Complaints of amnesia are usually referred to as the basis for beliefs that persistent brain damage ensues from a course of treatment. Those authors who profess this view with the most energy confuse the data of the early years of treatment, when anesthesia, oxygenation, and modern electrode placements and currents were not used, with our present practice (Friedberg, 1976; Breggin, 1979).

Depressive illness alone, without ECT, is associated with impairment in cognitive functions (Henry, Weingartner, & Murphy, 1973; Sternberg & Jarvik, 1976; Strömgren, 1977). Depressed patients have decrements in short term memory functions, which improve as they recover from their illness with antidepressant drug therapy or ECT.

Even this complaint of amnesia may be significantly reduced by the use of minimal currents and unilateral electrode placements. Amnesia is significantly reduced if the electrodes are placed over the nondominant hemisphere (d'Elia, 1970; d'Elia & Raotma, 1975; Squire & Slater, 1978; Fink, 1979; Strömgren et al., 1980; Kendell, 1981). Further, in the early studies of the selection of currents to induce a seizure, the amnesia was less in treatments which used brief stimulation methods (Liberson, 1953). Interest in the use of these modified currents was recently revived by Valentine, Keddie, and Dunne (1968) and Weaver and his coworkers (1976, 1978, 1979). Ongoing studies by Mandel and by Weiner using such currents suggest that there is indeed a reduction in cognitive defects with their use.

The efficacy of ECT is reflected in the presence of a seizure, and is not dependent on its mode of induction or other characteristics of the convulsion (Ottosson, 1960; d'Elia & Raotma, 1975; Fink, 1979). There has been much recent interest in whether the seizure is indeed necessary, and in four studies which have recently been reported from Great Britain, there is reasonable assurance that improvement is more rapid and more secure with seizures than with sham seizures (Palmer, 1981; Kendell, 1981).

Another complication, more prominent in the past than the present, is that of recurrent spontaneous seizures. The analogy to a kindling phenomenon has stimulated interest in this possibility, but a recent survey of 166 patients who had received more than 2,700 treatments revealed four patients who developed spontaneous fits after a course of ECT, and in only two was it likely to be a proximal cause (Blackwood et al., 1980). In kindling, there is a progressive decrease in the threshold for a seizure, while in ECT, the amount of current needed to induce a seizure generally increases (Green & Costain, 1981). In studies of the kindling phenomenon, anesthesia, particularly the use of barbiturates, is prophylactic for the recurrence of spontaneous seizures. The routine use of anesthesia remains a principal barrier to this complication.

The efficacy of ECT can be sustained without a reduction in therapeutic efficacy and with minimal effects on cognition by proper attention to anesthesia, oxygenation, electrode placement, selection of currents and current dosage, and monitoring. If these observations are put to routine use, then the safety of ECT, particularly with regard to the development of amnesia, will be evaluated more optimistically than at present.

Alternate Treatments

The risks of tricyclic antidepressants are not well defined, although they may be severe. Cardiovascular complications, particularly hypotension and disabling arrhythmias, are recognized with increasing frequency. Death by suicide using tricyclic compounds is frequently reported, although surveys of their incidence are not available. The onset of the therapeutic response is usually delayed, with the standard reference works suggesting that a minimum of 7 to 14 days are required for antidepressant efficacy. In older patients, the anticholinergic effects of tricyclic compounds may be associated with dry mouth and difficulty in urination and in reading (Klein & Davis, 1969; Hartshorn, 1974; Stimmel, 1979).

Avery and Winokur (1976, 1977, 1978) make a strong case for the safety of ECT compared to alternate therapies for depressive psychoses. They find lower suicide death rates in ECT-treated patients. This is also true for the efficacy of ECT in depressed patients with psychotic delusions (Hordern, Holt, Burt, & Gordon, 1963; Glassman, Kantor, & Shostak, 1975; Avery & Winokur, 1977; Davidson, McLeod, Kurland, & White, 1977; Kantor & Glassman, 1977; Nelson & Bowers, 1978; Minter & Mandel, 1979 a,b; Kaskey, Nasr, & Meltzer, 1980; Charney & Nelson, 1981).

The use of monoamine oxidase inhibitors is also restricted by hypertensive crises, cardiovascular and hepatic toxicity, and the interactions of these compounds with foodstuffs, tricyclic antidepressants, and some drugs used in common medical practice (Hartshorn, 1974). Their efficacy is low in depression, although recent studies of their use in neurotic anxiety states are more optimistic.

Comparisons with treatments for other mental illnesses are more difficult. In mania, the efficacy of lithium and the phenothiazines is well defined, but the risks of mortality, blood dyscrasia, organic psychosis, tardive dyskinesia, and other neurologic sequellae must be considered (Klein & Davis, 1969; Gershon & Shopsin, 1975). Lithium therapy has been associated with adverse effects on memory function (Schou, 1968; Kusomo & Vaughan, 1977). In a historical comparison of ECT and lithium, McCabe (1976) found the complications of lithium to be as severe as those for ECT.

In schizophrenia, the complications of ECT depend on the number and frequency of the treatments. Higher dosages are more effective, but the larger number of treatments increases the probability of persistent amnesia and spontaneous seizures. The hazards of antipsychotic drugs are also well defined, particularly tardive dyskinesia, hepatic dysfunction, lenticular opacities, and blood dyscrasia. Despite these hazards, pharmacotherapy seems to have significant advantages over ECT in chronic cases, particularly since maintenance therapy is more easily provided by the drug therapies.

ECT is, at the least, as effective as tricyclic antidepressants, and significantly superior to amine oxidase inhibitors and the various psychotherapies, in the treatment of the severe mentally ill. The latter therapies are particularly hazardous, since death by suicide is an everpresent feature of severe depressive illness.

Consequences of Non-Use of Treatments

Before a nihilistic attitude toward the use of convulsive therapy in the severely mentally ill is adopted, it is useful to consider the natural course of these illnesses before ECT and the drug therapies were introduced. During the 20th century, the number of mental hospital beds escalated until 1955-1960; since then, the number of beds for the hospitalized mentally ill has been sharply reduced. Records of these earlier periods describe many patients with depressive psychoses, mania, and schizophrenia who remained ill for decades. ECT was an important factor in the reduction of hospitalization periods to less than 6 months, and the increase in discharge rates to

80% (Huston & Locher, 1948 a,b), and in the reduction in mortality (Slater, 1951). It is difficult to cite suicide rates, but the recent reports by Avery and Winokur (1976, 1977, 1978), McCabe (1976), and McCabe and Norris (1977), reviewing the data from earlier periods, find greater efficacy, better discharge rates, fewer deaths and suicides, and shorter hospitalizations for patients treated with ECT and/or adequate doses of drugs than alternate treatments, usually milieu and the psychotherapies.

Some recent recollections by therapists who lived through that era of transition reflect on the remarkable effects of their introduction (Post, 1978; Rollin, 1981). A recent report by the scientists at the National Institute of Mental Health Clinical Center cites the successful treatment by ECT of nine cases in 6 years (Paul et al., 1981). There is some discrepancy in attitude when a major educational and research center finds so few cases for this treatment, a treatment which was more successful than a wide range of prior therapies. Similar anti-ECT bias must exist at other centers, particularly those public mental facilities which seem to treat less than 1% of their admissions, while university affiliated centers seem to find up to 5% of admissions to warrant ECT (Asnis, Fink, & Saferstein, 1979). The discrepancy in usage surely reflects political, economic, ideological, and experiential factors, but it does patients little service to be admitted to an institution which has restricted the range of treatments for nonmedical reasons, and to be denied the benefits of an otherwise useful treatment.

Conclusion

The benefits of the use of ECT clearly outweigh the risks and provide a clear indication, above all alternate treatments, for patients with psychotic depression. In these patients, and in those with suicidal risk, ECT is the treatment of choice. This is particularly true for patients with delusions or catatonic features.

A case may be made for the use of ECT in patients with mania and acute schizophrenia, but the indications are less clear, and the usefulness of alternate therapies is sufficiently well defined to warrant their initial use. When the treatment response is delayed, or where compliance for medication treatments is compromised, ECT is an effective and safe alternative.

In schizophrenia, the use of ECT is limited to those patients in whom pharmacotherapy has been unsuccessful. The use of ECT in all other conditions is poorly documented, and its use should be undertaken in research settings, under research protocols.

When the decision to use ECT is made, each patient deserves the full use of modern methods, including anesthesia, oxygenation, muscle relaxation, and the modifications of the induction procedure which minimize persistent effects on brain function. These include the use of unilateral nondominant electrode placements, and/or minimal current instruments. Pretreatment sedation should be minimized, to assure an adequate seizure. Seizures should be monitored, and those which are shorter in duration than some standard (we use 25 seconds) should be immediately repeated. Finally, treatments should be given in settings where the equipment and trained personnel for the emergency management of complications are readily available. In the further management of depressed patients, maintenance drug therapy with tricyclic antidepressants (or their equivalents) should be considered for at least 8 weeks, and probably for 6 months.

Finally, it is time that ECT is clearly recognized as a major treatment in psychiatry, similar to a surgical procedure, and it should be used only by therapists with demonstrated skills who maintain its active practice. Its occasional use, and its unsupervised use by trainees and physicians without special psychiatric skills, is not to be condoned. Only when therapists understand that ECT is a complex procedure, requiring special skills, and when they respect the dignity of their patients not to apply ECT except under optimal conditions, will ECT assume its proper role as a principal treatment of selected cases of the severely mentally ill.

References

Abrams, R., and Taylor, M. Catatonia. *Arch. Gen. Psychiatry*, 33:579-584, 1976.

Abrams, R., and Taylor, M. Catatonia: Prediction of response to somatic treatments. *Am. J. Psychiatry*, 134:78-80, 1977.

Abrams, R., Taylor, M., and Stolurow, K.A.C. Catatonia and mania: Patterns of cerebral dysfunction. *Biol. Psychiatry,* 13:111-117, 1978.

American Psychiatric Association. *Electroconvulsive Therapy.* Task Force Report #14. Washington, D.C., 1978, 200 pp.

Ananth, J., Samra, D., and Kolivakis, T. Amelioration of drug-induced parkinsonism by ECT. *Am. J. Psychiatry,* 136:1094, 1980.

Asnis, G. Parkinson's disease, depression, and ECT: A review and case study. *Am. J. Psychiatry,* 134:191-195, 1977.

Asnis, G., Fink, M., and Saferstein, S. ECT in metropolitan New York hospitals: A survey of practice, 1975-1976. *Am. J. Psychiatry,* 135:479-482, 1978.

Avery, D., and Lubrano, A. Depression treated with imipramine and ECT: The deCarolis study reconsidered. *Am. J. Psychiatry,* 136:559-562, 1979.

Avery, D., and Winokur, G. Mortality in depressed patients treated with electroconvulsive therapy and antidepressants. *Arch. Gen. Psychiatry,* 33:1029-1037, 1976.

Avery, D., and Winokur, G. The efficacy of electroconvulsive therapy and antidepressants in depression. *Biol. Psychiatry,* 12:507-523, 1977.

Avery, D., and Winokur, G. Suicide, attempted suicide, and relapse rate in depression. *Arch. Gen. Psychiatry,* 35:749-753, 1978.

Balldin, J., Eden, J., Granerus, A.-K., et al. Electroconvulsive therapy in Parkinson's syndrome with "On-Off" phenomenon. *J. Neural Transm.,* 47:11-21, 1980.

Blackwood, D.H.R., Cull, R., Freeman, C.P.L., et al. A study of the incidence of epilepsy following ECT. *J. Neurol. Neurosurg. Psychiatry,* 43:1098-1102, 1980.

Breggin, P.R. *Electroshock: Its Brain-Disabling Effects.* New York: Springer Publishing Co., 1979, 244 pp.

Charney, D.S., and Nelson, J.C. Delusional and nondelusional unipolar depression: Further evidence for distinct subtypes. *Am. J. Psychiatry,* 138:328-333, 1981.

Davidson, J.R.T., McLeod, M., Kurland, A.A., and White, H.L. Antidepressant drug therapy in psychotic depression. *Br. J. Psychiatry,* 131:493-496, 1977.

d'Elia, G. Unilateral electroconvulsive therapy. *Acta Psychiatr. Scand., (Suppl.),* 215:5-98, 1970.

d'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? *Br. J. Psychiatry,* 126:83-89, 1975.

Dornbush, R., and Williams, M. Memory and ECT. In: Fink, M., Kety, S., McGaugh, J., and Williams, T. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston & Sons, 1974, pp. 199-205.

Dysken, M., Evans, H.M., Chan, C.H., and Davis, J.M. Improvement of depression and parkinsonism during ECT: A case study. *Neuropsychobiology,* 2:81-86, 1976.

Dysken, M., Pandey, G.N., Chang, S.S., et al. Serial postdexamethasone cortisol levels in a patient undergoing ECT. *Am J. Psychiatry,* 136:1328-1329, 1979.

Fakhri, O., Fadhli, A.A., and El Rawi, R.M. Effect of electroconvulsive therapy on diabetes mellitus. *Lancet,* 1:775-777, 1980.

Fink, M. CNS sequellae of EST. Risks of therapy and their prophylaxis. In: Shagass, C., and Friedhoff, A. (eds.), *Psychopathology and Brain Dysfunction.* New York: Raven Press, 1977, pp. 223-229.

Fink, M. Efficacy and safety of induced seizures (EST) in man. *Compr. Psychiatry,* 19:1-18, 1978a.

Fink, M. Is ECT a useful therapy of schizophrenia? In: Brady, J.P., and Brodie, H.K.H. (eds.), *Controversy in Psychiatry.* Philadelphia, Pa.: W.B. Saunders Co., 1978b, pp. 183-193.

Fink, M. *Convulsive Therapy: Theory and Practice.* New York: Raven Press, 1979, 308 pp.

Fink, M. Convulsive and drug therapies of depression. *Ann. Rev. Med.,* 32:405-412, 1981.

Fraser, R.M., and Glass, I.B. Recovery from ECT in elderly patients. *Br. J. Psychiatry,* 133:524-528, 1978.

Fraser, R.M., and Glass, I.B. Unilateral and bilateral ECT in elderly patients: A comparative study. *Acta Psychiatr. Scand.,* 62:13-31, 1980.

Friedberg, J. *Shock Treatment Is Not Good for Your Brain.* San Francisco, Ca.: Glide Publications, 1976, 176 pp.

Gershon, S., and Shopsin, B. (eds.). *Lithium—Its Role in Psychiatric Research and Treatment.* New York: Plenum Press, 1973, 358 pp.

Glassman, A.H., Kantor, S.J., and Shostak, M. Depression, delusions, and drug response. *Am. J. Psychiatry,* 132:716-719, 1975.

Greden, J.F., and Carroll, B.J. The dexamethasone suppression test as a diagnostic aid in catatonia. *Am. J. Psychiatry,* 136:1199-1200, 1979.

Green, A.R., and Costain, D.W. *Pharmacology and Biochemistry of Psychiatric Disorders.* Chichester, England: John Wiley & Sons, 1981, 217 pp.

Harper, R.G., and Wiens, A.N. Electroconvulsive therapy and memory. *J. Nerv. Ment. Dis.,* 161:245-254, 1975.

Hartshorn, E.A. Interactions of CNS drugs—antidepressants. *Drug. Intel. Clin. Pharmacy,* 8:591-606, 1974.

Henry, G.M., Weingartner, H., and Murphy, D.L. The influence of affective states and psychoactive drugs on verbal learning and memory. *Am. J. Psychiatry,* 130:966-971, 1973.

Hoenig, J., and Chaulk, R. Delirium associated with lithium therapy and electroconvulsive therapy. *Can. Med. Assoc. J.* 116:837-838, 1977.

Hordern, A., Holt, H.F., Burt, C.G., and Gordon, W.F. Amitriptyline in depressive cases. *Br. J. Psychiatry,* 109: 815-825, 1963.

Huston, P.E., and Locher, L.M. Involutional psychosis. Course when untreated and when treated with electric shock. *Arch. Neurol. Psychiatry,* 59:385-394, 1948a.

Huston, P.E., and Locher, L.M. Manic-depressive psychosis. Course when treated and untreated with electric shock. *Arch. Neurol. Psychiatry,* 60:37-48, 1948b.

Kantor, S.J., and Glassman, A.H. Delusional depressions: Natural history and response to treatment. *Br. J. Psychiatry,* 131:351-360, 1977.

Kaskey, G.B., Nasr, S., and Meltzer, H.Y. Drug treatment in delusional depression. *Psychiatr. Res.,* 1:267-277, 1980.

Kendell, R.E. The present status of electroconvulsive therapy. *Br. J. Psychiatry,* 139:265-283, 1981.

Kiloh, L.G. The use of electroconvulsive treatment in depressive illness. In: Burrows, C.D. (ed.), *Handbook of Studies on Depression.* Amsterdam: Excerpta Media, 1977, pp. 229-252.

Klein, D.F., and Davis, J.M. *Diagnosis and Drug Treatment of Psychiatric Disorders*. Baltimore, Md.: Williams and Wilkins Co., 1969, 480 pp.

Kusumo, K.S., and Vaughan, M. Effects of lithium salts on memory. *Br. J. Psychiatry,* 131:453-457, 1977.

Lebensohn, Z.M., and Jenkins, R.B. Improvement of parkinsonism in depressed patients treated with ECT. *Am. J. Psychiatry,* 132:283-285, 1975.

Liberson, W.T. Current evaluation of electric convulsive therapy—correlations of the parameters of electric currents with physiologic and psychologic changes. *Res. Publ. Assoc. Nerv. Ment. Dis.,* 31:199-231, 1953.

Mandel, M.R., Madsen, J., Miller, A.L., and Baldessarini, R.J. Intoxication associated with lithium and ECT. *Am. J. Psychiatry,* 137:1107-1109, 1980.

McCabe, M.S. ECT in the treatment of mania: A controlled study. *Am J. Psychiatry,* 133:688-691, 1976.

McCabe, M.S., and Norris, B. ECT versus chlorpromazine in mania. *Biol. Psychiatry,* 12:245-254, 1977.

Minter, R.E., and Mandel, M.R. The treatment of psychotic major depressive disorder with drugs and electroconvulsive therapy. *J. Nerv. Ment. Dis.,* 167:726-733, 1979a.

Minter, R.E., and Mandel, M.R. A prospective study of the treatment of psychotic depression. *Am. J. Psychiatry,* 136:1470-1472, 1979b.

Nelson, J.C., and Bowers, M.B. Delusional unipolar depression—description and drug response. *Arch. Gen. Psychiatry,* 35: 1321-1328, 1978.

Ottosson, J.-O. Experimental studies of the mode of action of electroconvulsive therapy. *Acta Psychiatr. Neurol. Scand. (Suppl. 145),* 35:1-141, 1960.

Palmer, R.L. (ed.), *Electroconvulsive Therapy: An Appraisal*. New York: Oxford Press, 1981, 316 pp.

Paul, S.M., Extein, I., Calil, H.M., et al. Use of ECT with treatment-resistant depressed patients at the National Institute of Mental Health. *Am. J. Psychiatry,* 138:486-489, 1981.

Post, F. Then and now. *Br. J. Psychiatry,* 133:83-86, 1978.

Remick, R.A. Acute brain syndrome associated with ECT and lithium. *Can. J. Psychiatry,* 23:129-130, 1978.

Ries, R.K., Wilson, L., Bokan, J.A., and Chiles, J.A. ECT in medication resistant schizoaffective disorder. *Compr. Psychiatry,* 22:167-173, 1981.

Rollin, H.R. The impact of ECT. In: Palmer, R. (ed.), *Electroconvulsive Therapy: An Appraisal*. New York: Oxford Press, 1981, pp. 11-18.

Royal College of Psychiatrists. Memorandum on the use of electroconvulsive therapy. *Br. J. Psychiatry,* 131:261-272, 1977.

Salzman, C. The use of ECT in the treatment of schizophrenia. *Am. J. Psychiatry,* 137:1032-1041, 1980.

Schou, M. Lithium in psychiatric therapy and prophylaxis. *J. Psychiatr. Res.,* 6:67-95, 1968.

Slater, E.T. Evaluation of electric convulsion therapy as compared with conservative methods of treatment in depressive states. *J. Ment. Sci.,* 97:567-569, 1951.

Small, J.G., Kellams, J.J., Milstein, V., and Small, I.F. Complications with electroconvulsive treatment combined with lithium. *Biol. Psychiatry,* 15:103-112, 1980.

Squire, L.R. ECT and memory loss. *Am. J. Psychiatry,* 134:997-1001, 1977.

Squire, L.R., and Slater, P.C. Bilateral and unilateral ECT: Effects on verbal and nonverbal memory. *Am. J. Psychiatry,* 135:1316-1320, 1978.

Sternberg, D.E., and Jarvik, M.E. Memory functions in depression. *Arch. Gen. Psychiatry,* 33:219-224, 1976.

Stimmel, B. *Cardiovascular Effects of Mood-Altering Drugs*. New York: Raven Press, 1979, 290 pp.

Strömgren, L.S. The influence of depression on memory. *Acta Psychiatr. Scand.,* 56:109-128, 1977.

Strömgren, L.S., Dahl, J., Fjelborg, N., and Thomsen, A. Factors influencing seizure duration and number of seizures applied in unilateral electroconvulsive therapy. *Acta Psychiatr. Scand.,* 62:158-165, 1980.

Summers, W.K., Robins, E., and Reich, T. The natural history of acute organic mental syndrome after bilateral electroconvulsive therapy. *Biol. Psychiatry,* 14:905-912, 1979.

Taylor, P., and Fleminger, J.J. ECT for schizophrenia. *Lancet,* 1:1380-1383, 1980.

Turek, I.S., and Hanlon, T.E. The effectiveness and safety of electroconvulsive therapy (ECT). *J. Nerv. Ment. Dis.,* 164:419-431, 1977.

Valentine, M., Keddie, K.M.G., and Dunne, D. A comparison of techniques in electroconvulsive therapy. *Br. J. Psychiatry,* 114:989-996, 1968.

Weaver, L.A., Ives, J.O., Williams, R., and Nies, A. A comparison of standard alternating current and low-energy brief pulse electrotherapy. *Biol. Psychiatry,* 12:525-544, 1977.

Weaver, L.A., Ives, J.O., and Williams, R. The threshold number of pulses in bilateral and unilateral ECT. *Biol. Psychiatry,* 13:227-241, 1978.

Weaver, L.A., Williams, R., and Rush, S. Current density in bilateral and unilateral ECT. *Biol. Psychiatry,* 11:303-312, 1976.

Yudofsky, S.C. Parkinson's disease, depression, and electroconvulsive therapy: A clinical and neurobiologic synthesis. *Compr. Psychiatry,* 20:579-581, 1979.

Psychopharmacology—A Recurring Bibliography

The bibliography below is offered to our readers to alert them to recent papers on psychopharmacology from the world literature. It was computer-generated by the Medical Literature Analysis and Retrieval System (MEDLARS) of the National Library of Medicine, National Institutes of Health, and represents papers which were entered into the system during the 3 months before the *Bulletin* went to press.

The subject headings from Index Medicus were selected to reflect significant current interest of the international scientific community. Some nonrelevant citations may appear, and some relevant ones may be absent, but this is usual for machine-generated searches.

Each subsequent issue of the *Bulletin* will provide such a bibliography, which contains two parts—a Subject Section and an Author Section.

Comments and suggestions are invited.

ISSN 0048-5764

SUBJECT SECTION

ACEPROMAZINE

Acepromazine and droperidol inhibition of halothane-induced malignant hyperthermia (porcine stress syndrome) in swine. McGrath CJ, et al. **Am J Vet Res** 1981 Feb;42(2):195–8

Atypical conditions for quantitative recovery of acepromazine and chlorpromazine from plasma. Ballard S, et al. **J Toxicol Environ Health** 1981 May;7(5):745–51

ACETYLCHOLINE

A simplified enzymatic assay for the determination of acetylcholine and choline in discrete structures of rat brain. Bluth R, et al. **Acta Biol Med Ger** 1980;39(8–9):881–7

Acetylcarnitine as a contamination in the radiochemical assay of acetylcholine synthesis in salivary glands and urinary bladders. Banns H, et al. **Acta Physiol Scand** 1981 Feb;111(2):165–9

GABA and its interaction with ACh in the rabbit retina. Redburn DA, et al. **Adv Biochem Psychopharmacol** 1981;29:169–74

Differences in the effects of acetylcholine on the vas deferens from normal and castrated rats. A participation of adrenergic mechanisms. Agostini M del C, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):212–20

Sodium ion and the effect of acetylcholine on phospholipid and phosphoprotein phosphate turnover in the rabbit iris smooth muscle. Abdel-Latif AA. **Biochem Pharmacol** 1981 Jun 1;30(11):1371–4

Interaction of imipramine with the ionic channel of the acetylcholine receptor of motor endplate and electric organ. Eldefrawi ME, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1391–4

Mechanism of inactivation (desensitization) of acetylcholine receptor. Investigations by fast reaction techniques with membrane vesicles. Aoshima H, et al. **Biochemistry** 1981 Jun 9;20(12):3467–74

Effect of short electromagnetic pulses on brain acetylcholine content and spontaneous motor activity of mice. Modak AT, et al. **Bioelectromagnetics** 1981;2(1):89–92

Effects of mianserin, desipramine and maprotiline on blood pressure responses evoked by acetylcholine, histamine and 5-hydroxytryptamine in rats. Cavero I, et al. **Br J Pharmacol** 1981 Sep;74(1):143–8

Muscarinic acetylcholine receptors regulation and protein phosphorylation in primary cultures of rat cerebellum. Burgoyne RD, et al. **Brain Res** 1981 Aug;254(1):55–63

The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Coote JH, et al. **Brain Res** 1981 Jun 29;215(1–2):135–45

8-Br-cyclic GMP mimics activation of muscarinic autoreceptor and inhibits acetylcholine release from rat hippocampal slices. Nordström O, et al. **Brain Res** 1981 Jun 1;213(2):467–71

Acetylcholine (Ach) induced alterations of plasma growth hormone (GH) in normal and pimozide-treated ovariectomized rats. Vijayan E, et al. **Brain Res Bull** 1981 Jul;7(1):11–5

Prejunctional inhibition of norepinephrine release caused by acetylcholine in the human saphenous vein. Rorie DK, et al. **Circ Res** 1981 Aug;49(2):337–41

Calcium dependence of prejunctional inhibitory effects of adenosine and acetylcholine on adrenergic neurotransmission in canine saphenous veins. Vanhoutte PM, et al. **Eur J Pharmacol** 1981 Jun 19;72(2–3):189–98

The loss of muscarinic acetylcholine receptors in synaptic membranes under phosphorylating conditions is dependent on calmodulin. Burgoyne RD. **FEBS Lett** 1981 May 5;127(1):144–8

Acetylcholine receptor kinetics at slow fiber neuromuscular junctions. Dionne VE. **Fed Proc** 1981 Sep;40(11):2614–7

Effects of chemical transmitters on function of isolated canine parietal cells. Soll AH, et al. **Fed Proc** 1981 Aug;40(10):2519–23

Effects of exposure to trichloroethylene and tetrachloroethylene on the contents of acetylcholine, dopamine, norepinephrine and serotonin in rat brain. Honma T, et al. **Ind Health** 1980;18(4):171–8

The role of citrate derived from glucose in the acetylcholine synthesis in rat brain synaptosomes. Szutowicz A, et al. **Int J Biochem** 1981;13(8):887–92

Adrenergic neurotransmission in airways: inhibition by acetylcholine. Russell JA, et al. **J Appl Physiol** 1981 Aug;51(2):376–83

A proposed model for the synthesis, storage and release of acetylcholine at the neuromuscular junction. Hancox AJ, et al. **J Biomed Eng** 1981 Jul;3(3):183–95

Effect of acetylcholine on vascular capacity in the dog. Supple EW, et al. **J Clin Invest** 1981 Jul;68(1):64–74

Endplate channel block by guanidine derivatives. Farley JM, et al. **J Gen Physiol** 1981 Mar;77(3):273–93

Electrical Activity in canine sinus node cells during arrest produced by acetylcholine. Woods WT, et al. **J Mol Cell Cardiol** 1981 Apr;13(4):249–57

Acetylcholine incorporation by cholinergic synaptic vesicles from Torpedo marmorata. Diebler MF, et al. **J Neurochem** 1981 Aug;37(2):467–75

Utilization of citrate, acetylcarnitine, acetate, pyruvate and glucose for the synthesis of acetylcholine in rat brain slices. Doležal V, et al. **J Neurochem** 1981 Apr;36(4):1323–30

Decreases in amino acids and acetylcholine metabolism during hypoxia.

Gibson GE, et al. **J Neurochem** 1981 Jul;37(1):192-201

Acetylcholine synthesis and CO2 production from variously labeled glucose in rat brain slices and synaptosomes. Ksiezak HJ, et al. **J Neurochem** 1981 Jul;37(1):88-94

Oxygen dependence of glucose and acetylcholine metabolism in slices and synaptosomes from rat brain. Ksiezak HJ, et al. **J Neurochem** 1981 Aug;37(2):305-14

Quantitation of cholinergic synaptosomes from guinea pig brain. Richardson PJ. **J Neurochem** 1981 Jul;37(1):258-60

Inhibition of the synthesis of acetylcholine in rat brain slices by (-)-hydroxycitrate and citrate. Tuček S, et al. **J Neurochem** 1981 Apr; 36(4):1331-7

The immunocytochemical localization of tyrosine hydroxylase within rat sympathetic neurons that release acetylcholine in culture. Higgins D, et al. **J Neurosci** 1981 Feb,1(2):126-31

Snake alpha-toxin effects on cholinergic and noncholinergic responses of Aplysia californica neurons. Ono JK, et al. **J Neurosci** 1981 Mar; 1(3):259-70

On the role of Ca2+ in the transmitter choice made by cultured sympathetic neurons. Walicke PA, et al. **J Neurosci** 1981 Apr; 1(4):343-50

Use of the single electrode voltage clamp to perform noise and relaxation studies of acetylcholine-activated channels in Aplysia neurons. Wachtel RE, et al. **J Neurosci Methods** 1981 Jun;4(1):87-103

Effects of acetylcholine mustard analogs on schistosome and vertebrate neuromuscular preparations. Willcockson WS, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):330-6

The characteristics of synaptic currents and responses to acetylcholine of rat submandibular ganglion cells. Rang HP. **J Physiol (Lond)** 1981 Feb;311:23-55

Studies on secretion of catecholamines evoked by acetylcholine or transmural stimulation of the rat adrenal gland. Wakade AR. **J Physiol (Lond)** 1981;313:463-80

Redistribution of intramembrane particles related to acetylcholine release by cholinergic synaptosomes. Israël M, et al. **J Ultrastruct Res** 1981 May;75(2):162-78

Desensitization of the muscarinic acetylcholine receptor of atrium in bullfrogs. Tokimasa T, et al. **Jpn J Physiol** 1981;31(1):83-97

Determination of delta psi, delta pH and the proton electrochemical gradient in isolated cholinergic synaptic vesicles. Angel I, et al. **Life Sci** 1981 Jul 27;29(4):411-6

Increase in rat striatal acetylcholine content by bromocriptine: evidence for an indirect dopaminergic action. Consolo S, et al. **Life Sci** 1981 Aug 3;29(5):457-65

Biphasic dose-response relationship for acetylcholine in the chick jugular vein. Watanabe M, et al. **Life Sci** 1981 Aug 10;29(6):619-26

Brain cholinergic dysfunction and memory in aged rats. Lippa AS, et al. **Neurobiol Aging** 1980 Summer;1(1):13-9

Cholinergic actions of false neurotransmitters: acetylpyrrolidinecholine. Buccafusco JJ, et al. **Neurosci Lett** 1981 May 29;23(3):319-24

Subcellular fractionation of cat submandibular gland: comparative studies on the distribution of acetylcholine and vasoactive intestinal polypeptide (VIP). Lundberg JM, et al. **Neuroscience** 1981;6(6):1001-10

Effects of Cs on acetylcholine induced current. Is ik1 increased by acetylcholine in frog atrium? Ojeda C, et al. **Pflugers Arch** 1981 Jul; 391(1):57-9

The influence of taurine on acetylcholine content and synthesis in rat brain. Kleinrok AT, et al. **Pol J Pharmacol Pharm** 1980 May-Jun; 32(3):313-7

Acetylcholine-induced cation translocation across cell membranes and inactivation of the acetylcholine receptor: chemical kinetic measurements in the millisecond time region. Cash DJ, et al. **Proc Natl Acad Sci USA** 1981 Jun;78(6):3318-22

Does the motor nerve impulse evoke 'non-quantal' transmitter release? Katz B, et al. **Proc R Soc Lond [Biol]** 1981 May 7;212(1186):131-7

Acetylcholine turnover and aggression in related three strains of mice. Karczmar AG, et al. **Prog Neuropsychopharmacol** 1981;5(1):35-48

Cholinergic influences on escape deficits produced by uncontrollable stress. Anisman H, et al. **Psychopharmacology (Berlin)** 1981; 74(1):81-7

Acetylcholine synthesis in synaptosomes: mode of transfer of mitochondrial acetyl coenzyme A. Benjamin AM, et al. **Science** 1981 Sep 25;213(4515):1495-7

Brain acetylcholine synthesis declines with senescence. Gibson GE, et al. **Science** 1981 Aug 7;213(4508):674-6

Effect of acetylcholine and catecholamines on the enterochromaffin-like cells of the stomach. Sano M, et al. **Surg Gynecol Obstet** 1981 Sep; 153(3):337-40

[Concerning the quantum theory of acetylcholine release] Han JS. **Sheng Li Ko Hsueh Chin Chan** 1980 Mar;11(3):255-8 (Chi)

[Laminar distribution of excitatory responses to acetylcholine in rat somatic sensory cortex: a microionophoretic study] Lamour Y, et al. **C R Seances Acad Sci [III]** 1981 Jun 1;292(20):1121-4 (Eng. Abstr.) (Fre)

[Behavior of cellular cyclic nucleotides after hydrokinetic or ecbolic stimulation of the canine pancreas] Teufel H, et al. **Hoppe Seylers Z Physiol Chem** 1981 May;362(5):481-97 (Eng. Abstr.) (Ger)

[Studies on isolated smooth muscle cells. VI. Dispersion procedures for acetylcholine-sensitive smooth muscle cells of guinea pig (author's transl)] Momose K, et al. **Nippon Heikatsukin Gakkai Zasshi** 1980 Mar; 16(1):29-36 (Eng. Abstr.) (Jpn)

[Effect of iontophoretic application of acetylcholine on the discharge rate and action potential shape of pacemaker cells] Bochkina GI, et al. **Biull Eksp Biol Med** 1981 Mar;91(3):259-60 (Eng. Abstr.) (Rus)

[Regulation of the functioning of molluscan neuron cholinoreceptors by succinate and noradrenaline] Andreev AA, et al. **Dokl Akad Nauk SSSR** 1981;258(6):1466-9 (Rus)

[Acetylcholine diffusion through neuronal membranes] Poskonova MA, et al. **Dokl Akad Nauk SSSR** 1981;257(6):1496-9 (Rus)

[Desensitization of the isolated rat myometrium to biologically active substances] Bordunovskaia VP, et al. **Fiziol Zh SSSR** 1981 Mar; 67(3):390-7 (Eng. Abstr.) (Rus)

[Cholinergic shifts and nibufin therapy in food allergy in children] Khamidullina AKh, et al. **Pediatriia** 1981 Apr;(4):51-3 (Eng. Abstr.) (Rus)

[Effects of certain biologically active compounds and bivalent cations on lactate and malate dehydrogenase activities in cerebral cellular fractions] Bdovichenko LM. **Ukr Biokhim Zh** 1981 May-Jun; 53(3):66-70 (Eng. Abstr.) (Rus)

[Phospholipid metabolism in acetylcholine and substance P induced desensitization of guinea pig ileum smooth muscle] Minenko AN, et al. **Ukr Biokhim Zh** 1980 Sep-Oct;52(5):577-81 (Eng. Abstr.) (Rus)

[Spectrofluorimetric study of interaction between acetylcholine and brain proteins] Sergienko NG, et al. **Ukr Biokhim Zh** 1981 May-Jun; 53(3):18-21 (Eng. Abstr.) (Rus)

ACHIEVEMENT

Relationships between sex-related psychological characteristics during adolescence and catecholamine excretion during achievement stress. Rauste-von Wright M, et al. **Psychophysiology** 1981 Jul;18(4):362-70

AFFECT

Effects of an ACTH short chain neuropeptide in man. Dornbush RL, et al. **Am J Psychiatry** 1981 Jul;138(7):962-4

AFFECTIVE DISORDERS

Monoamines in affective illness. Is there a place for 5HT? Eccleston D. **Br J Psychiatry** 1981 Mar;138:257-8

Antinuclear antibodies and histocompatibility antigens in patients on long-term lithium therapy. Whalley LJ, et al. **J Affective Disord** 1981 Jun;3(2):123-30

Biochemical markers identify mental states [news] Maugh TH 2d. **Science** 1981 Oct 2;214(4516):39-41

[Clinical significance of the erythro-plasmatic ratio of lithium (author's transl)] Braccini T, et al. **Acta Psychiatr Belg** 1980 Jul-Aug; 80(4):413-9 (Eng. Abstr.) (Fre)

AFFECTIVE DISORDERS, PSYCHOTIC

CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Gerner RH, et al. **Am J Psychiatry** 1981 Aug;138(8):1098-101

Responders and non-responders to lithium therapy. Some potential biological indicators. Mendlewicz J. **Bibl Psychiatr** 1981;(161):63-8 (39 ref.)

Prophylactic and therapeutic profile of lithium. Peselow E, et al. **Bibl Psychiatr** 1981;(161):1-31 (158 ref.)

Mania, crime and the insanity defense: a case report. Ratner RA. **Bull Am Acad Psychiatry Law** 1981;9(1):23-32

Lithium excretion and therapeutic response in mania. Sampath G, et al. **Indian J Med Res** 1981 May;73:768-71

Kidney function in patients with affective disorders with and without lithium therapy. Wahlin A, et al. **Int Pharmacopsychiatry** 1980; 15(4):253-9

The activity of the lithium—sodium countertransport system in erythrocytes in depression and mania. Rybakowski J, et al. **J Affective Disord** 1981 Mar;3(1):59-64

Tricyclic antidepressants do not alter thyroid hormone levels in patients suffering from a major affective disorder. Linnoila M, et al. **Psychiatry Res** 1981 Jun;4(3):357-60

[Unsolved problems in the indications for lithium prophylaxis in affective and schizoaffective disorders] Angst J. **Bibl Psychiatr** 1981; (161):32-44 (Eng. Abstr.) (Ger)

[Effects of lithium on normal psychic functions as a restriction on prophylactic use] Kropf D. **Bibl Psychiatr** 1981;(161):141-51 (Eng. Abstr.) (Ger)

[Motor reactivity during lithium prophylaxis] Oppenoorth E, et al. **Bibl Psychiatr** 1981;(161):152-69 (Eng. Abstr.) (Ger)

[Clinico-psychopathologic research on prophylactic lithium therapy]

Teufel S, et al. **Bibl Psychiatr** 1981;(161):58-62 **(Ger)**

[A study on the prevention of recurrences of affective diseases using lithium] Felber W. **Psychiatr Neurol Med Psychol (Leipz)** 1981 Jun; 33(6):330-2 **(Ger)**

[Comparative characteristics of the preventive properties of short-acting and delayed-action lithium carbonate in endogenous affective psychoses] Panteleeva GP, et al. **Zh Nevropatol Psikhiatr** 1981; 81(3):406-12 (Eng. Abstr.) **(Rus)**

AGGRESSION

Regional changes in brain norepinephrine content in relation to mouse-killing behavior by rats. Yoshimura H, et al. **Brain Res Bull** 1981 Aug;7(2):151-5

Neurochemical correlates of muricidal behavior in rats. Valzelli L, et al. **Neuropsychobiology** 1981;7(4):172-8

Dietary tryptophan and aggressive behavior in rats. **Nutr Rev** 1981 Jul; 39(7):284-5

Beta-adrenoreceptor antagonists enhance the benzodiazepine-induced suppression of footshock induced fighting in mice. Roliński Z, et al. **Pol J Pharmacol Pharm** 1980;32(5):731-8

Acetylcholine turnover and aggression in related three strains of mice. Karczmar AG, et al. **Prog Neuropsychopharmacol** 1981;5(1):35-48

[GABA-ergic correlates of aggression and intraspecies sociability of mice subjected to isolation] Poshivalov VP. **Biull Eksp Biol Med** 1981 May; 91(5):584-7 (Eng. Abstr.) **(Rus)**

AMINO ACIDS

Amino acid neurotransmitters. **Adv Biochem Psychopharmacol** 1981; 29:1-572

Biochemistry of central active amino acids. Bachelard HS. **Adv Biochem Psychopharmacol** 1981;29:475-97 (57 ref.)

Amino acids and presynaptic inhibition. Davidoff RA. **Adv Biochem Psychopharmacol** 1981;29:249-55 (50 ref.)

Physiological study of amino acid uptake and receptor desensitization: the GABA system in dorsal root ganglia. Désarménien M, et al. **Adv Biochem Psychopharmacol** 1981;29:309-19

Neuron-glia interactions in the biosynthesis and release of transmitter amino acids. Hamberger A, et al. **Adv Biochem Psychopharmacol** 1981; 29:509-18 (29 ref.)

Uptake inhibitors, amino acids, and spinal neurones. Lodge D. **Adv Biochem Psychopharmacol** 1981;29:327-32 (32 ref.)

New insights into the mechanism of action of inhibitory amino acids on frog spinal neurones. Nistri A. **Adv Biochem Psychopharmacol** 1981; 29:263-9

Studies with excitatory amino acid antagonists in rat CNS: 2-amino-5-phosphonovaleric acid, phenytoin, and benzodiazepines. Stone TW. **Adv Biochem Psychopharmacol** 1981;29:223-30

Rat undercut cortex as a model for the study of central amino acid transmission. Ulmar G. **Adv Biochem Psychopharmacol** 1981; 29:105-13

Pharmacology of excitatory amino acid transmitters. Watkins JC. **Adv Biochem Psychopharmacol** 1981;29:205-12 (31 ref.)

Uptake and asymmetric efflux of amino acids at maternal and fetal sides of placenta. Eaton BM, et al. **Am J Physiol** 1981 Sep; 241(3):C106-12

Effects of ammonia infusion on plasma glucagon, insulin, and amino acids in intact, pancreatectomized, and adrenalectomized dogs. Strombeck DR, et al. **Am J Vet Res** 1981 May;42(5):810-8

Combined thin-layer chromatography/mass spectrometry without substance elution. Use of direct identification of phenols, steroids, nucleosides, biogenic amines, and amino acids. Kraft R, et al. **Anal Biochem** 1981 May 1;113(1):193-6

Amino acid degradation by anaerobic bacteria. Barker HA. **Annu Rev Biochem** 1981;50:23-40 (77 ref.)

In vivo chemical modification of proteins (post-translational modification). Wold F. **Annu Rev Biochem** 1981;50:783-814 (199 ref.)

Effects of amino acid analogues on protein degradation in isolated rat hepatocytes. Grinde B, et al. **Biochim Biophys Acta** 1981 Aug 5; 676(1):43-50

Utilization of amino acid analogues in diets of young turkeys. Parsons CM, et al. **Br J Nutr** 1981 Jul;46(1):77-86

Availability to pigs of amino acids in cereal grains. 2. Apparent and true ileal availability. Taverner MR, et al. **Br J Nutr** 1981 Jul; 46(1):159-71

Patterns of endogenous amino acid release from slices of rat and guinea-pig olfactory cortex. Collins GG, et al. **Brain Res** 1981 Jan 5; 204(1):103-20

Developmental changes in brain indoles, serum tryptophan and other serum neutral amino acids in the rat. Zeisel SH, et al. **Brain Res** 1981 Jul;227(4):551-64

Inhibitory actions of amino acids in the preoptic-anterior hypothalamus of the rat. Mayer ML. **Exp Brain Res** 1981;43(2):154-8

The differential distribution of label following uptake of 3H-labeled amino acids in the dorsal cochlear nucleus of the cat. An autoradiographic study. Schwartz IR. **Exp Neurol** 1981 Sep;73(3):601-17

The tsx protein of Escherichia coli can act as a pore for amino acids. Heuzenroeder MW, et al. **J Bacteriol** 1981 Sep;147(3):1113-6

Properties of abnormal proteins degraded rapidly in reticulocytes. Intracellular aggregation of the globin molecules prior to hydrolysis. Klemes Y, et al. **J Biol Chem** 1981 Aug 25;256(16):8436-44

Effect of beta-bungarotoxin on the release of endogenous amino aids from the sensorimotor cortex. Abdul-Ghani AS, et al. **J Neurochem** 1981 Jul;37(1):251-4

Decreases in amino acids and acetylcholine metabolism during hypoxia. Gibson GE, et al. **J Neurochem** 1981 Jul;37(1):192-201

Decreased glutamate uptake in subcortical areas deafferented by sensorimotor cortical ablation in the cat. Young AB, et al. **J Neurosci** 1981 Mar;1(3):241-9

Specificity of neutral amino acid uptake at the basolateral side of the epithelium in the cat salivary gland in situ. Bustamante JC, et al. **J Physiol (Lond)** 1981;313:65-79

Incorporation of various amino acids into non-histone chromatin protein fractions of spleen cells of mice immunized with IgG. Rakowicz-Szulczyńska EM, et al. **Mol Cell Biochem** 1981 Jun 9; 37(1):13-9

Effect of L-dopa treatment on cerebral amino acid levels in rats after portocaval anastomosis. Zanchin G, et al. **Neurochem Res** 1981 Jun; 6(6):649-58

The interaction between barbiturate anaesthetics and excitatory amino acid responses on cat spinal neurones. Lambert JD, et al. **Neuropharmacology** 1981 Mar;20(3):227-40

Motilin release by intravenous infusion of nutrients and somatostatin in conscious dogs. Mori K, et al. **Regul Pept** 1981 Jan;1(4):265-70

[Nutritional habits of children with portosystemic anastomoses--effects on serum ammonia and amino acid level] Cario RW, et al. **Kinderaerztl Prax** 1981 May;49(5):245-51 (Eng. Abstr.) **(Ger)**

[Deficiency of amino acid precursors of chemical mediators and of creatine in the aged] Bertolini AM, et al. **Minerva Med** 1981 Sep 8; 72(32):2157-60 **(Ita)**

AMITRIPTYLINE

Differential effect of REM stimulating and REM inhibiting drugs (reserpine and amitriptylin) on memory. Faber J, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):169-71

Pharmacokinetics and efficacy of maprotiline and amitriptyline in endogenous depression: a double-blind controlled trial. Montgomery SA, et al. **Clin Ther** 1980;3(4):292-310

Amitriptyline and nortriptyline plasma levels monitoring. Perspective in clinical practice. Corona GL, et al. **Commun Psychopharmacol** 1980; 4(4):309-16

Appropriate treatment of fibromyositis [letter] Labowitz RJ, et al. **Del Med J** 1981 Aug;53(8):389

Interaction of desipramine and amitriptyline with adrenergic mechanisms in the human iris in vivo. Szabadi E, et al. **Eur J Clin Pharmacol** 1981; 19(6):403-8

Reliability of tricyclic antidepressant levels — further questions [letter] Bank RL, et al. **J Clin Psychiatry** 1981 Sep;42(9):364

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633-9

Amitriptyline and scopolamine in an animal model of depression. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):265-71

Management of depressive neurosis. Shaw SH. **Practitioner** 1981 Feb; 225(1352):228-30

Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. Ananth J, et al. **Prog Neuropsychopharmacol** 1981; 5(3):257-62

Treatment validity of different diagnostic concepts of depression. Zisook S, et al. **Psychiatry Res** 1981 Aug;5(1):77-85

Continuation therapy with lithium and amitriptyline in unipolar depressive illness: a controlled clinical trial. A report by the Medical Research Council Drug Trials Subcommittee. **Psychol Med** 1981 May; 11(2):409-16

Amitriptyline pharmacokinetics. Single doses of Lentizol compared with ordinary amitriptyline tablets. Burch JE, et al. **Psychopharmacology (Berlin)** 1981;74(1):43-50

Amitriptyline pharmacokinetics. A crossover study with single doses of amitriptyline and nortriptyline. Burch JE, et al. **Psychopharmacology (Berlin)** 1981;74(1):35-42

[Pharmacological influences on the brain level and transport of GABA. II) Effect of various psychoactive drugs on brain level and uptake of GABA] Gabana MA, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30; 57(8):909-13 (Eng. Abstr.) **(Ita)**

AMOBARBITAL

Relationship between polymorphism and bioavailability of amobarbital in the rabbit. Kato Y, et al. **Chem Pharm Bull (Tokyo)** 1981 Jan; 29(1):268-72

AMPHETAMINE

Conformational analysis of pGlu-His-Amph and pGlu-His-Pro-Amph related to their central nervous system activity. Morier E, et al. **Biochimie** 1981 Jun;63(6):495-505

Endogenous hyperprolactinaemia enhances amphetamine- and apomorphine-induced stereotypy. Drago F, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):249-53

The regional distribution of d-amphetamine and local glucose utilization in rat brain during continuous amphetamine administration. Eison MS, et al. **Exp Brain Res** 1981;43(3-4):281-8

Stimulating effects of amphetamine on the visual system. Andreeva OG, et al. **Hum Physiol** 1980 May-Jun;6(3):199-205

Application of chiral lanthanide nuclear magnetic resonance shift reagents to pharmaceutical analysis. II. Determination of dextro- and levoamphetamine mixtures. Wainer IW, et al. **J Assoc Off Anal Chem** 1981 Jul;64(4):848-50

Impurities in illicit amphetamine. Huizer H, et al. **J Forensic Sci Soc** 1981 Jul;21(3):225-32

3H-amphetamine concentrations in the brains of young and aged rats: implications for assessment of drug effects in aged animals. Truex LL, et al. **Neurobiol Aging** 1980 Summer;1(1):93-5

Amphetamine and tranylcypromine in an animal model of depression: pharmacological specificity of the reversal effect. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):259-64

Amphetamine and increases in current intensity modulate reward in the hypothalamus and substantia nigra but not in the prefrontal cortex. Robertson A, et al. **Physiol Behav** 1981 May;26(5):809-13

Synergistic induction of pineal gland N-acetyltransferase activity by amphetamine and L-DOPA. Altar A, et al. **Proc West Pharmacol Soc** 1981;24:101-4

Chronic haloperidol treatment fails to alter the anorexic actions of dopaminergic agonists and cholinergic drugs. Hynes MD, et al. **Prog Neuropsychopharmacol** 1981;5(3):271-5

Amphetamine enhancement of reward asymmetry. Glick SD, et al. **Psychopharmacology (Berlin)** 1981;73(4):323-7

Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Leith NJ, et al. **Psychopharmacology (Berlin)** 1981;74(1):23-8

[Biotransformation of amphetamine derivatives by rat liver mitochondria/2nd communication; Oxidative deamination of amphetamine and reduction of phenylacetone] Blume H. **Arzneimittelforsch** 1981;31(6):994-7 (Eng. Abstr.) (Ger)

[Mechanism of pantogam potentiation of certain effects of hexobarbital and sodium barbital and inhibition of phenamine hyperactivity] Avakumov VM, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):30-4 (Eng. Abstr.) (Rus)

AMPHETAMINES

Methylenedioxyamphetamine. Clinical description of overdose, death, and review of pharmacology. Simpson DL, et al. **Arch Intern Med** 1981 Oct;141(11):1507-9

'Problem children' and stimulant drug treatment. Prior M. **Aust NZ J Psychiatry** 1981 Jun;15(2):117-21

Conformational analysis of pGlu-His-Amph and pGlu-His-Pro-Amph related to their central nervous system activity. Morier E, et al. **Biochimie** 1981 Jun;63(6):495-505

Emergence of supraependymal cells in rat third ventricle after administration of p-chloroamphetamine. Saland LC, et al. **Brain Res Bull** 1981 Jun;6(6):517-24

3-O-methyl-alpha-methyldopamine, a urinary metabolite of p-methoxyamphetamine in dog and monkey. Hubbard JW, et al. **Drug Metab Dispos** 1981 May-Jun;9(3):250-4

Violence: the ugly face of amphetamine abuse. Siomopoulos V. **IMJ** 1981 Jun;159(6):375-7

Studies on chiral interactions of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane and the corresponding N-hydroxy metabolites with cytochrome P-450. McGraw NP, et al. **J Med Chem** 1981 Mar;24(3):299-304

Different action of 5-hydroxytryptamine (5-HT) uptake inhibitors on fenfluramine- but not p-chloramphetamine-induced hyperthermia in rats. Pawlowski L. **J Pharm Pharmacol** 1981 Aug;33(8):538-40

Profiles of psychedelic drugs: 10. DOB. Shulgin A. **J Psychoactive Drugs** 1981 Jan-Mar;13(1):99

The acute effect of p-chloroamphetamine on the retention of fear conditioning in the rat: evidence for a role of serotonin in memory consolidation. Archer T, et al. **Neurosci Lett** 1981 Aug 7;25(1):75-81

Circadian variation in the head twitch response produced by 5-methoxy-N1,N1-dimethyltryptamine and p-chloroamphetamine in the mouse. Singleton C, et al. **Psychopharmacology (Berlin)** 1981;74(2):173-6

[The effects of Citrus aurantium and its active ingredient N-methyltyramine on the cardiovascular receptors (author's transl)] Chen X, et al. **Yao Hsueh Hsueh Pao** 1981 Apr;16(4):253-9 (Eng. Abstr.) (Chi)

[Biotransformation of amphetamine derivatives by rat liver mitochondria / 1st communication: Oxidative dealkylation of N,N-dialkyl- and N-alkylamphetamines (author's transl)] Blume H. **Arzneimittelforsch** 1981;31(5):805-9 (Eng. Abstr.) (Ger)

ANOREXIA NERVOSA

Prolactin secretion in anorexia nervosa. Caufriez A, et al. **Acta Psychiatr Belg** 1980 Jul-Aug;80(4):546-50

CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Gerner RH, et al. **Am J Psychiatry** 1981 Aug;138(8):1098-101

Catecholamine metabolism and body weight in anorexia nervosa. Abraham SF, et al. **Br J Psychiatry** 1981 Mar;138:244-7

Continuous infusion of luteinizing hormone releasing hormone (LHRH) in patients with anorexia nervosa. Beumont PJ, et al. **Psychol Med** 1981 Aug;11(3):477-84

ANTIDEPRESSIVE AGENTS

Drug treatment of depression in children. Pearce JB. **Acta Paedopsychiatr (Basel)** 1981 Feb;46(5-6):317-28

Effects of an ACTH short chain neuropeptide in man. Dornbush RL, et al. **Am J Psychiatry** 1981 Jul;138(7):962-4

Inhibition of rat liver tryptophan pyrrolase activity and elevation of brain tryptophan concentration by administration of antidepressants. Badawy AA, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1211-6

Effects of caroxazone, a reversible monoamine oxidase inhibitor, on the pressor response to intravenous tyramine in man. Martini A, et al. **Br J Clin Pharmacol** 1981 Jun;11(6):605-10

Effects of caroxazone, a reversible monoamine oxidase inhibitor, on the pressor response to oral tyramine in man. Martini A, et al. **Br J Clin Pharmacol** 1981 Jun;11(6):611-5

Effect of caroxazone, a new antidepressant drug, on monoamine oxidases in healthy volunteers. Moretti A, et al. **Br J Clin Pharmacol** 1981 May;11(5):511-5

Use of potentiation of thyrotrophin releasing hormone (TRH)-induced hyperthermia as a test for screening antidepressants which activate alpha-adrenoceptor systems. Desiles M, et al. **Br J Pharmacol** 1981 Sep;74(1):81-6

An experimental study of the clinical judgment of general physicians in evaluating and prescribing for depression. Fisch HU, et al. **Br J Psychiatry** 1981 Feb;138:100-9

The antidepressant effects of trazodone and inhibition of platelet serotonin reuptake. Mann JJ, et al. **Commun Psychopharmacol** 1980;4(4):293-301

Plasma levels, elimination and metabolic fate of 4a-amino-8-chloro-2-methyl-1,2,3,4,4a,10a-hexahydro-10H-benzopyr acid lactam, a new antidepressive agent, in rats and dogs. Belleville M, et al. **Drug Metab Dispos** 1981 May-Jun;9(3):233-9

Current antidepressant drugs: their clinical use. Hollister LE. **Drugs** 1981 Aug;22(2):129-52 (93 ref.)

Pharmacokinetics of zimelidine in humans--plasma levels and urinary excretion of zimelidine and norzimelidine after intravenous and oral administration of zimelidine. Love BL, et al. **Eur J Clin Pharmacol** 1981;20(2):135-9

Down-regulation of beta-adrenergic activity in astroglia by chronic treatment with an antidepressant drug. Hertz L, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):267-8

Differential effects of electroconvulsive shock and antidepressant drugs on serotonin-2 receptors in rat brain. Kellar KJ, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):515-8

Effects of antidepressants in the rat forced swimming test. Kitada Y, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):145-52

Refractory depression: prediction of non-response by clinical indicators. Kupfer DJ, et al. **J Clin Psychiatry** 1981 Aug;42(8):307-12

Immobility test: effects of 5-hydroxytryptaminergic drugs and role of catecholamines in the activity of some antidepressants. Borsini F, et al. **J Pharm Pharmacol** 1981 Jan;33(1):33-7

Studies on the effect of antidepressants on kinetics and metabolism of tyramine. Faraj BA, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):750-7

Multicentre depression [editorial] **Lancet** 1981 Sep 12;2(8246):563-4

Trazodone--a new antidepressant. Al-Yassiri MM, et al. **Life Sci** 1981 Jun 1;28(22):2449-58 (106 ref.)

Modification of affinity of postsynaptic serotonin receptors by antidepressant drugs. Fillion G, et al. **Nature** 1981 Jul 23;292(5821):349-51

Amitriptyline and scopolamine in an animal model of depression. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):265-71

Current concepts of the mechanisms of action of antidepressant drugs. Sugrue MF. **Pharmacol Ther** 1981;13(2):219-47 (262 ref.)

Clinical pharmacological studies with LM 5008, a new antidepressant. Iliopoulou A, et al. **Pharmatherapeutica** 1981;2(9):613-21

Double-blind assessment of the activity of minaprine (30038-CB) in child psychiatry. Maffia AG. **Pharmatherapeutica** 1981;2(9):601-6

The effect of antidepressants on behavioral despair in rats. Górka Z, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):463-8

Studies on the action of antidepressant drugs of second generation. Maj J. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):437-49

Preliminary study of the biotransformation of two new drugs, trazodone and etoperidone. Melzacka M, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):551-6

The central action of salbutamol, a beta-agonist with a potential antidepressant activity. Przegalinski E, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):485-93

Interaction between antidepressants and alpha-adrenergic receptor blocking agents. Zebrowska-Lupina I, et al. **Pol J Pharmacol Pharm** 1980;32(5):673-80

Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. van Kammen DP, et al. **Psychiatry Res** 1981 Jun;4(3):313-25

Involvement of the amygdala in the effect of antidepressants on the passive avoidance deficit in bulbectomised rats. Garrigou D, et al. **Psychopharmacology (Berlin)** 1981;74(1):66-70

Chronic treatment with some atypical antidepressants increases the brain level of 3-methoxy-4-hydroxyphenylglycol (MHPG) in rats. Przegaliński E, et al. **Psychopharmacology (Berlin)** 1981;74(2):187-90

Differences in presynaptic alpha-blockade, noradrenaline uptake inhibition, and potential antidepressant activity between (+)- and (-)mianserin. Schoemaker H, et al. **Psychopharmacology (Berlin)** 1981;74(2):137-42

[Pyrazidole in the treatment of endogenous depression: controlled study (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Feb;77(1):31-7 (Eng. Abstr.) **(Cze)**

[Mechanism of action and indications for psychopharmaceutic agents; possibilities and limitations in the elderly] Verhoeven WM. **Gerontologie** 1981 Aug;12(3):126-38 (Eng. Abstr.) **(Dut)**

[Physiopathology of inhibition and proposals for an original therapeutic response] Laborit H. **Agressologie** 1981;22(2):45-53 (90 ref.) (Eng. Abstr.) **(Fre)**

[Effects of minaprine hydrochloride on changes in body weight, blood pressure and cerebral amine concentrations induced by unavoidable planter electric shock] Laborit H, et al. **Agressologie** 1981;22(2):59-62 (Eng. Abstr.) **(Fre)**

[Influence of the procedure of administration in the activity of some antidepressant or disinhibiting drugs upon behavioural despair (author's transl)] Scotto di Tella AM, et al. **J Pharmacol** 1981 Apr-Jun;12(2):179-88 (Eng. Abstr.) **(Fre)**

[Antidepressive drugs] Rouillon F, et al. **Soins Psychiatr** 1981 Jan;(7):27-32 **(Fre)**

[Tiocromid, a psychopharmaceutical with antidepressive action] von Littrow C. **Agressologie** 1979;20(D):299-302 **(Ger)**

[Duration of prophylactic medication with antidepressives] Pöldinger W. **Bibl Psychiatr** 1981;(161):237-43 **(Ger)**

[Studies on the circulatory side-effects of 2-[3'-diethylaminopropyl-(1')-carbamoyl]-6,7-dimethoxy-1-thiaiso-chroxide ('16-252') (author's transl)] Rostock A, et al. **Pharmazie** 1981 Apr;36(4):287-90 **(Ger)**

[Comparative mydriatic effect of different groups of antidepressants] Polezhaeva AI, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):15-7 (Eng. Abstr.) **(Rus)**

ANTISOCIAL PERSONALITY DISORDER

[Psychopathy or mental disequilibrium] Massé G. **Infirm Fr** 1981 Jun;(726):3-5 **(Fre)**

ANXIETY

Alprazolam (Xanax, the Upjohn Company). Evans RL. **Drug Intell Clin Pharm** 1981 Sep;15(9):633-8

The how of anxiety [editorial] **Lancet** 1981 Aug 1;2(8240):237-9

Is the isolated animal a possible model for phobia and anxiety? Garattini S, et al. **Prog Neuropsychopharmacol** 1981;5(2):159-65 (56 ref.)

Animal models of anxiety. Gray JA, et al. **Prog Neuropsychopharmacol** 1981;5(2):143-57 (40 ref.)

Comparison of anti-conflict drug effects in three experimental animal models of anxiety. Kilts CD, et al. **Psychopharmacology (Berlin)** 1981;74(3):290-6

[The treatment of an anxiety - depression syndrome in young women. Report of a case (author's transl)] Leyne P. **Sem Hop Paris** 1981 Jun 18-25;57(25-28):1226-7 (Eng. Abstr.) **(Fre)**

[Neurophysiology of anxiety] Debray Q, et al. **Soins Psychiatr** 1981 Mar;(8):3-5 **(Fre)**

[Anxiety; pharmacological bases of treatment] de Andrés Rodriguez-Trelles F. **An R Acad Nac Med (Madr)** 1981;98(1):69-116 (68 ref.) **(Spa)**

ANXIETY DISORDERS

Treatment of spontaneous panic attacks with chlomipramine. Gloger S, et al. **Am J Psychiatry** 1981 Sep;138(9):1215-7

Interesting uses of beta blockers (3): Beta blockers in anxiety. Ogborne WL. **Aust Fam Physician** 1981 Jun;10(6):472-5

Trazodone: a review of its pharmacological properties and therapeutic use in depression and anxiety. Brogden RN, et al. **Drugs** 1981 Jun;21(6):401-29 (156 ref.)

Doxepin plasma levels and anxiolytic response. Norman TR, et al. **Int Pharmacopsychiatry** 1980;15(4):247-52

Multicenter double-blind efficacy and safety study comparing alprazolam, diazepam and placebo in clinically anxious patients. Cohn JB **J Clin Psychiatry** 1981 Sep;42(9):347-51

[Anxiety; pharmacological bases of treatment] de Andrés Rodriguez-Trelles F. **An R Acad Nac Med (Madr)** 1981;98(1):69-116 (68 ref) **(Spa)**

APOMORPHINE

Kainic acid induced lesion of ventral tegmental area: locomotor effect of apomorphine. Morgenstern R. **Acta Biol Med Ger** 1980;39(8-9):911-5

An analysis of the effects of apomorphine and haloperidol on the release of [3H]-dopamine and [3H]-noradrenaline from rabbit brain slices. Kelly MJ. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):18-29

Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Menniti FS, et al. **Brain Res** 1981 Jul 6;216(1):89-107

Changes in dopamine and DOPAC following systemic administration of apomorphine and 3,4-dihydroxyphenylamino-2-imidazoline (DPI) in rats. Springer J, et al. **Brain Res** 1981 Sep 7;220(1):226-30

Apomorphine in schizophrenia. Hollister LE, et al. **Commun Psychopharmacol** 1980;4(4):277-81

Apomorphine, haloperidol and the average evoked potentials in normal human volunteers. Rey AC, et al. **Commun Psychopharmacol** 1980;4(4):327-34

Apomorphine-induced stereotypy in mature and senescent rats following cessation of chronic haloperidol treatment. Roffman M, et al. **Commun Psychopharmacol** 1980;4(4):283-6

Endogenous hyperprolactinaemia enhances amphetamine- and apomorphine-induced stereotypy. Drago F, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):249-53

Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice. Joshi VV, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):499-502

Detailed analysis of the effects of apomorphine and d-amphetamine on spontaneous locomotor behaviour of rats as measured in a TV-based, automated open-field system. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):45-56

Potentiation by Des-Tyr-gamma-endorphin on apomorphine-induced changes in rat open field behavior. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):77-81

REM sleep deprivation induces subsensitivity of dopamine receptors mediating sedation in rats. Serra G, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):131-5

Injection of low doses of apomorphine into the nucleus accumbens of rats reduces locomotor activity. Van Ree JM, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):107-11

Induction of behavioral supersensitivity to apomorphine by DFP treatment. Davis KL, et al. **Life Sci** 1981 Apr 27;28(17):1953-9

Pharmacological difference of L-dopa, apomorphine, and bromocriptine against metoclopramide. Fang VS. **Life Sci** 1981 May 11;28(19):2143-9

The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour. Carter CJ, et al. **Neuropharmacology** 1981 Mar;20(3):261-5

Single or repeated administration of small doses of apomorphine on water intake and activity in water-deprived rats. Dourish CT, et al. **Neuropharmacology** 1981 Mar;20(3):257-60

Chronic haloperidol treatment fails to alter the anorexic actions of dopaminergic agonists and cholinergic drugs. Hynes MD, et al. **Prog Neuropsychopharmacol** 1981;5(3):271-5

[Toxicity of organic phosphates under the influence of neuroleptics] Andreas K, et al. **Acta Biol Med Ger** 1980;39(8-9):987-9 **(Ger)**

[Studies on the situational factors affecting the effect of psychotropic drugs. II. Circadian fluctuation of sedative and anti-apomorphine effects of chlorpromazine (author's transl)] Takagi A. **Seishin Shinkeigaku Zasshi** 1981;83(4):236-50 **(Jpn)**

APPETITE

Effect of lithium intake on sodium and lithium appetite in sodium deficient cattle. Sly J, et al. **Physiol Behav** 1981 Jul;27(1):147-52

AROMATIC AMINO ACID DECARBOXYLASES

Aromatic L-amino acid decarboxylase activity in central and peripheral tissues and serum of rats with L-DOPA and L-5-hydroxytryptophan as substrates. Rahman MK, et al. **Biochem Pharmacol** 1981 Mar 15;

30(6):645-9

Inhibition of the renin-angiotensin-aldosterone system by L-dopa with and without inhibition of extracerebral dopa decarboxylase in man. Barbieri C, et al. **Clin Sci** 1981 Aug;61(2):187-90

AROUSAL

A pilot study to evaluate the effect of acute and long-term administration of cyclandelate on the vigilance of subjects submitted to hypoxic conditions. Preliminary report. Schaffler K, et al. **Arzneimittelforsch** 1981;31(6):1032-5

ATTENTION

Tryptophan metabolism in children with attentional deficit disorder. Irwin M, et al. **Am J Psychiatry** 1981 Aug;138(8):1082-5

Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Solomon PR, et al. **Biol Psychiatry** 1981 Jun; 16(6):519-37

The influence of fragments of the LPH chains on learning, memory and attention in animals and man. Sandman CA, et al. **Pharmacol Ther [B]** 1981;13(1):39-60 (76 ref.)

Psychomotor performance and real driving performance of outpatients receiving diazepam. de Gier JJ, et al. **Psychopharmacology (Berlin)** 1981; 73(4):340-4

AUDITORY PERCEPTION

Early auditory and visual function in normal and hyperthyroid rats. Brunjes PC, et al. **Behav Neural Biol** 1981 Apr;31(4):393-412

[Analysis of auditory averaged evoked potentials (AEP)- description of a fully automated procedure for AEP analysis (author's transl)] Hofmann W, et al. **EEG EMG** 1981 Jun;12(2):84-9 (Eng. Abstr.) (Ger)

AUTISM, INFANTILE

Effects of vitamin B6 on averaged evoked potentials in infantile autism. Martineau J, et al. **Biol Psychiatry** 1981 Jul;16(7):627-41

AVOIDANCE LEARNING

Failure of albino guinea pigs to exhibit Lavin's poisoned partner effect. Revusky S, et al. **Behav Neural Biol** 1981 May;32(1):111-3

Extinction of a conditioned taste aversion in young, mid-aged, and aged C57/BL6 mice. Springer AD, et al. **Behav Neural Biol** 1981 Jul; 32(3):282-94

Effects of 60-Hz electric fields on avoidance behavior and activity of rats. Hjeresen DL, et al. **Bioelectromagnetics** 1980;1(3):299-312

Plasma catecholamines: effects of footshock level and hormonal modulators of memory storage. McCarty R, et al. **Horm Behav** 1981 Jun;15(2):168-82

Relation of consummatory responses and preabsorptive insulin release to palatability and learned taste aversions. Berridge K, et al. **J Comp Physiol Psychol** 1981 Jun;95(3):363-82

Effect of trigeminal tractotomy on behavioral response to dental pulp stimulation in the monkey. Young RF, et al. **J Neurosurg** 1981 Sep; 55(3):420-3

Effects of morphine and chlordiazepoxide on avoidance behaviour in two inbred strains of mice. Cuomo V, et al. **Neuropharmacology** 1981 Mar; 20(3):301-4

Effect of injury to the serotoninergic and noradrenergic brain systems on food and defensive conditioned reflexes in rats. Gromova EA, et al. **Neurosci Behav Physiol** 1981 Jan-Feb;11(1):10-5

Drugs and taste aversion. Rondeau DB, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):279-94 (135 ref.)

Effects of nortriptyline treatment on learned helplessness in the rat. Telner JI, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):823-6

Sexually dimorphic acquisition of a conditioned taste aversion in rats: effects of gonadectomy, testosterone replacement and water deprivation. Chambers KC, et al. **Physiol Behav** 1981 Jul;27(1):83-8

Paradoxical sleep deprivation and performance of an active avoidance task: impairment of c57BR mice and no effect in c57BL/6 mice. Kitahama K, et al. **Physiol Behav** 1981 Jul;27(1):41-50

Noradrenergic and dopaminergic interactions in escape behavior: analysis of uncontrollable stress effects. Anisman H, et al. **Psychopharmacology (Berlin)** 1981;74(3):263-8

Involvement of the amygdala in the effect of antidepressants on the passive avoidance deficit in bulbectomised rats. Garrigou D, et al. **Psychopharmacology (Berlin)** 1981;74(1):66-70

Pre-exposure effects of morphine, diazepam and delta 9-THC on the formation of conditioned taste aversions. Switzman L, et al. **Psychopharmacology (Berlin)** 1981;74(2):149-57

[Dopamine concentration in the nigro-striatal system during elaboration and performance of conditioned avoidance reactions of various complexity in rats] Saul'skaia NB. **Fiziol Zh SSSR** 1981 Jun; 67(6):797-803 (Eng. Abstr.) (Rus)

[Age and sex differences in the elaboration and maintenance of conditioned taste aversion in rats] Kassil' VG, et al. **Zh Vyssh Nerv Deiat** 1981 May-Jun;31(3):630-2 (Rus)

[Participation of hypothalamic noradrenergic structures in the reproduction of conditioned 'passive' avoidance reactions] Tolochko ZS. **Zh Vyssh Nerv Deiat** 1981;31(2):267-70 (Eng. Abstr.) (Rus)

AZEPINES

Pharmacoelectroencephalographic study of brotizolam, a novel hypnotic. Fink M, et al. **Clin Pharmacol Ther** 1981 Sep;30(3):336-42

Disposition of [14C]caprolactam in the rat. Unger PD, et al. **Food Cosmet Toxicol** 1981 Aug;19(4):457-62

Cyclic urea nucleosides. Cytidine deaminase activity as a function of aglycon ring size. Liu PS, et al. **J Med Chem** 1981 Jun;24(6):662-6

Characteristics of equilibrium reaction of zolazepam. Hong WH, et al. **J Pharm Sci** 1981 Jun;70(6):691-3

[Ordram transformation by microorganisms] Golovleva LA, et al. **Izv Akad Nauk SSSR [Biol]** 1981 May-Jun;(3):348-58 (Eng. Abstr.) (Rus)

BEHAVIOR

GABA systems and behavior. Koella WP. **Adv Biochem Psychopharmacol** 1981;29:11-21 (32 ref.)

Age-related behavioral and neurobiological changes: a review with an emphasis on memory. Kubanis P, et al. **Behav Neural Biol** 1981 Feb; 31(2):115-72

Effects of fluoxetine on a specific serotonergic syndrome in rats. Keshavan HJ, et al. **Indian J Med Res** 1981 Apr;73:653-7

[Neurophysiology of anxiety] Debray Q, et al. **Soins Psychiatr** 1981 Mar; (8):3-5 (Fre)

BEHAVIOR, ANIMAL

Central action of adrenaline. Jagiello-Wójtowicz E. **Acta Physiol Pol** 1981 Mar-Apr;32(2):169-80

Effects of intrahypothalamic injections of kainic acid on the behaviour of rats. Plech A, et al. **Acta Physiol Pol** 1981 Mar-Apr;32(2):145-54

Pharmacokinetics and behavioral effects of methylphenidate in Thoroughbred horses. Shults T, et al. **Am J Vet Res** 1981 May; 42(5):722-6

Behavioural recovery following transplantation of substantia nigra in rats subjected to 6-OHDA lesions of the nigrostriatal pathway. I. Unilateral lesions. Dunnett SB, et al. **Brain Res** 1981 Jun 29;215(1-2):147-61

Intrathecal substance P elicits a caudally-directed biting and scratching behavior in mice. Hylden JL, et al. **Brain Res** 1981 Jul 27; 217(1):212-5

Suppression of active sleep by chronic treatment with chlorimipramine during early postnatal development: effects upon adult sleep and behavior in the rat. Mirmiran M, et al. **Brain Res** 1981 Jan 5; 204(1):129-46

Behavioral pharmacology of tetrahydrocannabinol convulsions in rabbits. Consroe P, et al. **Commun Psychopharmacol** 1980;4(4):287-91

Effects of neonatal ACTH4-10 administration on adult adaptive behavior and brain tyrosine hydroxylase activity. Nyakas C, et al. **Dev Neurosci** 1981;4(3):225-32

Endocrine and behavioral effects of continuous exposure of male rats to a potent luteinizing hormone-releasing hormone (LHRH) agonist: evidence for central nervous system actions of LHRH. Dorsa DM, et al. **Endocrinology** 1981 Sep;109(3):729-35

Effect of chronic lithium treatment on isolation-induced behavioral and biochemical effects in mice. Frances H, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):337-41

Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice. Joshi VV, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):499-502

Behavioral effects of unilateral dopamine injection into dorsal or ventral striatum. Joyce JN, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):1-10

Presence of a particular subpopulation of dopamine receptors within the septal nuclei: a behavioural study on cats. Megens AA, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):247-58

Effects of fluoxetine on a specific serotonergic syndrome in rats. Keshavan HJ, et al. **Indian J Med Res** 1981 Apr;73:653-7

Relevance of the rodent area postrema to dopamine-dependent behavioural effects. Costall B, et al. **J Pharm Pharmacol** 1981 Apr; 33(4):257-9

Behavioral and neurochemical interactions of dextroamphetamine and methylphenidate in rats. Reigle TG, et al. **J Pharm Sci** 1981 Jul; 70(7):816-8

Effects of CDP-choline on striatal dopamine level and behavior in rats. Shibuya M, et al. **Jpn J Pharmacol** 1981 Feb;31(1):47-52

Induction of behavioral supersensitivity to apomorphine by DFP treatment. Davis KL, et al. **Life Sci** 1981 Apr 27;28(17):1953-9

Behavioral comparisons of the stereoisomers of tetrahydrocannabinols. Martin BR, et al. **Life Sci** 1981 Aug 10;29(6):565-74

Behavioral and neurochemical effects of the new opioid peptide dynorphin--(1-13): comparison with other neuropeptides. Zwiers H, et al. **Life Sci** 1981 Jun 1;28(22):2545-51

The effects of muscimol and picrotoxin injections into the cat substantia nigra. Wolfarth S, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):54-60

Pharmacological characterization of scratching behaviour induced by intracranial injection of substance P and somatostatin. Dobry PJ, et al. **Neuropharmacology** 1981 Mar;20(3):267-72

Behavioral effects of phencyclidine in the developing cat. Levine MS, et al. **Neuropharmacology** 1981 Aug;20(8):743-5

Antagonism of methylphenidate-induced behavior by neostigmine or hemicholinium-3. Ward HE Jr, et al. **Neuropharmacology** 1981 Jul; 20(7):703-9

Reciprocal antagonism between ACTH1-24 and beta-endorphin in rats. Fratta W, et al. **Neurosci Lett** 1981 Jun 12;24(1):71-4

Cardiovascular and behavior changes after ICV infusion of TRH in the conscious goat. Eriksson L, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):901-5

Behavioral assessment of norepinephrine and serotonin function and interaction in the hippocampal formation. Gage FH, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):815-21

Quipazine-induced behavior in neonatal rat pups. Spear LP, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):831-4

Effects of anorectic drugs and prior feeding on food-rewarded runway behavior. Thurlby PL, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):799-804

Melatonin and behavioral thermoregulation in the turtle, Terrapene carolina triunguis. Erskine DJ, et al. **Physiol Behav** 1981 Jun; 26(6):991-4

Effects on central dopaminergic systems of d-coclaurine and d-reticuline, extracted from Magnolia salicifolia. Watanabe H, et al. **Planta Med** 1981 Jul;42(3):213-22

The effect of antidepressants on behavioral despair in rats. Górka Z, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):463-8

The effect of imipramine and mianserin on the behavior and EEG afterdischarges induced by single electric stimulation of the rabbit amygdala. Ossowska K, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug; 32(4):513-22

Antianxiety agents and emotional behavior, an information processing analysis. Morris MD, et al. **Prog Neuropsychopharmacol** 1981; 5(3):219-40

Enduring behavioural and biochemical effects in the adult rat after prolonged postnatal administration of haloperidol. Cuomo V, et al. **Psychopharmacology (Berlin)** 1981;74(2):166-9

Supersensitivity to L-5-hydroxytryptophan after 5,7-dihydroxytryptamine injections in desmethylimipramine- and nomifensine-pretreated rats: behavioral evidence for postsynaptic supersensitivity. Ortmann R, et al. **Psychopharmacology (Berlin)** 1981; 74(2):109-14

Circadian variation in the head twitch response produced by 5-methoxy-N1,N1-dimethyltryptamine and p-chloroamphetamine in the mouse. Singleton C, et al. **Psychopharmacology (Berlin)** 1981; 74(2):173-6

Evidence against the involvement of serotonergic mechanisms in wet dog shake behavior induced by carbachol chloride in rats. Turski L, et al. **Psychopharmacology (Berlin)** 1981;73(4):376-80

A multivariate analysis of some operant variables used in behavioral pharmacology. Walker CH, et al. **Psychopharmacology (Berlin)** 1981; 74(2):182-6

Seasonal changes in the behavior and plasma titers of various hormones in barheaded geese, Anser indicus. Dittami JP. **Z Tierpsychol** 1981; 55(4):289-324

[Electrographic and behavioral changes induced by the administration of benzodiazepines in the restrained baboon] Rougeul A. **Actual Pharmacol (Paris)** 1981;33:77-90 (Fre)

[Influence of the procedure of administration in the activity of some antidepressant or disinhibiting drugs upon behavioural despair (author's transl)] Scotto di Tella AM, et al. **J Pharmacol** 1981 Apr-Jun; 12(2):179-88 (Eng. Abstr.) (Fre)

BENZAZEPINES

Differential effects of systemic and intracoronary calcium channel blocking agents on global and regional left ventricular function in conscious dogs. Walsh RA, et al. **Am Heart J** 1981 Sep; 102(3 Pt 1):341-50

Properties of 8,9-dichloro-2,3,4,5-tetrahydro-1H-2-benzazepine, an inhibitor of norepinephrine N-methyltransferase. Fuller RW, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1345-52

Actions of verapamil, diltiazem and other divalent cations on the calcium-current of Helix neurones. Akaike N, et al. **Br J Pharmacol** 1981 Sep;74(1):87-95

Plasma concentration of diltiazem after oral administration in normal volunteers. Koiwaya Y, et al. **Clin Ther** 1981;3(6):436-40

Effects of diltiazem hydrochloride on pressor and steroidogenic actions of angiotensins and norepinephrine in man. Ikeda F, et al. **Endocrinol Jpn** 1980 Dec;27(6):779-84

Inhibitory effect on calcium channel blockers on alpha -adrenergic activation of glycogenolysis and calcium efflux in perfused rat liver. Kimura S, et al. **Endocrinol Jpn** 1981 Feb;28(1):69-78

The pharmacokinetics and pharmacology of oral diltiazem in normal volunteers. Kinney EL, et al. **J Clin Pharmacol** 1981 Aug-Sep; 21(8-9):337-42

The effect of diltiazem and nisoldipine on spontaneously active human atrial tissue. Lathrop DA, et al. **J Mol Cell Cardiol** 1981 Jan; 13(1):111-5

The mechanism of inhibitory action of diltiazem on vascular smooth muscle contractility. van Breemen C, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):459-63

Effect of diltiazem, a calcium antagonist, on renin secretion from rat kidney slices. Churchill PC, et al. **Life Sci** 1981 Jul 27;29(4):383-9

Diltiazem and verapamil inhibit norepinephrine-stimulated 45Ca uptake in rabbit aorta. Flaim SF, et al. **Pharmacology** 1981;22(5):286-93

[Diltiazem and anaesthesia] Zerr C, et al. **Ann Cardiol Angeiol (Paris)** 1981 Mar-Apr;30(2):133-7 (Fre)

[Electrophysiologic effects of calcium channel blocking agents on the sinus node function in anesthetized dogs (author's transl)] Nakaya H, et al. **Nippon Yakurigaku Zasshi** 1980 Nov;76(8):697-707 (Eng. Abstr.) (Jpn)

[Effects of diltiazem on cardiac function in the dog (author's transl)] Narita H, et al. **Nippon Yakurigaku Zasshi** 1981 Jan;77(1):51-9 (Eng. Abstr.) (Jpn)

BENZODIAZEPINE TRANQUILIZERS

Effect of estazolam on the caudate spindle in the cat. Janicki P, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):172-3

Studies with excitatory amino acid antagonists in rat CNS: 2-amino-5-phosphonovaleric acid, phenytoin, and benzodiazepines. Stone TW. **Adv Biochem Psychopharmacol** 1981;29:223-30

Cimetidine-benzodiazepine drug interaction. Ruffalo RL, et al. **Am J Hosp Pharm** 1981 Sep;38(9):1365-6

Benzodiazepines--panacea or poison? Lader M. **Aust NZ J Psychiatry** 1981 Mar;15(1):1-9

Stimulation of benzodiazepine binding to rat brain membranes and solubilized receptor complex by avermectin B1a and gamma-aminobutyric acid. Pong SS, et al. **Biochim Biophys Acta** 1981 Aug 6;646(1):143-50

Withdrawal from long-term benzodiazepine treatment. Petursson H, et al. **Br Med J [Clin Res]** 1981 Sep 5;283(6292):643-5

Benzodiazepine binding and interactions with the GABA receptor complex in living cultures of rat cerebral cortex. White WF, et al. **Brain Res** 1981 Jun 29;215(1-2):162-76

More on lorazepam withdrawal [letter] Barton DF. **Drug Intell Clin Pharm** 1981 Feb;15(2):134

Alprazolam (Xanax, the Upjohn Company). Evans RL. **Drug Intell Clin Pharm** 1981 Sep;15(9):633-8

Effect of a short-acting benzodiazepine on brain electrical activity during sleep. Johnson LC, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jul;52(1):89-97

Action of pyrazolopyridines as modulators of [3H]flunitrazepam binding to the gaba/benzodiazepine receptor complex of the cerebellum. Supavilai P, et al. **Eur J Pharmacol** 1981 Mar 12;70(2):183-93

Neurochemical changes produced by acute treatment with clobazam, a new 1,5-benzodiazepine. Lapierre YD, et al. **Gen Pharmacol** 1981; 12(4):261-6

Assay of triazolam in plasma by capillary gas chromatography. Jochemsen R, et al. **J Chromatogr** 1981 May 8;223(2):438-44

Determination of tofisopam in serum by high-performance liquid chromatography. Sajgó M, et al. **J Chromatogr** 1981 Feb 13; 222(2):303-7

Multicenter double-blind efficacy and safety study comparing alprazolam, diazepam and placebo in clinically anxious patients. Cohn JB. **J Clin Psychiatry** 1981 Sep;42(9):347-51

Lack of effect of benzodiazepines on bicuculline-insensitive GABA-receptors in the field-stimulated guinea-pig vas deferens preparation. Doble A, et al. **J Pharm Pharmacol** 1981 Apr; 33(4):267-8

High-performance liquid chromatographic analysis of clorazepate dipotassium and monopotassium in solid dosage forms. Elrod L Jr, et al. **J Pharm Sci** 1981 Jul;70(7):793-5

Benzodiazepines reduce stress-augmented increase in rat urine monoamine oxidase inhibitor. Glover V, et al. **Nature** 1981 Jul 23; 292(5821):347-9

Benzodiazepine dependence: a general practice survey. Khan A, et al. **NZ Med J** 1981 Jul 8;93(687):19-21

Preliminary studies on the central action of new 1,5-benzodiazepine derivatives. Kleinrok Z, et al. **Pol J Pharmacol Pharm** 1980 May-Jun; 32(3):247-60

Beta-adrenoreceptor antagonists enhance the benzodiazepine-induced suppression of footshock induced fighting in mice. Rolinski Z, et al. **Pol J Pharmacol Pharm** 1980;32(5):731-8

The effect of chronic diazepam treatment on discrimination performance and 3H-flunitrazepam binding in the brains of shocked and nonshocked rats. Grimm VE, et al. **Psychopharmacology (Berlin)** 1981; 74(2):132-6

The halcion affair [letter] Rudnick HL. **S Afr Med J** 1981 Sep 5; 60(10):378

[Electrographic and behavioral changes induced by the administration of benzodiazepines in the restrained baboon] Rougeul A. **Actual Pharmacol (Paris)** 1981;33:77-90 (Fre)

[Comparative pharmacokinetics of diazepam and flunitrazepam] Cano JP, et al. **Ann Anesthesiol Fr** 1981;22(2):175-9 (Eng. Abstr.) (Fre)

[Clinical pharmacokinetics of flunitrazepam (Nacrozep) in intensive care patient (preliminary results)] Sumirtapura Y, et al. **Ann Anesthesiol Fr** 1981;22(2):180-4 (Eng. Abstr.) (Fre)

[Pharmacological and toxicological aspects of benzodiazepine compounds (author's transl)] Kapp W. **Anaesth Intensivther Notfallmed** 1981 Jun; 16(3):125-7 (Eng. Abstr.) (Ger)

[Clinical pharmacokinetics of midazolam, flunitrazepam and diazepam (author's transl)] Lauven PM, et al. **Anaesth Intensivther Notfallmed** 1981 Jun;16(3):135-42 (Eng. Abstr.) (Ger)

[The use of flunitrazepam in ICU patients (author's transl)] Pasch T. **Anaesth Intensivther Notfallmed** 1981 Jun;16(3):145-9 (Eng. Abstr.) (Ger)

[Molecular mechanism of action of benzodiazepines] Quast U. **Fortschr Med** 1981 May 28;99(20):788-94 (Eng. Abstr.) (Ger)

[Pharmacokinetic differentiation of benzodiazepines] Vollmer KO. **Fortschr Med** 1981 Jun 4;99(21):829-34 (Ger)

[Clinical relevance of pharmacokinetic differences in benzodiazepines] Weiershausen U. **Fortschr Med** 1981 Jun 28;99(23):919-24 (Eng. Abstr.) (Ger)

BENZODIAZEPINONES

Clonazepam acetylation in fast and slow acetylators. Miller ME, et al. **Clin Pharmacol Ther** 1981 Sep;30(3):343-7

Metabolism of pinazepam by rat liver microsomes. Marcucci F, et al. **Eur J Drug Metab Pharmacokinet** 1981;6(2):109-14

Neurochemical changes produced by acute treatment with clobazam, a new 1,5-benzodiazepine. Lapierre YD, et al. **Gen Pharmacol** 1981; 12(4):261-6

Structure of tomaymycin, a DNA binding antitumor antibiotic. Arora SK. **J Antibiot (Tokyo)** 1981 Apr;34(4):462-4

Benzodiazepine antagonist Ro 15-1788: binding characteristics and interaction with drug-induced changes in dopamine turnover and cerebellar cGMP levels. Möhler H, et al. **J Neurochem** 1981 Sep; 37(3):714-22

[New evidence for a GABA-ergic component in the mechanism of action of benzodiazepine tranquilizers] Zakusov VV, et al. **Biull Eksp Biol Med** 1981 May;91(5):571-4 (Eng. Abstr.) (Rus)

[Stimulation of prostaglandin E2 and F2a biosynthesis in the brains of mouse strain F1 (CBA X C57BL) by the tranquilizer phenazepam] Romantsev EF, et al. **Dokl Akad Nauk SSSR** 1981;258(1):239-42 (Rus)

[Dynamics of phenazepam concentration in the blood of pregnant mini-swine] Liubimov BI, et al. **Farmakol Toksikol** 1981 Jan-Feb; 44(1):43-6 (Eng. Abstr.) (Rus)

[Effect of stimulants on the tranquilizing, hypnotic and myorelaxant action of phenazepam] Voronina TA, et al. **Farmakol Toksikol** 1981 Mar-Apr; 44(2):155-9 (Eng. Abstr.) (Rus)

[Inhibitory effect of phenazepam on protein and RNA catabolism in the supraoptic nucleus during REM-sleep deprivation] Demin NN, et al. **Fiziol Zh SSSR** 1981 Mar;67(3):460-3 (Rus)

BIOGENIC AMINES

Effect of cholecystokinin octapeptide sulphate ester on brain monoamines in the rat. Fekete M, et al. **Acta Physiol Acad Sci Hung** 1981; 57(1):37-46

In vivo effect of danitracen on the uptake mechanism in monoaminergic neurons and platelets in rats. Wielosz M, et al. **Agressologie** 1979; 20(D):253-7

Combined thin-layer chromatography/mass spectrometry without substance elution. Use of direct identification of phenols, steroids, nucleosides, biogenic amines, and amino acids. Kraft R, et al. **Anal Biochem** 1981 May 1;113(1):193-6

Comparative histochemistry as a springboard for the discovery of biogenic amines and active peptides in molluscan tissues and amphibian skin. Erspamer V. **Basic Appl Histochem** 1981;25(1):3-14

Biogenic amine terminals in the goldfish cerebellum and optic tectum: a fluorescence and autoradiographic study. Niso R, et al. **Basic Appl Histochem** 1981;25(2):113-9

Characterization of eight biogenic indoleamines as substrates for type A and type B monoamine oxidase. Suzuki O, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1353-8

Detection of urinary primary amines through negative chemical ionization mass spectrometry of fluorescamine derivatives. Bergner EA, et al. **Biomed Mass Spectrom** 1981 May;8(5):208-10

Biogenic amines and the secretion of parathyroid hormone and calcitonin. Heath H 3d. **Endocr Rev** 1980 Fall;1(4):319-38 (141 ref.)

Gas chromatographic determination of some biogenic amines as their pentafluorobenzoyl derivatives in the picogram range and its applicability to biological materials. Bock UE, et al. **J Chromatogr** 1981 Sep 4;213(3):413-28

High-performance liquid chromatographic determination of biogenic amines. II. Comparison of detection methods. Svendsen H, et al. **J Chromatogr** 1981 Sep 4;213(3):429-37

Determination of picomole amounts of dopamine, noradrenaline, 3,4-dihydroxyphenylalanine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, and 5-hydroxyindolacetic acid in nervous tissue after one-step purification on Sephadex G-10, using high-performance liquid chromatography with a novel type of electrochemical detection. Westerink BH, et al. **J Neurochem** 1981 Apr;36(4):1449-62

Red blood cells: in vivo site for transport and inactivation of biogenic amines in man and rats. Alexander N, et al. **Life Sci** 1981 Aug 3; 29(5):477-82

Effects of antidepressant treatment with clomipramine on hormonal responses to thyrotropin-releasing hormone and insulin-induced hypoglycemia: implications for the 'monoamine-hypothesis'. Langer G, et al. **Pharmacopsychiatria** 1981 May;14(3):100-6

[Biogenic amines and biological control] **Tanpakushitsu Kakusan Koso** 1981 Jul;26(9 Suppl):1065-484 (Jpn)

[Progress in biochemical studies for biogenic amines] **Tanpakushitsu Kakusan Koso** 1981 Jul;26(9 Suppl):1071-288 (Jpn)

[Metabolism of biogenic amines and related enzymes] **Tanpakushitsu Kakusan Koso** 1981 Jul;26(9 Suppl):1289-484 (Jpn)

[Changes in the levels of adrenergic and serotoninergic indices in patients with depressive states] Misionzhnik EIu, et al. **Zh Nevropatol Psikhiatr** 1981;81(4):543-51 (Eng. Abstr.) (Rus)

BIPOLAR DISORDER

Lithium capsule. Holland PJ. **Am Fam Physician** 1981 Sep;24(3):147-8

Group therapy in the management of manic-depressive illness. Volkmar FR, et al. **Am J Psychother** 1981 Apr;35(2):226-34

Prophylactic lithium carbonate with and without imipramine for bipolar 1 patients. A double-blind study. Quitkin FM, et al. **Arch Gen Psychiatry** 1981 Aug;38(8):902-7

Practical guide-lines of lithium prophylaxis. Kerry RJ. **Bibl Psychiatr** 1981;(161):197-205

Differential sensitivity to the effects of psychotropic drugs: psychotics vs normals; Asian vs Western populations. Okuma T. **Folia Psychiatr Neurol Jpn** 1981;35(1):79-87

Bipolar affective disorder, lithium carbonate and Ca++ ATPase. Choi SJ, et al. **J Affective Disord** 1981 Jun;3(2):77-9

Bipolar affective disorder following coronary bypass surgery. Salinger R, et al. **J Clin Psychiatry** 1981 Sep;42(9):354-5

Manic depression—a disorder of central dopaminergic rhythm. Skutsch GM. **Med Hypotheses** 1981 Jun;7(6):737-46

Cell membrane anomaly in genetically determined manic-depressive illness. Verbanck PM, et al. **Neuropsychobiology** 1981;7(4):185-7

Leukocytosis during long-term lithium treatment. Yassa R. **NY State J Med** 1981 Sep;81(10):1479-80

[Manic-depressive psychosis. Efficacy of lithium in various disorders of carbohydrate metabolism (letter)] Gisselmann A, et al. **Nouv Presse Med** 1981 Jun 6;10(25):2121 (Fre)

[Lithium] Lemoine JM, et al. **Soins Psychiatr** 1981 Jan;(7):37-42 (Fre)

[Emotional stress and biochemical responses of completely recovered manic depressive patients (author's transl)] Nakahara T. **Seishin Shinkeigaku Zasshi** 1981;83(5):263-74 (Jpn)

[Slow-release lithium carbonate versus standard preparation in bipolar affective disorders (author's transl)] Bohaček N, et al. **Lijec Vjesn** 1980 Oct;102(10):575-9 (Eng. Abstr.) (Ser)

BLOOD-BRAIN BARRIER

Blood-brain transport of tryptophan and phenylalanine: effect of portacaval shunt in dogs. Huet PM, et al. **Am J Physiol** 1981 Aug; 241(2):G163-9

BOREDOM

The stress of boredom and monotony: a consideration of the evidence. Thackray RI. **Psychosom Med** 1981 Apr;43(2):165-76

BRADYKININ

Effects of high oxygen tension on the metabolism of vasoactive hormones in isolated perfused rat lungs. Toivonen H, et al. **Acta Physiol Scand** 1981 Feb;111(2):185-92

Bradykinin effects on adrenergic transmission in the canine kidney: relation to prostaglandins. Sušić H, et al. **Am J Physiol** 1981 Sep; 241(3):R146-51

Enkephalins, substance P, bradykinin and angiotensin II: differential sites of action on the hypothalamo-neurohypophysial system. Baertschi AJ, et al. **Brain Res** 1981 Sep 7;220(1):107-19

Thermoregulatory effects of centrally administered bombesin, bradykinin, and methionine-enkephalin. Francesconi R, et al. **Brain Res Bull** 1981 Jul;7(1):63–8

Inhibitory action of bradykinin on release of the adrenergic transmitter in the isolated lapine kidney. Malik KU, et al. **Experientia** 1981 May 15;37(5):496–7

BUTYLAMINES

Superiority of perfluorocarbon cardioplegia over blood or crystalloid cardioplegia. Kanter KR, et al. **Circulation** 1981 Aug; 64(2 Pt 2):75–80

Maintenance of rat liver viability enhanced by cold flushing with oxygenated perfluorochemicals. Konno T, et al. **Jpn J Surg** 1981; 11(3):209–13

BUTYROPHENONE TRANQUILIZERS

Influence of beta-adrenergic and cholinergic blockade on the electrophysiological effects of melperone in the dog heart in situ. Platou ES, et al. **Cardiovasc Res** 1981 Mar;15(3):137–43

Electrophysiological effects of melperone in the dog heart in situ - a new antiarrhythmic drug. Refsum H, et al. **Cardiovasc Res** 1981 Mar; 15(3):131–6

BUTYROPHENONES

Overall-response parameter analysis applied to butyrophenones. Mager PP. **Act Nerv Super (Praha)** 1981 Jun;23(2):130–5

Differential effects of itanoxone—a new hypolipidemic and hypouricemic drug—on platelet and vascular prostaglandin generation in rats. Livio M, et al. **Atherosclerosis** 1981 Jul;39(4):469–77

The interaction of chlorpromazine and butyrophenones with glutamate dehydrogenase. Tamir A, et al. **Biochem Pharmacol** 1981 Jun 15; 30(12):1469–73

[3H]Spiperone binding sites in brain: autoradiographic localization of multiple receptors. Palacios JM, et al. **Brain Res** 1981 Jun 1; 213(2):277–89

Influence of beta-adrenergic and cholinergic blockade on the electrophysiological effects of melperone in the dog heart in situ. Platou ES, et al. **Cardiovasc Res** 1981 Mar;15(3):137–43

Electrophysiological effects of melperone in the dog heart in situ - a new antiarrhythmic drug. Refsum H, et al. **Cardiovasc Res** 1981 Mar; 15(3):131–6

Kainic acid lesions dissociate [3H] spiperone and [3H]cis-flupenthixol binding sites in rat striatum. Cross AJ, et al. **Eur J Pharmacol** 1981 May 8;71(2–3):327–32

Decreased in vivo [3H]spiroperidol binding in rat brain after repeated methamphetamine administration. Kaneno S, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):101–5

Comparisons of rotamer populations of nialamide, azaperone, and chloroquine in solid state and in solution. Migliaccio GP, et al. **J Pharm Sci** 1981 Mar;70(3):284–7

Specific in vivo binding of 77Br-p-bromospiroperidol in rat brain: a potential tool for gamma ray imaging. Kulmala HK, et al. **Life Sci** 1981 Apr 27;28(17):1911–6

Effects of chronic haloperidol, thioridazine and zotepine treatment on apomorphine elicited stereotypic behavior and 3H-spiroperidol binding sites in the striatum of the rat. Lai HC, et al. **Proc West Pharmacol Soc** 1981;24:5–6

Lithium increases serotonin release and decreases serotonin receptors in the hippocampus. Treiser SL, et al. **Science** 1981 Sep 25; 213(4515):1529–31

CARBAMAZEPINE

Carbamazepine overdose. Lehrman SN, et al. **Am J Dis Child** 1981 Aug; 135(8):768–9

Saliva carbamazepine and phenytoin level monitoring. Rylance GW, et al. **Arch Dis Child** 1981 Aug;56(8):637–40

Rapid and sensitive high-pressure liquid chromatographic method for monitoring carbamazepine levels in serum. Furlanut M, et al. **Br J Clin Pharmacol** 1981 Apr;11(4):393–5

Comparison of anticonvulsant potencies of cyheptamide, carbamazepine, and phenytoin. Jones GL, et al. **J Pharm Sci** 1981 Jun;70(6):618–20

Competitive nephelometric immunoassay of carbamazepine and its epoxide metabolite in patient blood plasma. Nishikawa T, et al. **J Pharmacobiodyn** 1981 Jan;4(1):77–83

Carbamazepine poisoning: treatment by hemoperfusion. Gary NE, et al. **Nephron** 1981;27(4–5):202–3

An unexpected reaction to carbamazepine. Taylor MW, et al. **Practitioner** 1981 Feb;225(1352):219–20

Effect of carbamazepine on CSF opioid activity; relationship to antidepressant response. Post RM, et al. **Psychiatry Res** 1981 Aug; 5(1):59–66

[Carbamazepine poisoning] Krarup G, et al. **Ugeskr Laeger** 1981 Mar 2; 143(10):603–6 (Eng. Abstr.) (Dan)

[Carbamazepine (Tegretol) poisoning)] Wernberg M, et al. **Ugeskr Laeger** 1981 Mar 2;143(10):619–20 (Eng. Abstr.) (Dan)

[Pharmacological influences on the brain level and transport of GABA. I) Effect of various antipileptic drugs on brain levels of GABA] Varotto M, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30;57(8):904–8 (Eng. Abstr.) (Ita)

CARBIDOPA

Effects of benserazide and carbidopa on the metabolism of L-tryptophan by isolated rat liver cells. Smith SA, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):623–8

CATECHOLAMINES

Release of endogenous GABA from the rat brain: methodological aspects and the effects of catecholamines. van der Heyden JA, et al. **Adv Biochem Psychopharmacol** 1981;29:193–203

Stimulatory and inhibitory effects of catecholamines and of prostaglandin E2 on human fat cell adenylate cyclase. Kather H, et al. **Adv Cyclic Nucleotide Res** 1981;14:555–62

Role of guanine nucleotides in hormonal activation of adenylate cyclase. Selinger Z, et al. **Adv Cyclic Nucleotide Res** 1981;14:15–22

Peripheral metabolism of indoleamines and catecholamines in endogenous depressive syndrome. Puzynski S, et al. **Agressologie** 1979; 20(D):245–51

Stability of five catecholamines and terbutaline sulfate in 5% dextrose injection in the absence and presence of aminophylline. Newton DW, et al. **Am J Hosp Pharm** 1981 Sep;38(9):1314–9

Exercise plasma catecholamines in dogs: role of adrenals and cardiac nerve endings. Péronnet F, et al. **Am J Physiol** 1981 Aug;241(2):H243–7

A cellular activator of catecholamine-sensitive adenylate cyclase in rat reticulocytes and erythrocytes: changes during reticulocyte development and effects on the beta receptor. Shane E, et al. **Arch Biochem Biophys** 1981 May;208(2):418–25

The influence of sodium gamma-hydroxybutyrate on GABA receptors and catecholamine effect potentiation. Kozhechkin SN. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):242–53

Effects of Mg-pemoline on the central catecholaminergic system. Molina VA, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):66–79

Catecholamine levels and tyrosine hydroxylase activities in rat brain regions after chronic treatment with, and withdrawal of, methamphetamine. Bardsley ME, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1543–9

Influence of harmaline on the ability of pargyline to alter catecholamine metabolism in rats. Fuller RW, et al. **Biochem Pharmacol** 1981 Jun 1; 30(11):1295–8

Catecholamine-induced phosphorylation of cardiac muscle proteins. Dobson JG Jr. **Biochim Biophys Acta** 1981 Jun 11;675(1):123–31

High performance liquid chromatographic analysis of catecholamines in growing and non-growing Tetrahymena pyriformis. Goldman ME, et al. **Biochim Biophys Acta** 1981 Aug 17;676(2):221–5

Plasma catecholamines and pituitary adrenal hormones related to mental task demand under quiet and noise conditions. Brandenberger G, et al. **Biol Psychol** 1980 Jun;10(4):239–52

Evidence against an obligatory role for catecholamine release or prostacyclin synthesis in the effects of relaxin on the rat uterus. Sanborn BM, et al. **Biol Reprod** 1981 Jun;24(5):987–92

Prostacyclin and beta-adrenergic catecholamines inhibit arachidonate release and PGI2 synthesis by vascular endothelium. Adler B, et al. **Blood** 1981 Sep;58(3):514–7

Cell groups in the lower brain stem of the rabbit projecting to the spinal cord, with special reference to catecholamine-containing neurons. Blessing WW, et al. **Brain Res** 1981 Sep 21;221(1):35–55

Effect of manipulating central catecholamines on puberty and the surge of luteinizing hormone and gonadotropin releasing hormone induced by pregnant mare serum gonadotropin in female rats. Sarkar DK, et al. **Brain Res** 1981 Jun 1;213(2):335–49

Changes in dopamine and DOPAC following systemic administration of apomorphine and 3,4-dihydroxyphenylamino-2-imidazoline (DPI) in rats. Springer J, et al. **Brain Res** 1981 Sep 7;220(1):226–30

Effects of serotonin and catecholamines on RNA synthesis in planarians; in vitro and in vivo studies. Franquinet R, et al. **Cell Differ** 1981 Aug; 10(4):201–9

Projection of ventrolateral medullary (A1) catecholamine neurons toward nucleus tractus solitarii. Blessing WW, et al. **Cell Tissue Res** 1981; 220(1):27–40

Corticotropin-releasing factors (CRF) secreted by the rat median eminence in vitro in the presence or absence of ascorbic acid: quantitative role of vasopressin and catecholamines. Bény JL, et al. **Endocrinology** 1981 Sep;109(3):813–7

Characteristics of the alpha-adrenergic stimulation of adrenocorticotropin secretion in rat anterior pituitary cells. Giguere V, et al. **Endocrinology** 1981 Sep;109(3):757–62

Role of phosphorylation of the sarcoplasmic reticulum in the cardiac response to catecholamines. Katz AM. **Eur Heart J** 1980; Suppl A:29–33 (23 ref.)

Catecholaminergic involvement in the biphasic effect of ADATN on temperature in mice. Dooley DJ, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):269-76

Effect of prostaglandins D2, E2 and F2alpha on catecholamine release from slices of rat and rabbit brain. Reimann W, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):421-7

Effect of captopril on cardiovascular, sympathetic and vasopressin responses to hemorrhage. Zerbe RL, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):391-5

Gonadal steroids and brain monoamines: how do they interact? Wuttke W, et al. **Exp Brain Res** 1981;Suppl 3:130-41

Density of retinal catecholamine-accumulating cells in different-sized goldfish. Negishi K. **Exp Eye Res** 1981 Aug;33(2):223-32

Swim-stress induced changes of rat adrenal catecholamine level depending on metabolic state and different ambient temperature. Bargiel Z, et al. **Folia Histochem Cytochem (Krakow)** 1981;19(1):31-7

Plasma catecholamines: effects of footshock level and hormonal modulators of memory storage. McCarty R, et al. **Horm Behav** 1981 Jun;15(2):168-82

Stimulation of cyclic AMP production by vasoactive agents in cultured bovine aortic and pulmonary artery endothelial cells. Makarski JS. **In Vitro** 1981 May;17(5):450-8

Heterogeneity in the adrenomedullary storage of catecholamines, ATP, calcium and releasable dopamine beta-hydroxylase activity. Bolstad G, et al. **J Auton Nerv Syst** 1980 Dec;2(4):337-54

Tonic catecholaminergic inhibition of the spinal somato-sympathetic reflexes originating in the ventrolateral medulla oblongata. Dembowsky K, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):277-90

Effects of some catecholamines on the cat cardiovascular system: interactions with adrenoceptor antagonists. McPherson GA, et al. **J Cardiovasc Pharmacol** 1981 Jul-Aug;3(4):739-52

Determination of catecholamines by radioenzymatic assay using ion-pair liquid chromatography. Uchikura K, et al. **J Chromatogr** 1981 Apr 10;223(1):41-50

Cyclic adenosine monophosphate modulation of contractility via slow Ca2+ channels in chick heart. Azuma J, et al. **J Mol Cell Cardiol** 1981 Jun;13(6):577-87

Muscarinic receptors in chromaffin cell cultures mediate enhanced phospholipid labeling but not catecholamine secretion. Fisher SK, et al. **J Neurochem** 1981 Aug;37(2):491-7

Stimulus-secretion coupling in isolated adrenal chromaffin cells: calcium channel activation and possible role of cytoskeletal elements. Schneider AS, et al. **J Neurochem** 1981 Sep;37(3):567-75

On the role of Ca2+ in the transmitter choice made by cultured sympathetic neurons. Walicke PA, et al. **J Neurosci** 1981 Apr;1(4):343-50

Immobility test: effects of 5-hydroxytryptaminergic drugs and role of catecholamines in the activity of some antidepressants. Borsini F, et al. **J Pharm Pharmacol** 1981 Jan;33(1):33-7

Age-related changes in the central catecholaminergic function and its interaction with methamphetamine during postnatal life in the rat. Nomura Y, et al. **J Pharm Pharmacol** 1981 Apr;33(4):264-6

Physiological role of endogenous amines in the modulation of ventricular automaticity in the guinea-pig. Hume J, et al. **J Physiol (Lond)** 1980 Dec;309:275-86

Nitroglycerine and catecholamine actions on smooth muscle cells of the canine coronary artery. Ito Y, et al. **J Physiol (Lond)** 1980 Dec;309:171-83

Studies on secretion of catecholamines evoked by acetylcholine or transmural stimulation of the rat adrenal gland. Wakade AR. **J Physiol (Lond)** 1981;313:463-80

Facilitation of secretion of catecholamines from rat and guinea-pig adrenal glands in potassium-free medium or after ouabain. Wakade AR. **J Physiol (Lond)** 1981;313:481-98

Stress and age effects on catecholamines in normal subjects. Aslan S, et al. **J Psychosom Res** 1981;25(1):33-41

Influence of sino-aortic baroreceptor denervation on catecholamines, catecholamine-synthesizing enzymes and choline acetyltransferase activity in the brainstem nuclei of the rat. Nakamura K, et al. **Jpn J Pharmacol** 1981 Feb;31(1):95-105

Catecholamine biosynthesis in specific brain areas of the rat as determined by liquid chromatography and amperometric detection. Bennett BA, et al. **Life Sci** 1981 Jun 22;28(25):2811-7

Adrenal catecholamines during and following hypoxia in neonatal rats. Hedner T, et al. **Med Biol** 1980 Aug;58(4):228-31

Increase in catecholamine-stimulated cyclic AMP and progesterone synthesis in rat granulosa cells during culture. Kliachko S, et al. **Mol Cell Endocrinol** 1981 Jul;23(1):23-32

Catecholamines, dopamine, and endorphin levels during extreme exercise [letter] Bortz WM 2d, et al. **N Engl J Med** 1981 Aug 20;305(8):466-7

Liberation of catecholamines and 5-hydroxytryptamine from human blood-platelets. Peyer M, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):81-6

Endogenous dopa in rat brain. Occurrence, distribution and relationship to changes i catecholamine synthesis. Thiede HM, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jul;316(4):299-303

Catecholamines in the hypothalamus: an anatomical review. Palkovits M. **Neuroendocrinology** 1981 Aug;33(2):123-8

Scattered catecholaminergic cells in the dorsolateral tegmentum caudal to locus coeruleus in cat. Persson M, et al. **Neurosci Lett** 1981 May 29;23(3):275-80

alpha-MSH, MIF-I and melatonin: effects on novelty-induced defecation, plasma 11-OHCS and central catecholamines in rats. Datta PC, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:143-54

Presynaptic regulation of the release of catecholamines. Langer SZ. **Pharmacol Rev** 1980 Dec;32(4):337-62

Humoral indices of stress in rats. Natelson BH, et al. **Physiol Behav** 1981 Jun;26(6):1049-54

The effect of multiple imipramine administration on monoaminergic systems of the rat brain. Vetulani J, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):523-30

Effect of acute or chronic pentobarbital administration on the steady state levels and the turnover rates of catecholamines in discrete brain areas of mice. Nabeshima T, et al. **Prog Neuropsychopharmacol** 1981;5(2):121-8

Stimulatory effect of ouabain on catecholamine synthesis in bovine adrenal medullary slices. Yanagihara N. **Tokushima J Exp Med** 1980 Dec;27(3-4):63-8

[Plasma catecholamines and aerobic-anaerobic capacity in women during graduated treadmill exercise] Lehmann M, et al. **Eur J Applied Physiol** 1981;46(3):305-15 (Ger)

[Behavior of plasma catecholamines in relation to pressure changes induced with hemodialysis or ultrafiltration] Cannella G, et al. **Minerva Nefrol** 1979 Jul-Sep;26(3):365-72 (Ita)

[Effects of GSH on endocrine function and lysosomal enzyme levels during cardiopulmonary bypass in man (author's transl)] Matsuki A, et al. **Masui** 1981 Feb;30(2):150-7 (Eng. Abstr.) (Jpn)

[Catecholamines and potassium metabolism] Hishida A, et al. **Nippon Rinsho** 1981 Feb;39(2):304-9 (29 ref.) (Jpn)

[Studies on new radioenzymatic assay kit for catecholamine determination and plasma levels of catecholamines (author's transl)] Nakai T, et al. **Rinsho Byori** 1980 Sep;28(9):915-9 (Jpn)

[Metabolism of peripheral catecholamines and indole amines in healthy persons. Clinico-biochemical correlates] Krzyżowski J, et al. **Pol Tyg Lek** 1981 Mar 16;36(11):417-21 (Eng. Abstr.) (Pol)

[Correlation between the body's level of carbohydrates and the neurohormonal response to exercise in man] Nazar K. **Pol Tyg Lek** 1981 May 18;36(20):735-7 (Pol)

[Cerebral bioelectric activity and urinary catecholamine elimination in thermal stress in children] Stratone A, et al. **Rev Med Chir Soc Med Nat Iasi** 1981;85(1):113-6 (Eng. Abstr.) (Rum)

[Use of aluminum-formaldehyde to demonstrate catecholamines in cryostatic sections] Azhialis VP, et al. **Arkh Anat Gistol Embriol** 1981 Mar;80(3):102-6 (Rus)

[Luminescent-histochemical study of the effect of atropine and dimethoxydichlorvinylphosphate on catecholamine concentration in certain rat brain structures] Kutsenko SA, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):702-3 (Eng. Abstr.) (Rus)

[Effect of acetylcholine and histamine on electrolyte and catecholamine content of vessel walls exposed to x-rays and cystamine] Litvinov SA. **Farmakol Toksikol** 1981 Jan-Feb;44(1):55-9 (Eng. Abstr.) (Rus)

[Role of the kallikrein-kinin system in achieving the hemodynamic effects of catecholamines] Kiselev VI, et al. **Fiziol Zh SSSR** 1981 Apr;67(4):561-7 (Eng. Abstr.) (Rus)

[Catecholamines and the enzymes of their synthesis in the adrenal medulla of rats after a flight on the Cosmos-936 biosatellite] Kwietnanski R, et al. **Kosm Biol Aviakosm Med** 1981 Jun-Jul;15(4):64-5 (Eng. Abstr.) (Rus)

[Catecholamine metabolic state in the early stages of the development of chronic carbon disulfide poisoning (a review of the literature)] Lukhtai VA. **Vrach Delo** 1981 May;(5):110-4 (33 ref.) (Eng. Abstr.) (Rus)

[Identification of the catecholamines in tissue extracts of the trematode, Fasciola hepatica] Terenina NB. **Zh Evol Biokhim Fiziol** 1981 Jul-Aug;17(4):342-7 (Eng. Abstr.) (Rus)

CENTRAL NERVOUS SYSTEM AGENTS

Monophenolic 2-(dipropylamino)indans and related compounds: central dopamine-receptor stimulating activity. Hacksell U, et al. **J Med Chem** 1981 Apr;24(4):429-34

CHILD BEHAVIOR DISORDERS

The hyperactive child in adolescence: some pharmacologic approaches. White JH. **J Adolesc** 1981 Mar;4(1):79-86

Double-blind assessment of the activity of minaprine (30038-CB) in child psychiatry. Maffia AG. **Pharmatherapeutica** 1981;2(9):601-6

CHILD DEVELOPMENT DISORDERS, PERVASIVE

Use of stimulant medication in treating pervasive developmental disorder [letter] Sporn A, et al. **Am J Psychiatry** 1981 Jul;138(7):997

CHLORAMINES

The effect of the oxidizing agents chloramine-T and cigarette smoke on dog serum proteinase inhibitor(s). Abrams WR, et al. **Exp Lung Res** 1980 Aug;1(3):211-23

Investigations concerning the action of serveral chemical and biological agents on HBsAg. Morfei A, et al. **Virologie** 1980 Oct-Dec; 31(4):273-8

CHLORDIAZEPOXIDE

Hostility conflict and the effect of chlordiazepoxide on change in hostility level. Downing RW, et al. **Compr Psychiatry** 1981 Jul-Aug; 22(4):362-7

Lack of tolerance and rapid recovery of cimetidine-inhibited chlordiazepoxide (Librium) elimination. Patwardhan RV, et al. **Gastroenterology** 1981 Sep;81(3):547-51

Differential pulse amperometric detection of drugs in plasma using a dropping mercury electrode as a high-performance liquid chromatographic detector. Hackman MR, et al. **J Chromatogr** 1981 Feb 13;222(2):179-90

Benzodiazepines reduce stress-augmented increase in rat urine monoamine oxidase inhibitor. Glover V, et al. **Nature** 1981 Jul 23; 292(5821):347-9

Effects of morphine and chlordiazepoxide on avoidance behaviour in two inbred strains of mice. Cuomo V, et al. **Neuropharmacology** 1981 Mar; 20(3):301-4

The partial reinforcement extinction effect: influence of chlordiazepoxide in septal lesioned rats. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 74(3):280-9

P-CHLOROPHENYLALANINE

Diffuse noxious inhibitory controls (DNIC) in the rat with or without pCPA pretreatment. Dickenson AH, et al. **Brain Res** 1981 Jul 20; 216(2):313-21

Phasic activity induced by p-chlorophenylalanine in the auditory pathway. Ayala-Guerrero F, et al. **Neuropharmacology** 1981 Mar; 20(3):273-5

Modifications of brain steroidogenesis and plasma steroids after p-chlorophenylalanine-methyl-ester treatment in male rats and rabbits. Farabollini F, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):911-4

Does para-chlorophenylalanine produce disturbed waking, disturbed sleep or activation by ponto-geniculo-occipital waves in cats? Ursin R. **Waking Sleeping** 1980 Jul-Sep;4(3):211-21

CHLORPROMAZINE

Effect of chlorpromazine on conjugal plasmid transfer and sex pili. Mándi Y, et al. **Acta Microbiol Acad Sci Hung** 1981;28(2):205-10

Stability of chlorpromazine liquid in unit dose packaging [letter] Dugas JE. **Am J Hosp Pharm** 1981 Sep;38(9):1276

Membrane-active agents. Effect of various anesthetics and chlorpromazine on arterial lipid metabolism. Bell FP, et al. **Atherosclerosis** 1981 Jul;39(4):517-25

The interaction of chlorpromazine and butyrophenones with glutamate dehydrogenase. Tamir A, et al. **Biochem Pharmacol** 1981 Jun 15; 30(12):1469-73

Studies on the binding of chlorpromazine and chloroquine to melanin in vivo. Tjälve H, et al. **Biochem Pharmacol** 1981 Jul 1; 30(13):1845-7

Daytime variation in serum prolactin level in patients receiving oral and depot antipsychotic medication. Goode DJ, et al. **Biol Psychiatry** 1981 Jul;16(7):653-62

Phenothiazine withdrawal in schizophrenics in a hostel [letter] Mathur S, et al. **Br J Psychiatry** 1981 Mar;138:271-2

Synthesis of phosphatidyl-dCMP in human lymphocytes and its enhancement by chlorpromazine. Medrano E, et al. **Eur J Biochem** 1981 May 15;116(2):249-53

Differential sensitivity to the effects of psychotropic drugs: psychotics vs normals; Asian vs Western populations. Okuma T. **Folia Psychiatr Neurol Jpn** 1981;35(1):79-87

(Ca2+ + Mg2+)-ATPase of chlorpromazine containing rabbit erythrocyte membrane. Au KS. **Gen Pharmacol** 1981;12(4):285-90

Effect of dielectric discharge on drug treated mammalian cells. Mishra KP, et al. **Indian J Exp Biol** 1981 Jun;19(6):520-3

Failure of chlorpromazine to inhibit fluid accumulation caused by Escherichia coli heat-stable enterotoxin in suckling mice. Takeda T, et al. **Infect Immun** 1981 May;32(2):480-3

Protein binding of chlorpromazine in cerebrospinal fluid and serum. Alfredsson G, et al. **Int Pharmacopsychiatry** 1980;15(5):261-9

Selective inhibitory effects of chlorpromazine and imipramine on platelet aggregation. Ishigooka J, et al. **Int Pharmacopsychiatry** 1980; 15(5):270-80

Chronic chlorpromazine administration in rats: effects on ability to work in the heat. Francesconi R, et al. **J Appl Physiol** 1981 Mar; 50(3):509-12

Phototoxicity mechanisms: chlorpromazine photosensitized damage to DNA and cell membranes. Kochevar KE. **J Invest Dermatol** 1981 Jul; 77(1):59-64

Atypical conditions for quantitative recovery of acepromazine and chlorpromazine from plasma. Ballard S, et al. **J Toxicol Environ Health** 1981 May;7(5):745-51

Effects of various membrane phospholipid-interacting drugs on three species of multifunctional protein kinases. Mori T. **Kobe J Med Sci** 1981 Apr;27(2):77-89

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633-9

Effects of short- and long-term neuroleptic treatment on brain serotonin synthesis and turnover: focus on the serotonin hypothesis of schizophrenia. Rastogi RB, et al. **Life Sci** 1981 Aug 17;29(7):735-41

Modulation of platelet shape and membrane receptor binding by Ca2+-calmodulin complex. Kao KJ, et al. **Nature** 1981 Jul 2; 292(5818):82-4

Chlorpromazine: it leaves me cold! Hopkins SJ. **Nurs Mirror** 1981 Aug 12;153(7):34-5

Inactivation of bacteriophage lambda by near-ultraviolet irradiation in the presence of chlorpromazine. Fujita H, et al. **Photochem Photobiol** 1981 Feb;33(2):215-22

Substance P-like immunoreactivity in plasma of psychotic patients and effects of neuroleptics and electroconvulsive therapy. Kaiya H, et al. **Psychiatry Res** 1981 Aug;5(1):11-21

Effect of intramuscular chlorpromazine on serum prolactin levels in schizophrenic patients and normal controls. Meltzer HY, et al. **Psychiatry Res** 1981 Aug;5(1):95-105

[Studies on the situational factors affecting the effect of psychotropic drugs. II. Circadian fluctuation of sedative and anti-apomorphine effects of chlorpromazine (author's transl)] Takagi A. **Seishin Shinkeigaku Zasshi** 1981;83(4):236-50 **(Jpn)**

CHLORPROTHIXENE

The pathophysiology of acute renal failure after chlorprothixene overdosage. Rossen B, et al. **Acta Med Scand** 1981;209(6):525-7

Identification of 2-chlorothioxanthen-9-one in gastric aspirate in a case of chlorprothixene poisoning. Pettersen JE, et al. **J Pharm Sci** 1981 Jul;70(7):812-3

CHOICE BEHAVIOR

Effects of pentobarbital on delayed alternation performance. Terry WS, et al. **Behav Neural Biol** 1981 Jul;32(3):380-5

Temperature preferences and the effect of changes in serotonin in maturing mice. Goodrich C, et al. **Physiol Behav** 1981 Jun; 26(6):1041-7

CLOMIPRAMINE

Treatment of spontaneous panic attacks with chlomipramine. Gloger S, et al. **Am J Psychiatry** 1981 Sep;138(9):1215-7

School phobia: a therapeutic trial with clomipramine and short-term outcome. Berney T, et al. **Br J Psychiatry** 1981 Feb;138:110-8

Suppression of active sleep by chronic treatment with chlorimipramine during early postnatal development: effects upon adult sleep and behavior in the rat. Mirmiran M, et al. **Brain Res** 1981 Jan 5; 204(1):129-46

A double-blind multicentre trial comparing the efficacy and side-effects of mianserin and chlorimipramine in depressed in- and outpatients. Pinder RM, et al. **Int Pharmacopsychiatry** 1980;15(4):218-27

Effects of antidepressant treatment with clomipramine on hormonal responses to thyrotropin-releasing hormone and insulin-induced hypoglycemia: implications for the 'monoamine-hypothesis'. Langer G, et al. **Pharmacopsychiatria** 1981 May;14(3):100-6

Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. Ananth J, et al. **Prog Neuropsychopharmacol** 1981; 5(3):257-62

A multicenter controlled trial in phobic-obsessive psychoneurosis. The effect of chlorimipramine and of its combinations with haloperidol and diazepam. Cassano GB, et al. **Prog Neuropsychopharmacol** 1981; 5(2):129-38

[Clinical investigation comparing trazodone and clomipramine] Lange E, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1980 Dec;32(12):748-50 **(Ger)**

COCAINE

Pulmonary dysfunction in cocaine smokers. Weiss RD, et al.

Am J Psychiatry 1981 Aug;138(8):1110-2

Inverse relation of substance P-like immunoreactivity in dorsal raphe nucleus to serotonin levels in pons-medulla following administration of cocaine and 5-hydroxytryptophan. Pradhan S, et al. **Biochem Pharmacol** 1981 May 15;30(10):1071-6

The acquisition of responding with conditioned reinforcement: effects of cocaine, (+)-amphetamine and pipradrol. Beninger RJ, et al. **Br J Pharmacol** 1981 Sep;74(1):149-54

Cocaine cue in pigeons: time course studies and generalization to structurally related compounds (norcocaine, WIN 35,428 and 35,065-2) and (+)-amphetamine. Järbe TU. **Br J Pharmacol** 1981 Aug; 73(4):843-52

Cocaine facilitates the effects of alpha-agonists and antagonists on adrenergic neurotransmission. Nigro D, et al. **Gen Pharmacol** 1981; 12(4):255-9

Mass spectral quantitation of cocaine HCl in powders. Clark CC. **J Assoc Off Anal Chem** 1981 Jul;64(4):884-8

The 'body packer syndrome'-toxicity following ingestion of illicit drugs packaged for transportation. Wetli CV, et al. **J Forensic Sci** 1981 Jul; 26(3):492-500

Effect of cocaine on noradrenaline contractions of mesenteric vein: pre or postjunctional mechanism? O'Connor PC, et al. **J Pharm Pharmacol** 1981 Jan;33(1):58-60

Effect of cocaine on contractile responses to noradrenaline of canine isolated mesenteric vein. O'Connor PC, et al. **J Pharm Pharmacol** 1981 Jan;33(1):55-8

Effects of denervation, decentralization and cocaine on the responses of the guinea-pig vas deferens to phenylephrine in vivo and in vitro. Sannomiya P, et al. **J Pharm Pharmacol** 1981 Jun;33(6):388-9

Effects of cocaine on Ca-mobility in microsomal fraction from rat vas deferens. Hisayama T, et al. **Jpn J Pharmacol** 1981 Feb;31(1):1-6

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633-9

Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Leith NJ, et al. **Psychopharmacology (Berlin)** 1981;74(1):23-8

COGNITION

Brief fasting, stress, and cognition in children. Pollitt E, et al. **Am J Clin Nutr** 1981 Aug;34(8):1526-33

Cognition-activating properties of 3-(Aryloxy)pyridines. Butler DE, et al. **J Med Chem** 1981 Mar;24(3):346-50

Evaluation of information sequential aspects of schizophrenic performance. II. Research strategies and methodological issues. Neufeld RW, et al. **J Nerv Ment Dis** 1981 Sep;169(9):569-79 (77 ref.)

[Effect of phenobarbital on self-ratings of healthy subjects in comparison to the objective impairment of their performance] Walther H, et al. **Acta Biol Med Ger** 1980;39(8-9):949-60 (Eng. Abstr.) (Ger)

[Influence of thioridazine on cognitive, psychomotor, and reaction performance in patients with dysthymic-depressive syndrome (author's transl)] Meyer FP, et al. **Pharmacopsychiatria** 1981 May;14(3):94-9 (Ger)

COGNITION DISORDERS

Span of apprehension deficits during the postpsychotic stages of schizophrenia. A replication and extension. Asarnow RF, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1006-11

Cognitive dysfunction and imipramine in outpatient depressive. Glass RM, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1048-51

CONDITIONING (PSYCHOLOGY)

The acute effect of p-chloroamphetamine on the retention of fear conditioning in the rat: evidence for a role of serotonin in memory consolidation. Archer T, et al. **Neurosci Lett** 1981 Aug 7; 25(1):75-81

6-Hydroxydopamine and radiofrequency lesions of the lateral entorhinal cortex facilitate an operant appetitive conditioning task in mice. Gauthier M, et al. **Neurosci Lett** 1981 Jul 2;24(2):193-7

CONDITIONING, CLASSICAL

Extinction of a conditioned taste aversion in young, mid-aged, and aged C57/BL6 mice. Springer AD, et al. **Behav Neural Biol** 1981 Jul; 32(3):282-94

Forebrain norepinephrine and serotonin concentrations and cardiac conditioning in normal rabbits and rabbits with septal lesions. Hernández LL, et al. **Brain Res Bull** 1981 Jun;6(6):479-86

Effects of haloperidol and pimozide on classical conditioning of the rabbit nictitating membrane response. Harvey JA, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):712-9

Sexually dimorphic acquisition of a conditioned taste aversion in rats: effects of gonadectomy, testosterone replacement and water deprivation. Chambers KC, et al. **Physiol Behav** 1981 Jul;27(1):83-8

[Dopamine concentration in the nigro-striatal system during elaboration and performance of conditioned avoidance reactions of various complexity in rats] Saul'skaia NB. **Fiziol Zh SSSR** 1981 Jun; 67(6):797-803 (Eng. Abstr.) (Rus)

[Age and sex differences in the elaboration and maintenance of conditioned taste aversion in rats] Kassil' VG, et al. **Zh Vyssh Nerv Deiat** 1981 May-Jun;31(3):630-2 (Rus)

[Effect of scopolamine on temporary connection formation and fixation in rats with altered brain noradrenaline content] Orlova NV. **Zh Vyssh Nerv Deiat** 1981 May-Jun;31(3):571-6 (Eng. Abstr.) (Rus)

CONDITIONING, OPERANT

The acquisition of responding with conditioned reinforcement: effects of cocaine, (+)-amphetamine and pipradrol. Beninger RJ, et al. **Br J Pharmacol** 1981 Sep;74(1):149-54

Drug effects on multiple and alternating mixed-schedule performance. Leander JD. **J Pharmacol Exp Ther** 1981 Sep;218(3):728-33

The behavioral effects of hallucinogens in rats following 5,7-dihydroxytryptamine administration into the medial forebrain bundle. Commissaris RL, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):915-8

Effects of diazepam on operant behavior in man. Carlton PL, et al. **Psychopharmacology (Berlin)** 1981;73(4):314-7

A multivariate analysis of some operant variables used in behavioral pharmacology. Walker CH, et al. **Psychopharmacology (Berlin)** 1981; 74(2):182-6

CONFLICT (PSYCHOLOGY)

Effect of gamma-vinyl GABA alone or associated with diazepam on a conflict test in the rat. Huot S, et al. **Adv Biochem Psychopharmacol** 1981;29:45-52

Constructs and 'conflict' in depression. Sheehan MJ. **Br J Psychol** 1981 May;72(Pt 2):197-209

Hostility conflict and the effect of chlordiazepoxide on change in hostility level. Downing RW, et al. **Compr Psychiatry** 1981 Jul-Aug; 22(4):362-7

Effects of buspirone on conflict behavior of laboratory rats and monkeys. Hartmann RJ, et al. **Proc West Pharmacol Soc** 1981;24:179-81

Comparison of anti-conflict drug effects in three experimental animal models of anxiety. Kilts CD, et al. **Psychopharmacology (Berlin)** 1981; 74(3):290-6

CONSUMMATORY BEHAVIOR

Relation of consummatory responses and preabsorptive insulin release to palatability and learned taste aversions. Berridge K, et al. **J Comp Physiol Psychol** 1981 Jun;95(3):363-82

CORTICOSTERONE

Effect of ovariectomy, thyroidectomy and of thyroxine treatment on the plasma level of corticosterone of the female Japanese quail. Péczely P, et al. **Acta Biol Acad Sci Hung** 1981;32(1):1-6

Effect of electroconvulsive treatment on brain monoamine content, pituitary-adrenal function and plasma prolactin. Arató M, et al. **Acta Physiol Acad Sci Hung** 1980;56(2):163-71

Plasma corticosterone, thyroxine and triiodothyronine level in the collared dove (Streptopelia decaocto) during the reproductive cycle. Péczely P, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):421-30

Corticosterone levels in mice exposed to high-intensity electric fields. Hackman RM, et al. **Behav Neural Biol** 1981 Jun;32(2):201-13

In vitro effect of prostaglandins on corticosterone and aldosterone production by frog interrenal gland. Delarue C, et al. **Biochem Biophys Res Commun** 1981 May 29;100(2):769-77

Effect of escin on adrenocorticotropin and corticosterone levels in rat plasma. Hiai S, et al. **Chem Pharm Bull (Tokyo)** 1981 Feb; 29(2):490-4

Chemical structures and corticosterone secretion-inducing activities of saikosaponins. Yokoyama H, et al. **Chem Pharm Bull (Tokyo)** 1981 Feb; 29(2):500-4

Evaluation of the mineralocorticoid activity of 18-hydroxycorticosterone. Huston G, et al. **Clin Sci** 1981 Aug;61(2):201-6

Serotonin regulation of corticoid secretion in infant rats. Grota LJ. **Dev Psychobiol** 1981 May;14(3):221-8

Modulation of the direct effect of corticosterone upon glucose-induced insulin secretion of rat isolated islets of Langerhans. Billaudel B, et al. **Diabete Metab** 1981 Jun;7(2):91-6

Effect of thyroxine, testosterone, and corticosterone on nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations in adult female mouse submaxillary gland: dissociation of NGF and EGF responses. Walker P, et al. **Endocrinology** 1981 Aug;109(2):582-7

Tissue distribution of 3H-corticosterone in response to stress. Kolta MG, et al. **Endokrinologie** 1981 Apr;77(2):179-84

Effect or partial hepatectomy on secretion and metabolism of corticosterone in the rat. Malendowicz LK, et al. **Endokrinologie** 1981

Mar;77(3):291-6

Response of medial septal neurons to the iontophoretic application of glucocorticoids. Papir-Kricheli D, et al. **Exp Neurol** 1981 Sep; 73(3):801-11

Parenteral feeding abolishes the circadian adrenocortical rhythm in rats. Saito M, et al. **Experientia** 1981 Jul 15;37(7):754-5

The influence of exogenous ACTH on the levels of corticosterone and cortisol in the plasma of young chicks (Gallus domesticus). Kalliecharan R. **Gen Comp Endocrinol** 1981 Jun;44(2):249-51

Chronic and acute stress interrelationship: corticosterone response. Armario A, et al. **Horm Metab Res** 1981 Jul;13(7):413-4

Effects of sodium loading, desoxycorticosterone acetate, and corticosterone on urinary kallikrein excretion. Bönner G, et al. **Horm Res** 1981;14(2):87-94

Circadian periodicity of plasma corticosterone levels in rats subjected to hemorrhagic shock and surgical trauma. Levine RL, et al. **Horm Res** 1980;13(6):385-95

A simultaneous radioimmunoassay for aldosterone and its precursors: human plasma levels following the inhibition of converting enzyme, before and after blockade of prostaglandin biosynthesis. Witzgall H, et al. **J Clin Chem Clin Biochem** 1981 Jun;19(6):387-94

Binding of steroids by proteins in follicular fluid of the human ovary. Martin B, et al. **J Clin Endocrinol Metab** 1981 Aug;53(2):443-7

Protein-bound cyclic AMP and steroidogenesis in the adrenal gland of the rat. Guillemant J, et al. **J Endocrinol** 1981 Jul;90(1):77-82

Effect of glucocorticoids, butanol extraction of serum and adrenalectomy on somatomedin levels in the rat. Holder AT, et al. **J Endocrinol** 1981 Sep;90(3):411-20

Corticosterone catabolism by mouse liver homogenate: strain difference in dependence on added NADP. Shire JG. **J Endocrinol Invest** 1981 Apr-Jun;4(2):193-6

Effects of septic shock plasma on adrenocortical cell function. Keri G, et al. **Life Sci** 1981 Apr 27;28(17):1917-23

The effects of predictable and unpredictable schedules of physical restraint upon rats. Quirce CM, et al. **Life Sci** 1981 Apr 27;28(17):1897-902

Central epinergic inhibition of corticosterone release in rat. Roth KA, et al. **Life Sci** 1981 May 21;28(21):2389-94

Preferential accumulation of [3H] corticosterone in chick brain during embryonic development. Gremo F, et al. **Neurochem Res** 1981 Apr; 6(4):343-51

Effect of intrahypothalamic implantation of cortisone acetate on the onset of circadian corticosterone rhythm in neonatal female rats. Miyabo S, et al. **Neuroendocrinology** 1981 Jul;33(1):47-51

Phase relation between episodic fluctuations of spontaneous locomotor activity and plasma corticosterone in rats with suprachiasmatic nuclei lesions. Watanabe K, et al. **Neuroendocrinology** 1981 Jul;33(1):52-9

Hypothalamic multiunit activity correlates of the adrenocortical response to stress. Ramade F, et al. **Neurosci Lett** 1981 May 29;23(3):297-302

Labelling of Schwann and satellite cells by [3H]dexamethasone in a rat sympathetic ganglion and sciatic nerve. Warembourg M, et al. **Neuroscience** 1981;6(6):1039-43

Corticosterone response in group-housed rats exposed to psychogenic stresses in different social conditions. Armario A, et al. **Physiol Behav** 1981 Jul;27(1):179-81

Locomotor activity, defecation score and corticosterone levels during an openfield exposure: a comparison among individually and group-housed rats, and genetically selected rat lines. Gentsch C, et al. **Physiol Behav** 1981 Jul;27(1):183-6

Humoral indices of stress in rats. Natelson BH, et al. **Physiol Behav** 1981 Jun;26(6):1049-54

Effects of housing on corticosterone rhythm and stress responses in female mice. Nichols DJ, et al. **Physiol Behav** 1981 Jul;27(1):1-5

Circulating levels of corticosterone in the serum of developing chick embryos and newly hatched chicks. Scott TR, et al. **Poult Sci** 1981 Jun;60(6):1314-20

Corticosteroidogenesis in vitro: effects of parathyroid hormone, ACTH, and calcium. Carsia RV, et al. **Proc Soc Exp Biol Med** 1981 Jul; 167(3):402-6

Enzymatic changes in rat thymus after intraperitoneal injections of adrenocorticotrophic hormone and corticosterone. Deschaux P, et al. **Thymus** 1981 Apr;2(6):299-304

Changes in certain diurnal hormonal rhythms in developing male rats exposed to adiurnal environmental cues. Ooka-Souda S. **Mech Ageing Dev** 1981 Mar;15(3):227-33 (eng)

[Effect of calcium and magnesium ions on the interaction of corticosterone with the cytosol receptor(s) in the rat brain] Ueda M. **C R Trav Lab Carlsberg** 1981;175(3):372-6 (Eng. Abstr.) (Fre)

[Reaction between steroid hormones, the liver and its plasma membrane] Denisov IuP, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):722-5 (Eng. Abstr.) (Rus)

CORTICOTROPIN

Immunohistological demonstration of ACTH-like immunoreactivity in the foetal adrenal medulla in the 23rd week of gestation. Ito S, et al. **Acta Endocrinol (Copenh)** 1981;97(3):412-8

beta-Adrenergic stimulation of the release of ACTH- and LPH-related peptides from the pars intermedia of the rat pituitary gland. Tilders FJ, et al. **Acta Endocrinol (Copenh)** 1981;97(3):343-51

Effects of prolonged ACTH treatment on adrenal steroidogenesis and blood pressure in rats. Vazir H, et al. **Acta Endocrinol (Copenh)** 1981 Aug;97(4):533-42

Effects of an ACTH short chain neuropeptide in man. Dornbush RL, et al. **Am J Psychiatry** 1981 Jul;138(7):962-4

Strain differences in pituitary beta-endorphin and ACTH content in inbred mice. Crabbe JC Jr, et al. **Brain Res** 1981 Aug 24; 219(1):219-23

Pineal protein synthesis highly sensitive to ACTH-like neuropeptides. Schotman P, et al. **Brain Res** 1981 Aug 24;219(1):121-35

Ultrastructural immunocytochemical evidence of the presence of a peptide related to ACTH in granules of LHRH nerve terminals in the median eminence of the guinea pig. Beauvillain JC, et al. **Cell Tissue Res** 1981; 218(1):1-6

Immunocytochemistry of luteinizing hormone-releasing hormone, vasopressin, and corticotropin following deafferentation of the basal hypothalamus of the male rat brain. Scott PM, et al. **Cell Tissue Res** 1981;219(2):393-402

Effect of escin on adrenocorticotropin and corticosterone levels in rat plasma. Hiai S, et al. **Chem Pharm Bull (Tokyo)** 1981 Feb; 29(2):490-4

Processing, turnover and release of corticotropins, endorphins and melanotropin in the toad pituitary intermediate lobe. Loh YP. **Ciba Found Symp** 1981;(81):55-78

Comparison of rat anterior and intermediate pituitary in tissue culture: corticotropin (ACTH) and beta-endorphin. Mains RE, et al. **Ciba Found Symp** 1981;(81):32-54

Effects of neonatal ACTH4-10 administration on adult adaptive behavior and brain tyrosine hydroxylase activity. Nyakas C, et al. **Dev Neurosci** 1981;4(3):225-32

Characteristics of the alpha-adrenergic stimulation of adrenocorticotropin secretion in rat anterior pituitary cells. Giguere V, et al. **Endocrinology** 1981 Sep;109(3):757-62

The influence of exogenous ACTH on the levels of corticosterone and cortisol in the plasma of young chicks (Gallus domesticus). Kalliecharan R. **Gen Comp Endocrinol** 1981 Jun;44(2):249-51

Circadian and ultradian variations of ACTH and cortisol secretion. Désir D, et al. **Horm Res** 1980;13(4-5):302-16

The biologic activity of mast cell granules in rat skin: effects of adrenocorticosteroids on late-phase inflammatory responses induced by mast cell granules. Oertel H, et al. **J Allergy Clin Immunol** 1981 Sep; 68(3):238-45

Subcellular fractionation studies on the post-translational processing of pro-adrenocorticotropic hormone/endorphin in rat intermediate pituitary. Glembotski CC. **J Biol Chem** 1981 Jul 25;256(14):7433-9

Long-term treatment of rats with morphine reduces the activity of messenger ribonucleic acid coding for the beta-endorphin/ACTH precursor in the intermediate pituitary. Höllt V, et al. **J Neurochem** 1981 Sep;37(3):619-26

Peptide hormone degradation by a rat mast cell chymase-heparin complex. Jahnke GD, et al. **Life Sci** 1981 Jul 27;29(4):397-403

Parallel stimulation of ACTH, beta-LPH + beta-endorphin and alpha-MSH release by alpha-adrenergic agents in rat anterior pituitary cells in culture. Raymond V, et al. **Mol Cell Endocrinol** 1981 Jun; 22(3):295-303

Reciprocal antagonism between ACTH1-24 and beta-endorphin in rats. Fratta W, et al. **Neurosci Lett** 1981 Jun 12;24(1):71-4

Hypothalamic multiunit activity correlates of the adrenocortical response to stress. Ramade F, et al. **Neurosci Lett** 1981 May 29;23(3):297-302

Muscarinic cholinergic influences on ACTH and beta-endorphin release mechanisms in human subjects. Risch SC, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:95-7

Localization and opiate receptor binding of enkephalin, CCK and ACTH/beta-endorphin in the rat central nervous system. Stengaard-Pedersen K, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:3-19 (53 ref.)

ACTH-induced excessive grooming in the rat. Gispen WH, et al. **Pharmacol Ther [B]** 1981;12(1):209-46 (152 ref.)

Corticosteroidogenesis in vitro: effects of parathyroid hormone, ACTH, and calcium. Carsia RV, et al. **Proc Soc Exp Biol Med** 1981 Jul; 167(3):402-6

Characterization of a 41-residue ovine hypothalamic peptide that stimulates secretion of corticotropin and beta-endorphin. Vale W, et al. **Science** 1981 Sep 18;213(4514):1394-7

Enzymatic changes in rat thymus after intraperitoneal injections of adrenocorticotrophic hormone and corticosterone. Deschaux P, et al. **Thymus** 1981 Apr;2(6):299-304

[Biological and immunological activity similar to digitalis glycosides of synthetic ACTH and some sex hormone 14-hydroxyderivatives (author's transl)] Schreiber V, et al. **Cas Lek Cesk** 1981 May 21; 120(20):616-8 (Eng. Abstr.) (Cze)

[Hypothalamic control of ACTH secretion] Oliver C, et al. **Horm Res** 1980;13(4-5):230-41 (Eng. Abstr.) (Fre)

[ACTH measurement in the hypophysis after adrenalectomy and adrenal

cortex hormone therapy by means of microphotometry and radioimmunoassay method (author's transl)] Lange F. **Microsc Acta** 1981 Jul;84(4):329–37 (Eng. Abstr.) (Ger)
[ACTH, endorphins and related peptides (author's transl)] Imura H, et al. **Tanpakushitsu Kakusan Koso** 1981 Feb;26(2):90–101 (56 ref.) (Jpn)

CORTICOTROPIN RELEASING HORMONE

A different distribution of corticotropin releasing factor and arginine vasopressin contents in the hypothalamic nuclei after estrogen administration. Hashimoto K, et al. **Acta Med Okayama** 1981 Feb; 35(1):37–43
Characterization of corticotropin releasing factor (CRF) and arginine vasopressin in median eminence extracts on sephadex gel-filtration. Hashimoto K, et al. **Endocrinol Jpn** 1981 Feb;28(1):1–7
Corticotropin-releasing factors (CRF) secreted by the rat median eminence in vitro in the presence or absence of ascorbic acid: quantitative role of vasopressin and catecholamines. Bény JL, et al. **Endocrinology** 1981 Sep;109(3):813–7
Dynamics of the formation and release of corticotrophin releasing activity by the rat hypothalamus in vitro. Gillham B, et al. **J Endocrinol** 1981 Aug;90(2):201–10
Studies on the corticotrophin releasing activity of a posterior pituitary extract. Kirkland SC, et al. **J Endocrinol** 1981 Jun;89(3):423–9
Characterization of corticotropin-releasing factor activity from sheep hypothalamic extracts. Jutisz M, et al. **Life Sci** 1981 Jun 15; 28(24):2761–8
Characterization of a 41-residue ovine hypothalamic peptide that stimulates secretion of corticotropin and beta-endorphin. Vale W, et al. **Science** 1981 Sep 18;213(4514):1394–7

CROSS-CULTURAL COMPARISON

[Treatment of schizophrenic patients with clomacran. A transcultural study (author's transl)] Torres Ruiz A, et al. **Arch Neurobiol (Madr)** 1981 Mar-Apr;44(2):117–24 (Eng. Abstr.) (Spa)

CROWDING

Cageing density and dopamine striatal elimination after amphetamine in the rat. Lokiec F, et al. **Psychopharmacology (Berlin)** 1981; 73(4):402–3

DANSYL COMPOUNDS

Hapten-induced changes in pig anti-dansyl antibodies revealed by EPR spectra of spin-labelled antibodies. Käiväräinen AI, et al. **Immunol Lett** 1981 Apr;3(1):5–11

DEPRESSION

Drug treatment of depression in children. Pearce JB. **Acta Paedopsychiatr (Basel)** 1981 Feb;46(5–6):317–28
An experimental study of the clinical judgment of general physicians in evaluating and prescribing for depression. Fisch HU, et al. **Br J Psychiatry** 1981 Feb;138:100–9
Current antidepressant drugs: their clinical use. Hollister LE. **Drugs** 1981 Aug;22(2):129–52 (93 ref.)
Effects of antidepressants in the rat forced swimming test. Kitada Y, et al. **Eur J Pharmacol** 1981 Jun 19;72(2–3):145–52
The significance of secondary depression. Clayton PJ, et al. **J Affective Disord** 1981 Mar;3(1):25–35
Relevance of tryptophan and tyrosine availability in endogenous and 'non-endogenous' depressives treated with imipramine or clomipramine. Møller SE, et al. **J Affective Disord** 1981 Sep;3(3):231–44
Differential effects of cognitive therapy and pharmacotherapy on depressive symptoms. Rush AJ, et al. **J Affective Disord** 1981 Sep; 3(3):221–9
Multicentre depression [editorial] **Lancet** 1981 Sep 12;2(8246):563–4
Amitriptyline and scopolamine in an animal model of depression. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):265–71
Amphetamine and tranylcypromine in an animal model of depression: pharmacological specificity of the reversal effect. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):259–64
Animal model of depression: effects of electroconvulsive shock therapy. Katz RJ. **Neurosci Biobehav Rev** 1981 Summer;5(2):273–7
Further studies on a novel animal model of depression: therapeutic effects of a tricyclic antidepressant. Roth KA, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):253–8
The effect of antidepressants on behavioral despair in rats. Górka Z, et al. **Pol J Pharmacol Pharm** 1980 Jul–Aug;32(4):463–8
Flupenthixol versus combined fluphenazine-nortriptyline in depressive illness. Conway JF. **Practitioner** 1981 Mar;225(1353):400–4
[The treatment of an anxiety - depression syndrome in young women. Report of a case (author's transl)] Leyne P. **Sem Hop Paris** 1981 Jun 18–25;57(25–28):1226–7 (Eng. Abstr.) (Fre)
[Urinary excretion of MHPG in endogenous depression. Clinico-therapeutic index] Roccatagliata G, et al. **Minerva Psichiat** 1981 Apr–Jun;22(2):75–8 (Eng. Abstr.) (Ita
[A diagram illustrating experimental evaluation of psychotropic drug (author's transl)] Brzeziński J. **Psychiatr Pol** 1981 Jan–Feb; 15(1):37–47 (Eng. Abstr.) (Pol
[Changes in the levels of adrenergic and serotoninergic indices in patien with depressive states] Misionzhnik EIu, et al. **Zh Nevropatol Psikhiatr** 1981;81(4):543–51 (Eng. Abstr.) (Rus

DEPRESSIVE DISORDER

The polysymptomatic melancholic as patient in the internist's office. Ros BE. **Acta Med Scand** 1981;209(6):433–6
Drug treatment of depression in children. Pearce JB. **Acta Paedopsychiatr (Basel)** 1981 Feb;46(5–6):317–28
TSH, HGH, HPr, and cortisol response to TRH in depressed patien Ramseier F, et al. **Acta Psychiatr Belg** 1980 Jul–Aug;80(4):399–409
Changes in the electrocardiogram during treatment with tricyclic antidepressant drugs in endogenous depression. Bilikiewicz A, et al **Agressologie** 1979;20(D):287–9
Peripheral metabolism of indoleamines and catecholamines in endogenou depressive syndrome. Puzynski S, et al. **Agressologie** 1979; 20(D):245–51
Clinical experience with some beta blocking agents and their derivatives in endogenous depressions. Svestka J, et al. **Agressologie** 1979; 20(D):295–8
CSF GABA in normal subjects and patients with depressio schizophrenia, mania, and anorexia nervosa. Gerner RH, et al. **Am J Psychiatry** 1981 Aug;138(8):1098–101
Cognitive dysfunction and imipramine in outpatient depressive. Glass RM, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1048–51
Lithium carbonate in the treatment of acute depressive illness. Khan MC **Bibl Psychiatr** 1981;(161):244–8
Memory performances in depressed patients during prophylactic treatme with lithium salts. Zerbi F, et al. **Bibl Psychiatr** 1981;(161):190–6
Blood platelets and psychiatry. Campbell IC. **Br J Psychiatry** 1981 Jan; 138:78–80
A pilot study of the mechanism of action of desipramine. Checkley SA, et al. **Br J Psychiatry** 1981 Mar;138:248–51
Lithium induces rapid relief of depression in tricyclic antidepressant drug non-responders. Dé Montigny C, et al. **Br J Psychiatry** 1981 Mar; 138:252–6
Constructs and 'conflict' in depression. Sheehan MJ. **Br J Psychol** 1981 May;72(Pt 2):197–209
The new psychiatry [editorial] **Br Med J [Clin Res]** 1981 Aug 22; 283(6290):513–4
Psychodynamic aspects in the use of monoamine oxidase inhibito antidepressants. Roskos SR, et al. **Bull Menninger Clin** 1981 Mar; 45(2):143–8
Elderly depressives: treatment and follow-up. Gordon WF. **Can J Psychiatry** 1981 Mar;26(2):110–3
Pharmacokinetics and efficacy of maprotiline and amitriptyline i endogenous depression: a double-blind controlled trial. Montgomery SA, et al. **Clin Ther** 1980;3(4):292–310
Comparison of midday serum dopamine-beta-hydroxylase activity i depressed patients and normal controls. Nasr S, et al. **Commun Psychopharmacol** 1980;4(4):263–7
Trazodone: a review of its pharmacological properties and therapeutic use in depression and anxiety. Brogden RN, et al. **Drugs** 1981 Jun; 21(6):401–29 (156 ref.)
Current antidepressant drugs: their clinical use. Hollister LE. **Drugs** 1981 Aug;22(2):129–52 (93 ref.)
Multicentre study with viloxazine (Vivalan) in depressed patients. Kabe J, et al. **Int Pharmacopsychiatry** 1980;15(4):228–39
A double-blind multicentre trial comparing the efficacy and side-effects of mianserin and chlorimipramine in depressed in- and outpatients. Pinder RM, et al. **Int Pharmacopsychiatry** 1980;15(4):218–27
Trazodone in depression. Wheatley D. **Int Pharmacopsychiatry** 1980; 15(4):240–6
Cerebrospinal fluid amine metabolites, tryptophan and clinical parameters in depression. Part 1. Background variables. Banki CM, et al. **J Affective Disord** 1981 Jun;3(2):81–9
Relevance of tryptophan and tyrosine availability in endogenous an 'non-endogenous' depressives treated with imipramine or clomipram Møller SE, et al. **J Affective Disord** 1981 Sep;3(3):231–44
The activity of the lithium—sodium countertransport system i erythrocytes in depression and mania. Rybakowski J, et al. **J Affective Disord** 1981 Mar;3(1):59–64
Comparison of molindone and tranylcypromine in the treatment o refractory depression. Small JG, et al. **J Clin Pharmacol** 1981 Aug-Sep; 21(8–9):351–8
Refractory depression: prediction of non-response by clinical indicators. Kupfer DJ, et al. **J Clin Psychiatry** 1981 Aug;42(8):307–12
Amoxapine: once versus divided daily doses in neurotic and endogeno depression. Ragheb M, et al. **J Clin Psychiatry** 1981 Aug; 42(8):318–21
CSF-MHPG in depressive syndromes: basal values and

imipramine-induced modifications. Roccatagliata G, et al. **Neuropsychobiology** 1981;7(4):169–71

Animal models and human depressive disorders. Katz RJ. **Neurosci Biobehav Rev** 1981 Summer;5(2):231–46 (243 ref.)

Influence of unilateral ECT on tryptophan metabolism in endogenous depression. Smith DF, et al. **Pharmacopsychiatria** 1981 Jul; 14(4):135–8

Management of depressive neurosis. Shaw SH. **Practitioner** 1981 Feb; 225(1352):228–30

Decreased tryptophan availability in endogenous depression caused by disturbed plasma leucine clearance. Møller SE, et al. **Prog Neuropsychopharmacol** 1981;5(3):277–9

Electroconvulsive therapy in the medically ill patient. Bidder TG. **Psychiatr Clin North Am** 1981 Aug;4(2):391–405 (60 ref.)

Depression in the medically ill. Klerman GL. **Psychiatr Clin North Am** 1981 Aug;4(2):301–17

Effect of carbamazepine on CSF opioid activity; relationship to antidepressant response. Post RM, et al. **Psychiatry Res** 1981 Aug; 5(1):59–66

Relationship between urinary free cortisol and CSF opioid binding activity in depressed patients and normal volunteers. Rubinow DR, et al. **Psychiatry Res** 1981 Aug;5(1):87–93

Treatment validity of different diagnostic concepts of depression. Zisook S, et al. **Psychiatry Res** 1981 Aug;5(1):77–85

Continuation therapy with lithium and amitriptyline in unipolar depressive illness: a controlled clinical trial. A report by the Medical Research Council Drug Trials Subcommittee. **Psychol Med** 1981 May; 11(2):409–16

Monoamine oxidase inhibitor efficacy in depression and the 'cheese effect'. Sandler M. **Psychol Med** 1981 Aug;11(3):455–8

[Results of the clinical trial with nomifensine (author's transl)] Kabeš J, et al. **Cesk Psychiatr** 1981 Feb;77(1):42–9 (Eng. Abstr.) (Cze)

[Pyrazidole in the treatment of endogenous depression: controlled study (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Feb; 77(1):31–7 (Eng. Abstr.) (Cze)

[Biochemical aspects of depression (author's transl)] Duchemin AM. **Sem Hop Paris** 1981 Apr 18–25;57(15–16):745–50 (Eng. Abstr.) (Fre)

[Planning the treatment of depressive states with psychopharmaceuticals] Guensberger E, et al. **Agressologie** 1979;20(D):315–8 (Eng. Abstr.) (Ger)

[Noveril in depression] Medvecký J, et al. **Agressologie** 1979; 20(D):311–2 (Eng. Abstr.) (Ger)

[Noveril in high doses in the treatment of depression] Molcan J, et al. **Agressologie** 1979;20(D):307–9 (Eng. Abstr.) (Ger)

[Tisocromid, a psychopharmaceutical with antidepressive action] von Littrow C. **Agressologie** 1979;20(D):299–302 (Ger)

[Duration of prophylactic medication with antidepressives] Pöldinger W. **Bibl Psychiatr** 1981;(161):237–43 (Ger)

[Enduring structure of the 'depressive personality' in lithium prophylaxis. With special reference to the social partners] Schuster P, et al. **Bibl Psychiatr** 1981;(161):170–8 (Eng. Abstr.) (Ger)

[Depression in rheumatic diseases or somatic symptoms in depression] Carrière B. **Fortschr Med** 1981 Aug 27;99(31–32):1226–30 (Eng. Abstr.) (Ger)

[Depression, somatization, suicide. Part 2: Masked depression, suicide] Hertrich O. **Fortschr Med** 1981 Jul 2;99(25):973–7 (Ger)

[Nomifensin-induced immune haemolytic anaemias (author's transl)] Eckstein R, et al. **Klin Wochenschr** 1981 Jun 1;59(11):567–9 (Eng. Abstr.) (Ger)

[Influence of thioridazine on cognitive, psychomotor, and reaction performance in patients with dysthymic-depressive syndrome (author's transl)] Meyer FP, et al. **Pharmacopsychiatria** 1981 May;14(3):94–9 (Ger)

[Clinical investigation comparing trazodone and clomipramine] Lange E, et al. **Psychiatr Neurol Med Psychol (Leipz)** 1980 Dec;32(12):748–50 (Ger)

[Tricyclics, MAOI and electroshock therapy in the treatment of depressive syndromes] Carolei A, et al. **Clin Ter** 1981 Jul 15;98(1):75–86 (29 ref.) (Ita)

[Third-generation antidepressive agents. Experience with 100 cases of primary depression treated with viloxazine, nomifensine and mianserin] Faravelli C, et al. **Minerva Psichiatr** 1981 Apr–Jun;22(2):79–83 (Eng. Abstr.) (Ita)

[Clinical experience with treatment of depressions by nomiphenzine (author's transl)] Pogády J, et al. **Cesk Psychiatr** 1981 Feb; 77(1):11–6 (Eng. Abstr.) (Slo)

DESIPRAMINE

Concentrations of desipramine in elderly women. Cutler NR, et al. **Am J Psychiatry** 1981 Sep;138(9):1235–7

A pilot study of the mechanism of action of desipramine. Checkley SA, et al. **Br J Psychiatry** 1981 Mar;138:248–51

Plasma concentration monitoring of hydroxylated metabolites of imipramine and desipramine. DeVane CL, et al. **Drug Intell Clin Pharm** 1981 Apr;15(4):263–6

Interaction of desipramine and amitriptyline with adrenergic mechanisms in the human iris in vivo. Szabadi E, et al. **Eur J Clin Pharmacol** 1981; 19(6):403–8

High-affinity [3H] DMI binding is associated with neuronal noradrenaline uptake in the periphery and the central nervous system. Langer SZ, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):423–4

Simultaneous determination of imipramine, desipramine, and their 2-hydroxy metabolites in plasma by ion-pair reversed-phase high-performance liquid chromatography with amperometric detection. Suckow RF, et al. **J Pharm Sci** 1981 Mar;70(3):257–61

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633–9

Prediction of steady state plasma and saliva levels of desmethylimipramine using a single dose, single time point procedure. Cooper TB, et al. **Psychopharmacology (Berlin)** 1981;74(2):115–21

Supersensitivity to L-5-hydroxytryptophan after 5,7-dihydroxytryptamine injections in desmethylimipramine- and nomifensine-pretreated rats: behavioral evidence for postsynaptic supersensitivity. Ortmann R, et al. **Psychopharmacology (Berlin)** 1981; 74(2):109–14

DESOXYCORTICOSTERONE

Effect of cortisol, deoxycorticosterone and 19-nortestosterone on the gametogenesis of the snail Helix pomatia. Csaba G, et al. **Acta Biol Acad Sci Hung** 1981;32(1):15–8

Inner medullary osmolality and sodium concentration are decreased in rats during escape from DOCA-induced salt retention. Düsing R, et al. **Clin Sci** 1981 Apr;60(4):467–9

Effects of sodium loading, desoxycorticosterone acetate, and corticosterone on urinary kallikrein excretion. Bönner G, et al. **Horm Res** 1981;14(2):87–94

A simultaneous radioimmunoassay for aldosterone and its precursors: human plasma levels following the inhibition of converting enzyme, before and after blockade of prostaglandin biosynthesis. Witzgall H, et al. **J Clin Chem Clin Biochem** 1981 Jun;19(6):387–94

[Histochemical localization of Na+, K+-ATPase in rat submandibular gland. The effects of mineralocorticoid and sodium ion (author's transl)] Kida T, et al. **Josai Shika Daigaku Kiyo** 1980;(9):155–8 (Eng. Abstr.) (Jpn)

DEXTROAMPHETAMINE

Amphetamine behavioral toxicity: rotational behavior after chronic intrastriatal infusion. Dougherty GG Jr, et al. **Biol Psychiatry** 1981 May; 16(5):479–88

Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Solomon PR, et al. **Biol Psychiatry** 1981 Jun; 16(6):519–37

The acquisition of responding with conditioned reinforcement: effects of cocaine, (+)-amphetamine and pipradrol. Beninger RJ, et al. **Br J Pharmacol** 1981 Sep;74(1):149–54

Cocaine cue in pigeons: time course studies and generalization to structurally related compounds (norcocaine, WIN 35,428 and 35,065-2) and (+)-amphetamine. Järbe TU. **Br J Pharmacol** 1981 Aug; 73(4):843–52

Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Menniti FS, et al. **Brain Res** 1981 Jul 6; 216(1):89–107

Detailed analysis of the effects of apomorphine and d-amphetamine on spontaneous locomotor behaviour of rats as measured in a TV-based, automated open-field system. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):45–56

The regional distribution of d-amphetamine and local glucose utilization in rat brain during continuous amphetamine administration. Eison MS, et al. **Exp Brain Res** 1981;43(3–4):281–8

Application of chiral lanthanide nuclear magnetic resonance shift reagents to pharmaceutical analysis. II. Determination of dextro- and levoamphetamine mixtures. Wainer IW, et al. **J Assoc Off Anal Chem** 1981 Jul;64(4):848–50

Neuronal responses of the globus pallidus to systemic administration of d-amphetamine: investigation of the involvement of dopamine, norepinephrine, and serotonin. Bergstrom DA, et al. **J Neurosci** 1981 Mar;1(3):292–9

Behavioral and neurochemical interactions of dextroamphetamine and methylphenidate in rats. Reigle TG, et al. **J Pharm Sci** 1981 Jul; 70(7):816–8

3H-amphetamine concentrations in the brains of young and aged rats: implications for assessment of drug effects in aged animals. Truex LL, et al. **Neurobiol Aging** 1980 Summer;1(1):93–5

Effects of chronic amphetamine treatment on the glutamate concentration in cerebrospinal fluid and brain: implications for a theory of schizophrenia. Kim JS, et al. **Neurosci Lett** 1981 Jun 12;24(1):93–6

Post-amphetamine depression of self-stimulation behavior in rats: prophylactic effects of lithium. Predy PA, et al. **Neurosci Lett** 1981

May 29;23(3):343–7

Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. van Kammen DP, et al. **Psychiatry Res** 1981 Jun;4(3):313–25

Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Leith NJ, et al. **Psychopharmacology (Berlin)** 1981;74(1):23–8

Cageing density and dopamine striatal elimination after amphetamine in the rat. Lokiec F, et al. **Psychopharmacology (Berlin)** 1981; 73(4):402–3

Effect of chronic amphetamine administration on central dopaminergic mechanisms in the vervet. Owen F, et al. **Psychopharmacology (Berlin)** 1981;74(3):213–6

DIAZEPAM

Alterations in human memory following acute maprotiline, diazepam and codeine administration. Liljequist R, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Feb;48(2):190–2

Effect of gamma-vinyl GABA alone or associated with diazepam on a conflict test in the rat. Huot S, et al. **Adv Biochem Psychopharmacol** 1981;29:45–52

Promotion of intramuscular diazepam questioned [letter] Watson DM, et al. **Am J Hosp Pharm** 1981 Jul;38(7):968, 970–1

Hazards of mistaking haloperidol for diazepam [letter] Nininger JE, et al. **Am J Psychiatry** 1981 Aug;138(8):1130

Effect of propranolol on circulatory responses to induction of diazepam-nitrous oxide anesthesia and to endotracheal intubation. McCammon RL, et al. **Anesth Analg (Cleve)** 1981 Aug;60(8):579–83

Interaction of depressant, convulsant, and anticonvulsant barbiturates with the [3H]diazepam binding site of the benzodiazepine-GABA-receptor-ionophore complex. Ticku MK. **Biochem Pharmacol** 1981 Jun 15;30(12):1573–9

Clinical evaluation of diazepam for relief of postoperative pain. Singh PN, et al. **Br J Anaesth** 1981 Aug;53(8):831–6

Effects of phenytoin on [3H]diazepam binding in dissociated primary cortical cell culture. Gallager DW, et al. **Brain Res** 1981 Aug 10; 218(1–2):319–30

Ethyl beta-carboline-3-carboxylate antagonizes the action of GABA and benzodiazepines in the hippocampus. Polc P, et al. **Brain Res** 1981 Jul 27;217(1):216–20

Diazepam binding of dissociated hippocampal cultures from fetal mice. Walker CR, et al. **Brain Res** 1981 Jul;227(4):565–78

Benzodiazepine binding and interactions with the GABA receptor complex in living cultures of rat cerebral cortex. White WF, et al. **Brain Res** 1981 Jun 29;215(1–2):162–76

Effects of diazepam on body temperature of the aged squirrel monkey. Clark SM, et al. **Brain Res Bull** 1981 Jul;7(1):5–9

Estimation of diazepam adsorbed on glass surfaces and silicone-coated surfaces as models of surfaces of containers. Mizutani T, et al. **Chem Pharm Bull (Tokyo)** 1981 Apr;29(4):1182–3

Promethazine and diazepam potentiate the haloperidol induced prolactin responses. Arató M. **Commun Psychopharmacol** 1980;4(4):317–22

Drug-specific EEG frequency spectra and their time courses produced in the cat by antidepressants and a benzodiazepine. Fairchild MD, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jul;52(1):81–8

3-hydroxymethyl-beta-carboline antagonizes some pharmacologic actions of diazepam. Skolinick P, et al. **Eur J Pharmacol** 1981 Feb 19; 69(4):525–7

Comparative protein binding of diazepam and desmethyldiazepam. Allen MD, et al. **J Clin Pharmacol** 1981 May–Jun;21(5–6):219–23

Multicenter double-blind efficacy and safety study comparing alprazolam, diazepam and placebo in clinically anxious patients. Cohn JB. **J Clin Psychiatry** 1981 Sep;42(9):347–51

Altered drug binding to serum proteins in pregnant women: therapeutic relevance. Perucca E, et al. **J R Soc Med** 1981 Jun;74(6):422–6

Norharman inhibition of [3H]diazepam binding in mouse brain. Morin AM, et al. **Life Sci** 1981 May 18;28(20):2257–63

Diazepam and driving ability. Landauer AA. **Med J Aust** 1981 Jun 13; 1(12):624–6

Pentobarbital enhances [3H]diazepam binding to soluble receptors at the benzodiazepine--GABA-receptor-ionophore complex. Davis WC, et al. **Neurosci Lett** 1981 May 6;23(2):209–13

Fibre-optic gastroscopy and intravenous diazepam: their combined effect on arterial oxygen saturation. Harrison RN, et al. **Pharmatherapeutica** 1981;2(9):565–7

Effect of chloro-N-desmethyldiazepam on serum and brain tryptophan and serotonin in relation to the activity of central serotonergic neurons. Valzelli L, et al. **Pol J Pharmacol Pharm** 1981 Jan–Feb;33(1):37–42

A multicenter controlled trial in phobic-obsessive psychoneurosis. The effect of chlorimipramine and of its combinations with haloperidol and diazepam. Cassano GB, et al. **Prog Neuropsychopharmacol** 1981; 5(2):129–38

Effects of diazepam on operant behavior in man. Carlton PL, et al. **Psychopharmacology (Berlin)** 1981;73(4):314–7

Psychomotor performance and real driving performance of outpatients receiving diazepam. de Gier JJ, et al. **Psychopharmacology (Berlin)** 1981; 73(4):340–4

The effect of chronic diazepam treatment on discrimination performance and 3H-flunitrazepam binding in the brains of shocked and nonshocked rats. Grimm VE, et al. **Psychopharmacology (Berlin)** 1981; 74(2):132–6

Pre-exposure effects of morphine, diazepam and delta 9-THC on the formation of conditioned taste aversions. Switzman L, et al. **Psychopharmacology (Berlin)** 1981;74(2):149–57

Diazepam-cimetidine drug interaction: a clinically significant effect. Ruffalo RL, et al. **South Med J** 1981 Sep;74(9):1075–8 (20 ref.)

Diazepam-induced neural tube closure defects in explanted early chick embryos. Nagele RG, et al. **Teratology** 1981 Jun;23(3):343–9

The effect of diazepam on meiosis in the CF-1 mouse. Stenchever MA, et al. **Teratology** 1981 Apr;23(2):279–81

[Interrelationship of the tranquilizers diazepam and lonetil with dopamine mediation in the central nervous system] Ovcharov R, et al. **Eksp Med Morfol** 1981;20(2):88–96 (Eng. Abstr.) (Bul)

[Diazepam levels in the ventricular cerebrospinal fluid and peripheral venous blood in man] Boulard G, et al. **Ann Anesthesiol Fr** 1981; 22(2):185–90 (Eng. Abstr.) (Fre)

[Comparative pharmacokinetics of diazepam and flunitrazepam] Cano JP, et al. **Ann Anesthesiol Fr** 1981;22(2):175–9 (Eng. Abstr.) (Fre)

[Physico-chemical study of diazepam and hydrophilic excipients interaction (author's transl)] Neamtu M, et al. **Ann Pharm Fr** 1980; 38(6):507–11 (Eng. Abstr.) (Fre)

[Clinical pharmacokinetics of midazolam, flunitrazepam and diazepam (author's transl)] Lauven PM, et al. **Anaesth Intensivther Notfallmed** 1981 Jun;16(3):135–42 (Eng. Abstr.) (Ger)

[Plasma levels following high diazepam doses in intensive-care medicine (author's transl)] Ochs HR. **Anaesth Intensivther Notfallmed** 1981 Jun; 16(3):143–4 (Eng. Abstr.) (Ger)

[A floating capsule with slow release of drugs: a new method of oral drug medication (author's transl)] Müller-Lissner SA, et al. **Dtsch Med Wochenschr** 1981 Sep 4;106(36):1143–7 (Eng. Abstr.) (Ger)

[Effects of diazepam and thiamylal on reticular multi-unit activity, visual evoked responses, EEG and arterial blood pressure in rabbits (author's transl)] Ueda Y. **Nippon Geka Hokan** 1980 Sep 1;49(5):595–607 (Eng. Abstr.) (Jpn)

[Effect of GABA-negative preparations on the anxiolytic and sedative effects of diazepam] Andreev BV, et al. **Biull Eksp Biol Med** 1981 Jun; 91(6):685–7 (Eng. Abstr.) (Rus)

DIBENZAZEPINES

Differential actions of mianserin and iprindole on the sensitivity of cortical neurons to noradrenaline: effect of chronic treatment. Olpe HR, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):381–5

A double-blind multicentre trial comparing the efficacy and side-effects of mianserin and chlorimipramine in depressed in- and outpatients. Pinder RM, et al. **Int Pharmacopsychiatry** 1980;15(4):218–27

Clozapine inhibition of metenkephalin binding to synaptosome-enriched fractions of rat whole brain and hippocampus. Somoza E, et al. **Neurochem Res** 1981 Apr;6(4):413–24

The effect of imipramine and mianserin on the behavior and EEG afterdischarges induced by single electric stimulation of the rabbit amygdala. Ossowska K, et al. **Pol J Pharmacol Pharm** 1980 Jul–Aug; 32(4):513–22

Differences in presynaptic alpha-blockade, noradrenaline uptake inhibition, and potential antidepressant activity between (+)- and (-)mianserin. Schoemaker H, et al. **Psychopharmacology (Berlin)** 1981; 74(2):137–42

[Noveril in depression] Medvecký J, et al. **Agressologie** 1979; 20(D):311–2 (Eng. Abstr.) (Ger)

[Noveril in high doses in the treatment of depression] Molcan J, et al. **Agressologie** 1979;20(D):307–9 (Eng. Abstr.) (Ger)

[Hemoperfusion and forced diuresis in dibenzepine poisoning (letter)] Vlachoyannis J, et al. **Dtsch Med Wochenschr** 1981 Oct 2; 106(40):1314–5 (Ger)

[Alkylation of 6-benzyl-5H-dibenzo(d,f)-(1,3)diazepine] Boido A, et al. **Boll Soc Ital Biol Sper** 1981 Apr 15;57(7):759–65 (Eng. Abstr.) (Ita)

[Third-generation antidepressive agents. Experience with 100 cases of primary depression treated with viloxazine, nomifensine and mianserin] Faravelli C, et al. **Minerva Psichiatr** 1981 Apr–Jun;22(2):79–83 (Eng. Abstr.) (Ita)

[The most common complications in neuroleptic therapy. A case report] Preradović M. **Vojnosanit Pregl** 1981 May–Jun;38(3):211–2 (Ser)

DIBENZOTHIEPINS

Further clinical experiences with optical isomers of the L and D clorothepin. Náhunek K, et al. **Agressologie** 1979;20(D):275–8

Reduction of octoclothepine-N-oxide by rat liver microsomes. Helia O, et al. **Eur J Drug Metab Pharmacokinet** 1981;6(2):155–8

Effects of microinjection of 2-chloro-11 (2-dimethylaminoethoxy)-dibenzo[b,f]-thiepine (zotepine), thioridazine and haloperidol into the striatum and nucleus accumbens on stereotypic

behaviour and motor activity. Lai H, et al. **J Pharm Pharmacol** 1981 Apr;33(4):252-4
[Effects of the intraventricular injection of methiothepin and methergoline on the sleep of rats] Laguzzi R. **C R Soc Biol (Paris)** 1981; 175(2):160-3 (Eng. Abstr.) **(Fre)**

DIBENZOXAZEPINES

Physostigmine in amoxapine overdose [letter] Ross SR, et al. **Am J Hosp Pharm** 1981 Aug;38(8):1121-2
Very high dose loxapine in refractory schizophrenic patients. Lehmann CR, et al. **Am J Psychiatry** 1981 Sep;138(9):1212-4
Acutely ill schizophrenic patients treated with loxapine. A clinical study in a community mental health center. Rasul M. **Clin Ther** 1980; 3(4):242-9
Amoxapine: once versus divided daily doses in neurotic and endogenous depression. Ragheb M, et al. **J Clin Psychiatry** 1981 Aug; 42(8):318-21
The effects of amoxapine and ethanol on psychomotor skills related to driving: a placebo and standard controlled study. Wilson WH, et al. **Prog Neuropsychopharmacol** 1981;5(3):263-70
Treatment validity of different diagnostic concepts of depression. Zisook S, et al. **Psychiatry Res** 1981 Aug;5(1):77-85

DIIODOTYROSINE

Experimental study of hormone receptor development in a unicellular model system. Csaba G, et al. **Exp Cell Biol** 1981;49(3):173-6

DISCRIMINATION LEARNING

Changes in brain biogenic amines in cats performing a symmetrically reinforced go-nogo visual discrimination task. Kitsikis A, et al. **Behav Neural Biol** 1981 Jun;32(2):133-47
Effects of pentobarbital on delayed alternation performance. Terry WS, et al. **Behav Neural Biol** 1981 Jul;32(3):380-5
Age and neurochemical correlates of radial maze performance in rats. Ingram DK, et al. **Neurobiol Aging** 1981 Spring;2(1):41-7

DOPA

Rapid and simple analysis of DOPA and 5-HTP using high performance liquid chromatography with electrochemical detection. Arnerić SP, et al. **Brain Res Bull** 1981 May;6(5):407-11
Monoamine precursor uptake in ganglia of a mollusc Anodonta cygnea L. (Bivalvia) An autoradiographic and ultrastructural study. Elekes K. **Cell Tissue Res** 1981;219(2):403-15
Endogenous dopa in rat brain. Occurrence, distribution and relationship to changes i catecholamine synthesis. Thiede HM, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jul;316(4):299-303
[Interaction of dihydroxyphenylalanine with the acid proteins of rat brain chromatin] Tret'iak TM, et al. **Dokl Akad Nauk SSSR** 1981; 257(5):1262-4 **(Rus)**

DOPAMINE

Interaction at the synaptic level of fusaric acid with neurotransmitters. Fischer HD, et al. **Acta Biol Med Ger** 1980;39(8-9):935-40
Further studies of the chemical sensitivity of the oscillatory potentials of the electroretinogram (ERG). II. Glutamate-aspartate-and dopamine antagonists. Wachtmeister L. **Acta Ophthalmol (Copenh)** 1981 Apr; 59(2):247-58
Density of amine accumulating neurons in rabbit and guinea-pig retina. Ehinger B, et al. **Acta Physiol Scand** 1981 May;112(1):111-2
Dopamine uptake in platelets: two different low-affinity, saturable mechanisms. Lingjaerde O, et al. **Agents Actions** 1981 Jul; 11(4):410-6
A functional analysis of dopaminergic innervation of the neurohypophysis. Passo SS, et al. **Am J Physiol** 1981 Sep;241(3):E186-90
Reverse-phase high-performance liquid chromatographic separation and electrochemical detection of norepinephrine, dopamine, serotonin, and related major metabolites. Kempf E, et al. **Anal Biochem** 1981 Apr; 112(2):223-31
Application of high-performance liquid chromatography with a chemiluminescence detection system to determine catecholamines in urine. Kobayashi S, et al. **Anal Biochem** 1981 Mar 15;112(1):99-104
Effect of neonatal administrations of 6-OHDA on the brain development. I. Alteration in the striatum. Imamoto K, et al. **Arch Histol Jpn** 1980 Oct;43(4):347-64
The influence of dopamine and dopaminergic agonists on the contractions of field stimulated rat vas deferens. György L, et al. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):55-64
An analysis of the effects of apomorphine and haloperidol on the release of [3H]-dopamine and [3H]-noradrenaline from rabbit brain slices. Kelly MJ. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):18-29
Effects of intracerebroventricular administration of dopamine and metoclopramide on blood pressure in rats. Kondo K, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):273-8
Analysis of responses to dopamine in the mesenteric vascular bed of the cat. Lippton HL, et al. **Arch Int Pharmacodyn Ther** 1981 May; 251(1):136-49
Effects of dopamine and its antagonist domperidone cannot be explained by an effect on alpha 1-adrenergic receptors. Schuurkes JA, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):324-7
Barrel rotation induced by vasopressin and involvement of dopaminergic and cholinergic functions in rats. Yamada K, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):88-94
Striatal dopamine turnover and L-dopa treatment after short-term exposure of rats to manganese. Shukla GS, et al. **Arch Toxicol** 1981 Jun;47(3):191-6
High-affinity stereospecific binding of 3H-dopamine in rat brain: interaction with endogenous dopamine. Bacopoulos NG. **Biochem Pharmacol** 1981 Jul 15;30(14):2037-40
Amfonelic acid antagonism of dopamine and norepinephrine depletion by alpha-methyl-m-tyrosine in rat brain. Fuller RW, et al. **Biochem Pharmacol** 1981 Jul 15;30(14):2025-6
Changes in plasma catecholamine concentrations during endotracheal intubation. Russell WJ, et al. **Br J Anaesth** 1981 Aug;53(8):837-9
Evidence for an inhibitory presynaptic component of neuroleptic drug action. de Belleroche JS, et al. **Br J Pharmacol** 1981 Mar; 72(3):427-33
Dopamine-like properties of ephedrine in rat brain. Zarrindast MR. **Br J Pharmacol** 1981 Sep;74(1):119-22
Positive and negative schizophrenic symptoms and the role of dopamine [letter] Ashcroft GW, et al. **Br J Psychiatry** 1981 Mar;138:268-9
Dopamine hypothesis in acute psychosis [letter] Marsden CD. **Br J Psychiatry** 1981 Mar;138:269-70
Differential effects of gonadal steroids on dopamine metabolism in mesolimbic and nigro-striatal pathways of male rat brain. Alderson LM, et al. **Brain Res** 1981 Aug 10;218(1-2):189-206
Modulation of slow postsynaptic potentials by dopamine, in rabbit sympathetic ganglion. Ashe JH, et al. **Brain Res** 1981 Jul 27; 217(1):93-106
Mesocortical dopamine neurons: rapid transmitter turnover compared to other brain catecholamine systems. Bannon MJ, et al. **Brain Res** 1981 Aug 10;218(1-2):376-82
The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Coote JH, et al. **Brain Res** 1981 Jun 29;215(1-2):135-45
Release of endogenous catecholamines from slices of hypothalamus of rats. Hamlet MA, et al. **Brain Res** 1981 Aug 3;217(2):315-25
Opposite changes in dopamine utilization in the nucleus accumbens and the frontal cortex after electrolytic lesion of the median raphe in the rat. Herve D, et al. **Brain Res** 1981 Jul 20;216(2):422-8
Puberty of female rats may in part be explained by decreased hypothalamic dopamine receptor sensitivity. Lamberts R, et al. **Brain Res** 1981 Jun 29;215(1-2):375-81
Release of somatostatin from extra-hypothalamic rat brain slices: inhibition by dopamine and morphine. Lee CM, et al. **Brain Res** 1981 Aug 31;219(2):355-61
Chemical deafferentation of the olfactory bulb: plasticity of the levels of tyrosine hydroxylase, dopamine and norepinephrine. Nadi NS, et al. **Brain Res** 1981 Jun 1;213(2):365-77
High resolution radioautography of central dopaminergic fibers labelled in vitro with [3H]dopamine or [3H]norepinephrine. Nguyen-Legros J, et al. **Brain Res** 1981 Jun 1;213(2):265-76
Selective activation of tuberoinfundibular dopaminergic neurons in the chronically restrained rat. Seegal RF. **Brain Res** 1981 Jul 20; 216(2):460-5
Differential functional ontogeny of dopamine presynaptic receptor regulation. Shalaby IA, et al. **Brain Res** 1981 Jun;227(3):434-9
Changes in dopamine and DOPAC following systemic administration of apomorphine and 3,4-dihydroxyphenylamino-2-imidazoline (DPI) in rats. Springer J, et al. **Brain Res** 1981 Sep 7;220(1):226-30
Effects of ventral tegmental area stimulation and microiontophoretic application of dopamine and norepinephrine on hypothalamic neurons. Barone FC, et al. **Brain Res Bull** 1981 Aug;7(2):181-93
Secretion of hypothalamic dopamine into pituitary stalk blood of aged female rats. Reymond MJ, et al. **Brain Res Bull** 1981 Jul;7(1):69-73
Catecholamines and 5-hydroxytryptamine in photophores of Porichthys notatus. Radioenzymatic detection and radioautographic localization. Anctil M, et al. **Cell Tissue Res** 1981;219(3):557-66
In normal young men acute dopaminergic blockade does not impair free water excretion following a standard water load. Cohen M, et al. **Commun Psychopharmacol** 1980;4(4):323-6
Activation of adenylate cyclase in rat striatum by an ergoline dopamine agonist, pergolide. Wong DT, et al. **Commun Psychopharmacol** 1980; 4(4):269-75
Dilated fixed pupils due to administration of high doses of dopamine hydrochloride. Ong GL, et al. **Crit Care Med** 1981 Sep;9(9):658-9
3-O-methyl-alpha-methyldopamine, a urinary metabolite of p-methoxyamphetamine in dog and monkey. Hubbard JW, et al. **Drug Metab Dispos** 1981 May-Jun;9(3):250-4
Intraventricular administration of vasopressin and oxytocin effects the

steady-state levels of serotonin, dopamine and norepinephrine in rat brain. Schwarzberg H, et al. **Endocrinol Exp (Bratisl)** 1981; 15(2):75–80

Dopaminergic and serotonergic involvement in opiate-induced prolactin release in monkeys. Wehrenberg WB, et al. **Endocrinology** 1981 Aug; 109(2):544–7

Clinical tolerability of ibopamine hydrochloride (SB 7505). Melloni GF, et al. **Eur J Clin Pharmacol** 1981;19(6):409–11

Pharmacological studies with several analogs of mazindol: correlation between effects on dopamine uptake and various in vivo responses. Heikkila RE, et al. **Eur J Pharmacol** 1981 May 8;71(2–3):277–86

Behavioral effects of unilateral dopamine injection into dorsal or ventral striatum. Joyce JN, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):1–10

Differential effects of dopamine agonists in mature and immature rats. McDevitt JT, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):69–75

Endogenous alpha-melanotropin and central dopamine systems in physical and psychological stress. Monnet F, et al. **Exp Brain Res** 1981; 42(2):203–11

Effect of dopamine agonists and antagonists on the electrical activity of substantia nigra neurons transplanted into the lateral ventricle of the rat. Wuerthele SM, et al. **Exp Brain Res** 1981;44(1):1–10

3-Hydroxy-4-methoxyphenethylamine, the cardioactive constituent of a soft coral. Gregson RP, et al. **Experientia** 1981 May 15;37(5):493–4

The acute effects of sulpiride on the central dopamine turnover in rats: a quantitative histochemical study. Yoshida M, et al. **Experientia** 1981 May 15;37(5):491–2

Effects of exposure to trichloroethylene and tetrachloroethylene on the contents of acetylcholine, dopamine, norepinephrine and serotonin in rat brain. Honma T, et al. **Ind Health** 1980;18(4):171–8

Effects of dopamine on chemoreflexes in breathing. Nishino T, et al. **J Appl Physiol** 1981 Apr;50(4):892–7

Stereospecific antagonism by d-butaclamol of dopamine-induced relaxation of the isolated rabbit mesenteric artery. Brodde OE, et al. **J Cardiovasc Pharmacol** 1981 Jul–Aug;3(4):828–37

Studies on dopamine-converting enzymes in human plasma. Allenmark S, et al. **J Chromatogr** 1981 Apr 10;223(1):188–92

Effects of L-dopa on dopamine and norepinephrine concentrations in rat brain assessed by gas chromatography. Doshi PS, et al. **J Chromatogr** 1981 Jun 19;210(3):505–11

Effect of gonadectomy on the concentrations of catecholamines in discrete areas of the diencephalon of the domestic fowl. Knight PG, et al. **J Endocrinol** 1981 Jun;89(3):389–97

Synthesis and pharmacological evaluation of sulfonium analogues of dopamine: nonclassical dopamine agonists. Anderson K, et al. **J Med Chem** 1981 Jun;24(6):683–7

Synthesis and evaluation of novel alkylpiperazines as potential dopamine antagonists. Glennon RA, et al. **J Med Chem** 1981 Jun;24(6):678–83

Cyclic adenosine monophosphate modulation of contractility via slow Ca2+ channels in chick heart. Azuma J, et al. **J Mol Cell Cardiol** 1981 Jun;13(6):577–87

Characterisation of inhibitory 5-hydroxytryptamine receptors that modulate dopamine release in the striatum. Ennis C, et al. **J Neurochem** 1981 Apr;36(4):1515–20

Effect of guanine nucleotides on dopaminergic agonist and antagonist affinity for [3H]sulpiride binding sites in rat striatal membrane preparations. Freedman SB, et al. **J Neurochem** 1981 Sep; 37(3):608–12

Involvement of brain monoamines in the delta-9-tetrahydrocannabinol-induced reduction of hippocampal choline uptake. Lindamood C 3d, et al. **J Neurochem** 1981 Sep; 37(3):788–91

Diurnal variations in monoamine contents in discrete brain regions of the mongolian gerbil (Meriones unguiculatus). Matsumoto M, et al. **J Neurochem** 1981 Sep;37(3):792–4

Benzodiazepine antagonist Ro 15–1788: binding characteristics and interaction with drug-induced changes in dopamine turnover and cerebellar cGMP levels. Möhler H, et al. **J Neurochem** 1981 Sep; 37(3):714–22

A rapid and simple method for the determination of picogram levels of 3-methoxytyramine in brain tissue using liquid chromatography with electrochemical detection. Ponzio F, et al. **J Neurochem** 1981 Apr; 36(4):1361–7

Alteration of dopamine synthesis in rat striatum subsequent to selective type A monoamine oxidase inhibition. Schoepp DD, et al. **J Neurochem** 1981 Aug;37(2):527–30

Neuronal responses of the globus pallidus to systemic administration of d-amphetamine: investigation of the involvement of dopamine, norepinephrine, and serotonin. Bergstrom DA, et al. **J Neurosci** 1981 Mar;1(3):292–9

High-performance liquid chromatography with electrochemical detection as a highly efficient tool for studying catecholaminergic systems. I. Quantification of noradrenaline, adrenaline and dopamine in cultured adrenal medullary cells. Müller TH, et al. **J Neurosci Methods** 1981 Jun;4(1):39–52

Relevance of the rodent area postrema to dopamine-dependent behavioural effects. Costall B, et al. **J Pharm Pharmacol** 1981 Apr; 33(4):257–9

Lowering of dopamine metabolites in rat brain by harmaline. Fuller RW, et al. **J Pharm Pharmacol** 1981 Apr;33(4):255–6

Effect of GABAergic drugs on dopamine catabolism in the nigrostriatal and mesolimbic dopaminergic pathways of the rat. Gundlach AL, et al. **J Pharm Pharmacol** 1981 Jan;33(1):41–3

Comparative effects of classical and atypical antipsychotic drugs in combination with a non-amphetamine stimulant on rat brain dopamine metabolism. McMillen BA. **J Pharm Pharmacol** 1981 Aug; 33(8):544–6

Influence of deaminated metabolites on the relaxing effect of dopamine on dog saphenous vein. Teixeira F, et al. **J Pharm Pharmacol** 1981 Aug; 33(8):529–33

Dopamine and its antagonists on molluscan smooth muscle. Yoshida Y, et al. **J Pharmacobiodyn** 1981 Mar;4(3):226–8

Haloperidol-induced reduction of nigral substance P-like immunoreactivity: a probe for the interactions between dopamine and substance P neuronal systems. Hanson GR, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):568–74

Alteration of aminophylline-induced respiratory stimulation by perturbation of biogenic amine systems. Mueller RA, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):593–9

Effects of CDP-choline on striatal dopamine level and behavior in rats. Shibuya M, et al. **Jpn J Pharmacol** 1981 Feb;31(1):47–52

Increase in rat striatal acetylcholine content by bromocriptine: evidence for an indirect dopaminergic action. Consolo S, et al. **Life Sci** 1981 Aug 3;29(5):457–65

Striatal muscarinic receptors: regulation by dopaminergic agonists. Ehlert FJ, et al. **Life Sci** 1981 May 21;28(21):2441–8

Acute choline administration in rat and mouse: no effect on dopamine metabolism in brain. Flentge F, et al. **Life Sci** 1981 Jul 27; 29(4):331–5

Differential effects of several dopamine uptake inhibitors and releasing agents on locomotor activity in normal and in reserpinized mice. Heikkila RE. **Life Sci** 1981 Apr 27;28(17):1867–73

Studies on axonal transport in dopaminergic neurons: effect of neuropharmacologic lesions. Iwamoto ET. **Life Sci** 1981 May 11; 28(19):2179–86

Dopamine independent rotational response to unilateral intranigral injection of serotonin. Oberlander C, et al. **Life Sci** 1981 Jun 8; 28(23):2595–601

Biochemical effects of quipazine on rat striatal dopaminergic system. Ponzio F, et al. **Life Sci** 1981 Jul 6;29(1):83–91

Dopaminergic agonist and antagonist effects on striatal tyrosine hydroxylase distribution. Smith CP, et al. **Life Sci** 1981 Jan 12; 28(2):193–7

Tyrosine availability and dopamine synthesis in the striatum: studies with gamma-butyrolactone. Svod A, et al. **Life Sci** 1981 Aug 17; 29(7):743–8

Stimulation of dopamine synthesis and release by morphine and D-ala2-D-leu5-enkephalin in the mouse striatum in vivo. Urwyler S, et al. **Life Sci** 1981 May 18;28(20):2277–86

Manic depression—a disorder of central dopaminergic rhythm. Skutsch GM. **Med Hypotheses** 1981 Jun;7(6):737–46

Dopamine receptor mediated inhibition by pergolide of electrically-evoked 3H-dopamine release from striatal slices of cat and rat: slight effect of ascorbate. Lehmann J, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):31–5

Pathways of dopamine metabolism in the rabbit caudate nucleus in vitro. Zumstein A, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun; 316(3):205–17

Age-related changes in dopamine, LHRH and somatostatin in the rat hypothalamus. Hoffman GE, et al. **Neurobiol Aging** 1980 Summer; 1(1):27–37

The effect of hypoxia on monoamine levels in discrete regions of aged rat brain. Roubein IF, et al. **Neurobiol Aging** 1981 Spring;2(1):37–40

Release of radiolabeled dopamine, p-tyramine, and m-tyramine from rat striatal slices by some aminotetralins. Dyck LE. **Neurochem Res** 1981 Apr;6(4):365–75

Hyperprolactinemia counteracts the testosterone-induced inhibition of the preoptic area dopamine turnover. Kalra PS, et al. **Neuroendocrinology** 1981 Aug;33(2):118–22

Characteristics of dopamine release from isolated nerve endings of the tuberoinfundibular neurones. Annunziato L, et al. **Neuropharmacology** 1981 Aug;20(8):727–31

The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour. Carter CJ, et al. **Neuropharmacology** 1981 Mar; 20(3):261–5

Altered paw preference after unilateral 6-hydroxy-dopamine injections into lateral hypothalamus. Uguru-Okorie DC, et al. **Neuropsychologia** 1981;19(3):463–7

Brain levels of noradrenalin, dopamine, and serotonin in rats with different levels of motor activity. Semenova TP, et al. **Neurosci Behav Physiol** 1981 Mar–Apr;11(2):153–5

Dopamine-induced ventilatory depression in the rat, mediated by carotid nerve afferents. Cardenas H, et al. **Neurosci Lett** 1981 Jun 12;

24(1):29-33

Histochemical evidence for a catecholaminergic (presumably dopaminergic) projection from the ventral mesencephalic tegmentum to visual cortex in the cat. Törk I, et al. **Neurosci Lett** 1981 Jul 17; 24(3):215-9

Membrane activation of smooth muscle from rabbit basilar artery by dopamine. Harder DR. **Pflugers Arch** 1981 Jun;390(3):296-8

Effects on central dopaminergic systems of d-coclaurine and d-reticuline, extracted from Magnolia salicifolia. Watanabe H, et al. **Planta Med** 1981 Jul;42(3):213-22

Effect of combined treatment with dopaminergic and GABA-ergic drugs on the threshold for maximal electroconvulsions in mice. Czuczwar SJ. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):25-35

Dopaminergic regulation of muscarinic receptor binding in the corpus striatum. Ehlert FJ, et al. **Proc West Pharmacol Soc** 1981;24:93-5

Noradrenergic and dopaminergic interactions in escape behavior: analysis of uncontrollable stress effects. Anisman H, et al. **Psychopharmacology (Berlin)** 1981;74(3):263-8

Differential effects of IV and IP muscimol on central dopamine metabolism. Gundlach AL, et al. **Psychopharmacology (Berlin)** 1981; 74(1):71-3

Cathinone, an alkaloid from khat leaves with an amphetamine-like releasing effect. Kalix P. **Psychopharmacology (Berlin)** 1981; 74(3):269-70

Cageing density and dopamine striatal elimination after amphetamine in the rat. Lokiec F, et al. **Psychopharmacology (Berlin)** 1981; 73(4):402-3

Role of dopamine in the diuresis caused by stimulation of atrial receptors. Linden RJ, et al. **Q J Exp Physiol** 1981 Apr;66(2):155-61

Effect of imipramine on high potassium evoked 3H-dopamine release in the rat striatum. Kamiya H, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):49-60

Concomitant analysis of normetanephrine and 3-methoxytyramine in brain: a new gas-liquid chromatography procedure. LeGatt DF, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):61-8

The posterior pituitary: regulation of anterior pituitary prolactin secretion. Peters LL, et al. **Science** 1981 Aug 7;213(4508):659-61

Effect of dopamine on renal haemodynamics in the denervated dog kidney. Huland H, et al. **Urol Res** 1981 Mar 17;9(1):5-11

[Effect of the organophosphorus compound neguvon on the dopamine content in the rat brain] Dishovski K, et al. **Eksp Med Morfol** 1981; 20(2):62-6 (Eng. Abstr.) (Bul)

[Effect of piracetam and dihydroergotoxine on the release of dopamine from the corpus striatum of the rat] Wustmann C, et al. **Acta Biol Med Ger** 1980;39(8-9):383-5 (Ger)

[Effect of dopamine and its antagonists on contractile activity of the lower esophageal sphincter and the stomach (author's transl)] Itoh Z, et al. **Nippon Heikatsukin Gakkai Zasshi** 1980 Jun;16(2):99-107 (Eng. Abstr.) (Jpn)

[Increase in the affinity of hypothalamic tyrosine hydroxylase for tyrosine as a result of the action of dopamine on the synaptosome membrane] Mineeva MF, et al. **Dokl Akad Nauk SSSR** 1981;258(2):501-4 (Rus)

[Effect of certain GABA-ergic substances on dopamine metabolism in the rat brain] Malikova LA, et al. **Farmakol Toksikol** 1981 Jan-Feb; 44(1):37-40 (Eng. Abstr.) (Rus)

[Dopamine concentration in the nigro-striatal system during elaboration and performance of conditioned avoidance reactions of various complexity in rats] Saul'skaia NB. **Fiziol Zh SSSR** 1981 Jun; 67(6):797-803 (Eng. Abstr.) (Rus)

[Participation of the thymus in effecting the modulating influence of the dopaminergic system on immunogenesis] Al'perina EL. **Vestn Akad Med Nauk SSSR** 1981;(5):30-3 (Eng. Abstr.) (Rus)

DOPAMINE BETA-HYDROXYLASE

Immunofluorescence of dopamine-beta-hydroxylase in small intensely fluorescent cells of human sympathetic ganglia. Schröder H, et al. **Acta Anat (Basel)** 1981 Jan;109(1):47-50

The effect of intracerebroventricularly administered dibutyryl adenosine 3',5'-cyclic monophosphate on cerebrospinal fluid and serum dopamine-beta-hydroxylase in rabbits. Fraeyman NH, et al. **Biochem Pharmacol** 1981 Jul 1;30(13):1765-9

Studies on the interaction of Cibacron Blue and Procion Red with dopamine beta-monooxygenase. Skotland T. **Biochim Biophys Acta** 1981 Jun 15;659(2):312-25

Comparison of midday serum dopamine-beta-hydroxylase activity in depressed patients and normal controls. Nasr S, et al. **Commun Psychopharmacol** 1980;4(4):263-7

Estradiol concentration in dopamine-beta-hydroxylase containing neurons of lower brain stem demonstrated by combined autoradiography and immunohistochemistry. Sar M, et al. **Exp Brain Res** 1981; Suppl 3:29-36

Palmar skin potential reflex and serum dopamine-beta-hydroxylase activity of the aged. Nomura S, et al. **Folia Psychiatr Neurol Jpn** 1981; 35(1):3-9

Heterogeneity in the adrenomedullary storage of catecholamines, ATP, calcium and releasable dopamine beta-hydroxylase activity. Bolstad G, et al. **J Auton Nerv Syst** 1980 Dec;2(4):337-54

Dopamine beta-hydroxylase. Comparative specificities and mechanisms of the oxygenation reactions. May SW, et al. **J Biol Chem** 1981 Aug 25;256(16):8470-5

Studies on dopamine-converting enzymes in human plasma. Allenmark S, et al. **J Chromatogr** 1981 Apr 10;223(1):188-42

Ultrastructural demonstration of noradrenergic synapses in the rat central nervous system by dopamine-beta-hydroxylase immunocytochemistry. Olschowka JA, et al. **J Histochem Cytochem** 1981 Feb;29(2):271-80

Influence of sino-aortic baroreceptor denervation on catecholamines, catecholamine-synthesizing enzymes and choline acetyltransferase activity in the brainstem nuclei of the rat. Nakamura K, et al. **Jpn J Pharmacol** 1981 Feb;31(1):95-105

Compensatory increase in adrenal weight and dopamine-beta-hydroxylase activity after unilateral adrenalectomy: experimental evidence for a pineal-dependent contribution. Banerji TK, et al. **Proc Soc Exp Biol Med** 1981 Sep;167(4):514-8

DOSE-RESPONSE RELATIONSHIP, DRUG

Dose dependence of the thyrotropin (TSH) receptor damaging effect of gonadotropin in the newborn rats. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):417-20

DOXEPIN

Doxepin plasma levels and anxiolytic response. Norman TR, et al. **Int Pharmacopsychiatry** 1980;15(4):247-52

Malignant breast change in man given two drugs associated with breast hyperplasia [letter] Smedley HM. **Lancet** 1981 Sep 19; 2 Pt 1(8247):638-9

DRUG EVALUATION

Guidelines for the evaluation of drugs in the elderly neuropsychiatric patient (demented and non-demented). **Pharmacopsychiatria** 1981 Jul; 14(4):150-4 contd

[Effectiveness of drug testing with the help of psychometric methods. Possibilities and problems] Oswald WD. **Med Welt** 1981 Aug 21; 32(34):1225-31 (Ger)

ELECTROCONVULSIVE THERAPY

Effect of electroconvulsive treatment on brain monoamine content, pituitary-adrenal function and plasma prolactin. Arató M, et al. **Acta Physiol Acad Sci Hung** 1980;56(2):163-71

Animal model of depression: effects of electroconvulsive shock therapy. Katz RJ. **Neurosci Biobehav Rev** 1981 Summer;5(2):273-7

Influence of unilateral ECT on tryptophan metabolism in endogenous depression. Smith DF, et al. **Pharmacopsychiatria** 1981 Jul; 14(4):135-8

Electroconvulsive therapy in the medically ill patient. Bidder TG. **Psychiatr Clin North Am** 1981 Aug;4(2):391-405 (60 ref.)

Substance P-like immunoreactivity in plasma of psychotic patients and effects of neuroleptics and electroconvulsive therapy. Kaiya H, et al. **Psychiatry Res** 1981 Aug;5(1):11-21

Studies on possible mechanisms of action of electroconvulsive therapy; effects of repeated electrically induced seizures on rat brain receptors for monoamines and other neurotransmitters. Deakin JF, et al. **Psychopharmacology (Berlin)** 1981;73(4):345-9

[Tricyclics, MAOI and electroshock therapy in the treatment of depressive syndromes] Carolei A, et al. **Clin Ter** 1981 Jul 15;98(1):75-86 (29 ref.) (Ita)

ELECTROENCEPHALOGRAPHY

Effect of estazolam on the caudate spindle in the cat. Janicki P, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):172-3

Pharmacoelectroencephalographic study of brotizolam, a novel hypnotic. Fink M, et al. **Clin Pharmacol Ther** 1981 Sep;30(3):336-42

Drug-specific EEG frequency spectra and their time courses produced in the cat by antidepressants and a benzodiazepine. Fairchild MD, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jul;52(1):81-8

Effect of a short-acting benzodiazepine on brain electrical activity during sleep. Johnson LC, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jul;52(1):89-97

Effects of gonadal steroids on EEG and performance in the human. Becker D, et al. **Exp Brain Res** 1981;Suppl 3:309-17

Bilateral skin conductance, finger pulse volume, and EEG orienting response to tones of differing intensities in chronic schizophrenics and controls. Bernstein AS, et al. **J Nerv Ment Dis** 1981 Aug; 169(8):513-28

The effect of imipramine and mianserin on the behavior and EEG afterdischarges induced by single electric stimulation of the rabbit amygdala. Ossowska K, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug; 32(4):513-22

The effects of haloperidol on the EEG spectrum. Wieneke GH, et al. **Psychopharmacology (Berlin)** 1981;74(1):33-4

[Analysis of auditory averaged evoked potentials (AEP)– description of a fully automated procedure for AEP analysis (author's transl)] Hofmann W, et al. **EEG EMG** 1981 Jun;12(2):84–9 (Eng. Abstr.) (Ger)

[Effects of diazepam and thiamylal on reticular multi–unit activity, visual evoked responses, EEG and arterial blood pressure in rabbits (author's transl)] Ueda Y. **Nippon Geka Hokan** 1980 Sep 1;49(5):595–607 (Eng. Abstr.) (Jpn)

[Cerebral bioelectric activity and urinary catecholamine elimination in thermal stress in children] Stratone A, et al. **Rev Med Chir Soc Med Nat Iasi** 1981;85(1):113–6 (Eng. Abstr.) (Rum)

ELECTROLYTES

Endogenous norepinephrine release induced by tyramine modulates intestinal ion transport. Tapper EJ, et al. **Am J Physiol** 1981 Sep; 241(3):G264–9

Measurement of active ion transport in man. Utilizing intact human erythrocytes. Micheis RC, et al. **Ann Clin Lab Sci** 1981 Mar–Apr; 11(2):158–64

The effect of lithium on electrolyte transport by the in situ choroid plexus of the cat. Reed DJ, et al. **J Physiol (Lond)** 1980 Dec;309:329–39

[Effect of acetylcholine and histamine on electrolyte and catecholamine content of vessel walls exposed to x–rays and cystamine] Litvinov SA. **Farmakol Toksikol** 1981 Jan–Feb;44(1):55–9 (Eng. Abstr.) (Rus)

ELECTROSHOCK

Effect of electroconvulsive shock on beta–endorphin immunoreactivity of rat brain, pituitary gland, and plasma. Dias RD, et al. **Behav Neural Biol** 1981 Jun;32(2):265–8

Differential effects of electroconvulsive shock and antidepressant drugs on serotonin–2 receptors in rat brain. Kellar KJ, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):515–8

Effect of combined treatment with dopaminergic and GABA–ergic drugs on the threshold for maximal electroconvulsions in mice. Czuczwar SJ. **Pol J Pharmacol Pharm** 1981 Jan–Feb;33(1):25–35

EMOTIONS

Psychophysiological responses of schizophrenic patients to high and low expressed emotion relatives. Sturgeon D, et al. **Br J Psychiatry** 1981 Jan;138:40–5

The effect of five tricyclic antidepressants on salivary flow and mood in healthy volunteers. Blackwell B, et al. **Commun Psychopharmacol** 1980;4(4):255–61

Antianxiety agents and emotional behavior, an information processing analysis. Morris MD, et al. **Prog Neuropsychopharmacol** 1981; 5(3):219–40

ENDORPHINS

The investigation of [(4'–amino)–PHE]4–enkephalin conformation in water by the spectrofluorimetric procedure. Jankowski A, et al. **Acta Biochim Pol** 1981;28(1):11–20

Interaction of tritiated beta–endorphin with rat brain membranes. Hammonds RG Jr, et al. **Anal Biochem** 1981 Jun;114(1):75–84

Effect of electroconvulsive shock on beta–endorphin immunoreactivity of rat brain, pituitary gland, and plasma. Dias RD, et al. **Behav Neural Biol** 1981 Jun;32(2):265–8

Evidence for an opiate–inactive N–acetylated derivative of leucine–enkephalin in the rat neurointermediate pituitary. Seizinger BR, et al. **Biochem Biophys Res Commun** 1981 Jul 16;101(1):289–97

Synthetic N–dimethyl beta–endorphin, a stabilized opioid peptide. Boarder MR, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1289–93

A reaction of acetaldehyde with enkephalins and related peptides. Summers MC, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1621–7

Acetaldehyde––enkephalins: structure proof and some conformational deductions from one– and two–dimensional proton nuclear magnetic resonance spectra. Gidley MJ, et al. **Biochemistry** 1981 Jun 23; 20(13):3880–3

Conformational properties of central nervous system myelin basic protein, beta–endorphin, and beta–lipotropin in water and in the presence of anionic lipids. Mattice WL, et al. **Biopolymers** 1981 Jul; 20(7):1421–34

The effects of morphine and methionine–enkephalin on the release of purines from cerebral cortex slices of rats and mice. Stone TW. **Br J Pharmacol** 1981 Sep;74(1):171–6

Enkephalins, substance P, bradykinin and angiotensin II: differential sites of action on the hypothalamo–neurohypophysial system. Baertschi AJ, et al. **Brain Res** 1981 Sep 7;220(1):107–19

Strain differences in pituitary beta–endorphin and ACTH content in inbred mice. Crabbe JC Jr, et al. **Brain Res** 1981 Aug 24; 219(1):219–23

Development of acute tolerance during exposure of hippocampal explants to an opioid peptide. Gähwiler BH. **Brain Res** 1981 Jul 27; 217(1):196–200

Differential response to methionine–enkephalin in basal hypothalamus and preoptic area following hypothalamic deafferentation. Kalra SP, et al. **Brain Res** 1981 Jun 29;215(1–2):410–3

Met–enkephalin concentrations in individual brain nuclei of ansa lenticularis and stria terminalis transected rats. Palkovits M, et al. **Brain Res** 1981 Jul 6;216(1):203–9

Opiate effects on rabbit vagus nerve: electrophysiology and radioligand binding. Shefner SA, et al. **Brain Res** 1981 Sep 21;221(1):109–16

Mechanism of kyotorphin–induced release of Met–enkephalin from guinea pig striatum and spinal cord. Shiomi H, et al. **Brain Res** 1981 Sep 21; 221(1):161–9

Comparative immunocytochemical localization of enkephalin and somatostatin in the median eminence, hypothalamus and adjacent areas of the guinea–pig brain. Tramu G, et al. **Brain Res** 1981 Jun 29; 215(1–2):235–55

Thermoregulatory effects of centrally administered bombesin, bradykinin, and methionine–enkephalin. Francesconi R, et al. **Brain Res Bull** 1981 Jul;7(1):63–8

Immunohistochemical localisation of substances reactive to antisera against alpha– and beta–endorphin and met–enkephalin in the brain of Rana temporaria L. Doerr–Schott J, et al. **Cell Tissue Res** 1981; 217(1):79–92

Immunohistochemical evidence of methionine enkephalin–like material in the brain of the migratory locust. Rémy C, et al. **Cell Tissue Res** 1981;218(2):271–8

Processing, turnover and release of corticotropins, endorphins and melanotropin in the toad pituitary intermediate lobe. Loh YP. **Ciba Found Symp** 1981;(81):55–78

Comparison of rat anterior and intermediate pituitary in tissue culture: corticotropin (ACTH) and beta–endorphin. Mains RE, et al. **Ciba Found Symp** 1981;(81):32–54

beta–lipotrophin and beta–endorphin plasma levels during pregnancy. Genazzani AR, et al. **Clin Endocrinol (Oxf)** 1981 Apr;14(4):409–18

Alpha–adrenergic stimulation by clonidine increases plasma concentrations of immunoreactive beta–endorphin in rats. Pettibone DJ, et al. **Endocrinology** 1981 Sep;109(3):798–802

Evidence that a serotonergic mechanism stimulates the secretion of pituitary beta–endorphin–like immunoreactivity in the rat. Sapun DI, et al. **Endocrinology** 1981 Aug;109(2):421–6

Epinephrine as a potent releaser of immunoreactive beta–endorphin in rats. Berkenbosch F, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):97–100

Effect of chronic morphine treatment on beta–endorphin biosynthesis by the rat neurointermediate lobe. Gianoulakis C, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):313–21

Comparison of the effects of beta–endorphin and morphine on exploratory and socio–sexual behaviour in the male rat. Meyerson BJ. **Eur J Pharmacol** 1981 Feb 19;69(4):453–63

Potentiation by Des–Tyr–gamma–endorphin on apomorphine–induced changes in rat open field behavior. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):77–81

Bombesin, calcitonin and leu–enkephalin immunoreactivity in endocrine cells of human lung. Cutz E, et al. **Experientia** 1981 Jul 15; 37(7):765–7

(D–Ala2, N–Val5), (D–Ala2, Met5) enkephalins and enkephalinamides. Correlation between biological activity and NMR features. Gairin JE, et al. **FEBS Lett** 1981 Jun 1;128(1):51–4

N–(9–Xanthenyl)amino acid N–carboxyanhydrides in the solid–phase synthesis of a Lys–Lys–linked cyclic leucine–enkephalin. Halstrøm J, et al. **Hoppe Seylers Z Physiol Chem** 1981 Jun;362(6):593–9

Effect of glucose and arginine on L–enkephalin secretion of the isolated perfused rat pancreas. Sachse G, et al. **Horm Metab Res** 1981 Jun; 13(6):360

Subcellular fractionation studies on the post–translational processing of pro–adrenocorticotropic hormone/endorphin in rat intermediate pituitary. Glembotski CC. **J Biol Chem** 1981 Jul 25;256(14):7433–9

Distribution of methionine–enkephalin immunoreactivity in the chick brain: an immunohistochemical study. de Lanerolle NC, et al. **J Comp Neurol** 1981 Jul 10;199(4):513–33

The immunocytochemical localization of enkephalin in the central nervous system of the rat. Finley JC, et al. **J Comp Neurol** 1981 Jun 1; 198(4):541–65

Immunohistochemical localization of enkephalin in the central nervous system and pituitary of the lizard, Anolis carolinensis. Naik DR, et al. **J Comp Neurol** 1981 Jun 1;198(4):583–601

Neuropeptides in striato–nigral pathways. Cuello AC, et al. **J Neural Transm** 1981;51(1–2):83–96

Long–term treatment of rats with morphine reduces the activity of messenger ribonucleic acid coding for the beta–endorphin/ACTH precursor in the intermediate pituitary. Höllt V, et al. **J Neurochem** 1981 Sep;37(3):619–26

Methionine–enkephalin and morphine: amount ejected microiontophoretically. Hosford DA, et al. **J Neurosci Methods** 1981 Aug;4(2):135–9

The effect of barbiturates on the degradation of enkephalin by brain enzymes. Altstein M, et al. **Life Sci** 1981 Jun 12;28(2):185-91

Neurochemical studies in the hypoxic brain: substance P, met-enkephalin, GABA and angiotensin converting enzyme. Arregui A, et al. **Life Sci** 1981 Jun 29;28(26):2925-9

A distinct peptidyl dipeptidase that degrades enkephalin: exceptionally high activity in rabbit kidney. Benuck M, et al. **Life Sci** 1981 Jun 8; 28(23):2643-50

Opioid activities of beta-casomorphins. Brantl V, et al. **Life Sci** 1981 Apr 27;28(17):1903-9

Intracerebral des-tyrosine-gamma-endorphin inhibits methylphenidate induced locomotor activity. Davis KL, et al. **Life Sci** 1981 May 21; 28(21):2421-4

Rapid depletion and restoration of striatal met-enkephalin after ketamine. Fratta W, et al. **Life Sci** 1981 Jul 6;29(1):93-7

Peptide hormone degradation by a rat mast cell chymase-heparin complex. Jahnke GD, et al. **Life Sci** 1981 Jul 27;29(4):397-403

Sensitive and specific high performance liquid chromatographic method for methionine and leucine enkephalins. Mousa S, et al. **Life Sci** 1981 Jul 6;29(1):61-8

Stimulation of dopamine synthesis and release by morphine and D-ala2-D-leu5-enkephalin in the mouse striatum in vivo. Urwyler S, et al. **Life Sci** 1981 May 18;28(20):2277-86

Behavioral and neurochemical effects of the new opioid peptide dynorphin--(1-13): comparison with other neuropeptides. Zwiers H, et al. **Life Sci** 1981 Jun 1;28(22):2545-51

Parallel stimulation of ACTH, beta-LPH + beta-endorphin and alpha-MSH release by alpha-adrenergic agents in rat anterior pituitary cells in culture. Raymond V, et al. **Mol Cell Endocrinol** 1981 Jun; 22(3):295-303

Endorphins and ventilatory control [letter] **N Engl J Med** 1981 Oct 15; 305(16):958-60

What makes us run? [editorial] Appenzeller O. **N Engl J Med** 1981 Sep 3;305(10):578-80

Catecholamines, dopamine, and endorphin levels during extreme exercise [letter] Bortz WM 2d, et al. **N Engl J Med** 1981 Aug 20; 305(8):466-7

Physical conditioning facilitates the exercise-induced secretion of beta-endorphin and beta-lipotropin in women. Carr DB, et al. **N Engl J Med** 1981 Sep 3;305(10):560-3

An opiate system in the goldfish retina. Djamgoz MB, et al. **Nature** 1981 Aug 13;292(5824):620-3

Super-active enkephalin analogues. Simple tripeptide hydroxyalkylamides exhibit surprisingly high and long-lasting opioid activities. Kiso Y, et al. **Naturwissenschaften** 1981 Apr;68(4):210-2

Vasopressin stimulates release of beta-lipotropin and beta-endorphin in conscious rats as measured by radioimmunoassay of unextracted plasma. Anhut H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb; 316(1):59-63

Clozapine inhibition of metenkephalin binding to synaptosome-enriched fractions of rat whole brain and hippocampus. Somoza E, et al. **Neurochem Res** 1981 Apr;6(4):413-24

Immunocytochemical localization of beta-endorphin-containing neurons in the rat brain. Finley JC, et al. **Neuroendocrinology** 1981 Jul; 33(1):28-42

In vivo characterization of the mechanisms that secrete enkephalin-like peptides stored in dog adrenal medulla. Govoni S, et al. **Neuropharmacology** 1981 Jul;20(7):639-45

Multi-dimensional analyses of behavior in mice treated with alpha-endorphin. Kameyama T, et al. **Neuropharmacology** 1981 Mar; 20(3):247-50

Isolation and identification of an analgesic opioid dipeptide kyotorphin (Tyr-Arg) from bovine brain. Shiomi H, et al. **Neuropharmacology** 1981 Jul;20(7):633-8

In vivo release of enkephalin from the globus pallidus. Bayon A, et al. **Neurosci Lett** 1981 Jun 12;24(1):65-70

Diffuse enkephalin innervation from caudate to globus pallidus. Correa FM, et al. **Neurosci Lett** 1981 Aug 7;25(1):63-8

Reciprocal antagonism between ACTH1-24 and beta-endorphin in rats. Fratta W, et al. **Neurosci Lett** 1981 Jun 12;24(1):71-4

Release of immunoreactive-dynorphin from the isolated guinea-pig small intestine is reduced during peristaltic activity. Kromer W, et al. **Neurosci Lett** 1981 Aug 7;25(1):53-6

The influence of foot-shock stress upon brain, pituitary and spinal cord pools of immunoreactive dynorphin in rats. Millan MJ, et al. **Neurosci Lett** 1981 Jun 12;24(1):75-9

Effects of bromocriptine on receptor binding of methionine-enkephalin. Ogawa N, et al. **Neurosci Lett** 1981 May 6;23(2):215-8

Correlation between Met-enkephalin and substance P immunoreactivity in the primate globus pallidus. Haber S, et al. **Neuroscience** 1981; 6(7):1291-7

Co-localization of neurophysin- and enkephalin-like immunoreactivity in cat pituitary. Coulter HD, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:51-5

Regional distribution of gamma- and beta-endorphin-like peptides in the pituitary and brain of the rat. Dorsa DM, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:71-7

Effects of alpha-MSH and beta-endorphin on startle reflex in rat. Hoehler FK, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:137-41

Substance P and leucine-enkephalin changes after chordotomy and morphine treatment. Naftchi NE, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:61-70

Presence of leucine-enkephalin in organotypic explants of fetal mouse spinal cord. Naftchi NE, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:57-60

Muscarinic cholinergic influences on ACTH and beta-endorphin release mechanisms in human subjects. Risch SC, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:95-7

Localization and opiate receptor binding of enkephalin, CCK and ACTH/beta-endorphin in the rat central nervous system. Stengaard-Pedersen K, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:3-19 (53 ref.)

Peptides as neurotransmitters: focus on the enkephalins and endorphins. Miller RJ. **Pharmacol Ther [B]** 1981;12(1):73-108 (214 ref.)

Endogenous opioids and cyclic AMP. Wollemann M. **Prog Neurobiol** 1981;16(2):145-54 (76 ref.)

Effect of carbamazepine on CSF opioid activity; relationship to antidepressant response. Post RM, et al. **Psychiatry Res** 1981 Aug; 5(1):59-66

(Des-Tyr)-gamma-endorphin in the treatment of schizophrenia. Manchanda R, et al. **Psychol Med** 1981 May;11(2):401-4

Effects of opioid peptides on synaptic potentials in explants of rat hippocampus. Gähwiler BH, et al. **Regul Pept** 1981 Feb;1(5):317-26

Presence of dynorphin-like immunoreactivity in rat pituitary gland and hypothalamus. Nakao K, et al. **Regul Pept** 1981 Jun;2(3):201-8

Immunohistochemical localization of gastrin C-terminus, gastric inhibitory peptide (GIP) and endorphin in the pancreas of lizards with special reference to the hibernation period. El-Salhy M, et al. **Regul Pept** 1981 May;2(2):97-111

Anatomical distribution and physiological effects of enkephalin in rat inferior olive. Schulman JA. **Regul Pept** 1981 May;2(2):125-37

Endogenous opiates and fasting [letter] Ettenberg A, et al. **Science** 1981 Sep 11;213(4513):1282

Characterization of a 41-residue ovine hypothalamic peptide that stimulates secretion of corticotropin and beta-endorphin. Vale W, et al. **Science** 1981 Sep 18;213(4514):1394-7

[Endogenous opiate-like substances and cardiovascular activity (author's transl)] Zhang F, et al. **Sheng Li Ko Hsueh Chin Chan** 1980 Apr; 11(4):365-7 **(Chi)**

[Endorphins -- new regulating peptides (author's transl)] Horáček J, et al. **Cas Lek Cesk** 1981 Jun 25;120(25):753-5 (Eng. Abstr.) **(Cze)**

[Endorphins in psychiatry] Rimón R. **Duodecim** 1980;96(21):1387-9 **(Fin)**

[Effects of intrathecal injection of beta-endorphin on endocrine function in man (author's transl)] Yamaya R. **Masui** 1981 May;30(5):445-52 (Eng. Abstr.) **(Jpn)**

[ACTH, endorphins and related peptides (author's transl)] Imura H, et al. **Tanpakushitsu Kakusan Koso** 1981 Feb;26(2):90-101 (56 ref.) **(Jpn)**

[Chemical studies of enkephalin precursors in adrenal medulla (author's transl)] Kimura S. **Tanpakushitsu Kakusan Koso** 1981 Feb; 26(2):125-37 (67 ref.) **(Jpn)**

[New endogenous 'big' enkephalins (author's transl)] Matsuo H, et al. **Tanpakushitsu Kakusan Koso** 1981 Feb;26(2):102-14 (44 ref.) **(Jpn)**

[Dynorphin---A potent opioid peptide (author's transl)] Tachibana S. **Tanpakushitsu Kakusan Koso** 1981 Feb;26(2):115-24 (20 ref.) **(Jpn)**

[Interaction of D-Ala2-[Tyr-3,5-3H]enkephalin(5-D-Leu) with opiate receptors of rat brain] Balashov AM, et al. **Biokhimiia** 1981 Jun; 46(6):1067-72 (Eng. Abstr.) **(Rus)**

[Effect of enkephalins on central processes regulating hemodynamics] Medvedev OS, et al. **Biull Eksp Biol Med** 1981 May;91(5):574-6 (Eng. Abstr.) **(Rus)**

[Endogenous opioids in the central nervous system] Hedner T. **Lakartidningen** 1981 Jul 22;78(30-31):2689-93 (Eng. Abstr.) **(Swe)**

ENURESIS

Voiding dysfunction in the child with problem 'wetting'. Noe HN. **JDBP** 1980 Mar;1(1):29-33

EPHEDRINE

Experimental motion sickness: efficacy of transdermal scopolamine plus ephedrine. Graybiel A, et al. **Aviat Space Environ Med** 1981 Jun; 52(6):337-9

Dopamine-like properties of ephedrine in rat brain. Zarrindast MR. **Br J Pharmacol** 1981 Sep;74(1):119-22

Sensitive assay for pseudoephedrine and its metabolite, norpseudoephedrine in plasma and urine using gas-liquid chromatography with electron-capture detection. Lo LY, et al. **J Chromatogr** 1981 Feb 13;222(2):297-302

Stereospecific radioimmunoassays for d-pseudoephedrine in human plasma and their application to bioequivalency studies. Findlay JW, et al. **J Pharm Sci** 1981 Jun;70(6):624-31

EPINEPHRINE

Central action of adrenaline. Jagiello-Wójtowicz E. **Acta Physiol Pol** 1981 Mar-Apr;32(2):169-80

Responses to catecholamines and nerve stimulation of the perfused rete tibiotarsale and associated blood vessels in the hind limb of the Mallard (Anas platyrhynchos). Midtgård U, et al. **Acta Physiol Scand** 1981 May; 112(1):77-81

Use of endotracheally administered epinephrine in a pediatric patient. Greenberg MI, et al. **Am J Dis Child** 1981 Aug;135(8):767-8

Catecholamine excretion rates in relation to life-styles in the male population of Otmoor, Oxfordshire. Reynolds V, et al. **Ann Hum Biol** 1981 May-Jun;8(3):197-209

Antidiuretic effects of intracerebroventricular infusion of adrenaline in conscious goats. Vendeputte-van Messom G, et al. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):137-46

Different sedimentation properties of agonist- and antagonist-labelled platelet alpha 2 adrenergic receptors. Michel T, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):1131-6

The effects of epinephrine on guinea pig placental glycogen metabolism and on cellular cyclic AMP. Sezer Yarimağan H, et al. **Biochem Med** 1981 Apr;25(2):125-34

Habitual catecholamine excretion and its relation to habitual distress. Forsman L. **Biol Psychol** 1980 Sep;11(2):83-97

ADP and epinephrine-induced release of platelet fibrinogen. Kaplan KL, et al. **Blood** 1981 Oct;58(4):797-802

Changes in plasma catecholamine concentrations during endotracheal intubation. Russell WJ, et al. **Br J Anaesth** 1981 Aug;53(8):837-9

The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Coote JH, et al. **Brain Res** 1981 Jun 29;215(1-2):135-45

Effects of an epinephrine synthesis inhibitor, SKF64139, on the secretion of luteinizing hormone in ovariectomized female rats. Crowley WR, et al. **Brain Res** 1981 Jan 5;204(1):231-5

Release of endogenous catecholamines from slices of hypothalamus of rats. Hamlet MA, et al. **Brain Res** 1981 Aug 3;217(2):315-25

High resolution radioautography of central dopaminergic fibers labelled in vitro with [3H]dopamine or [3H]norepinephrine. Nguyen-Legros J, et al. **Brain Res** 1981 Jun 1;213(2):265-76

Catecholamines and 5-hydroxytryptamine in photophores of Porichthys notatus. Radioenzymatic detection and radioautographic localization. Anctil M, et al. **Cell Tissue Res** 1981;219(3):557-66

Correlative light-, fluorescence- and electron-microscopic studies of catecholamine-storing cells in the adrenal medulla of the domestic fowl. Chungsamarnyart N, et al. **Cell Tissue Res** 1981;217(3):471-7

Catecholamine-storing cells in the adrenal medulla of the pre- and postnatal rat. Acetylcholinesterase as a means for early discrimination of cell types. Millar TJ, et al. **Cell Tissue Res** 1981;217(1):155-70

Total circulatory capacity in the rat. Effects of epinephrine and vasopressin on compliance and unstressed volume. Trippodo NC. **Circ Res** 1981 Oct;49(4):923-31

Influence of adrenal epinephrine on postnatal development of tyrosine hydroxylase activity in the superior cervical ganglion. Markey KA, et al. **Dev Neurosci** 1981;4(4):267-72

Direct phosphorylation effects of epinephrine on the plasma membranes of intact rat fat cells. Kang ES, et al. **Dev Pharmacol Ther** 1981; 2(1):55-66

Inhibitory effect of prostaglandins on the stimulation by glucagon and adrenaline of formation of cyclic AMP in rat hepatocytes. Brønstad GO, et al. **Eur J Biochem** 1981 Jul;117(2):369-74

Epinephrine as a potent releaser of immunoreactive beta-endorphin in rats. Berkenbosch F, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):97-100

The effects of topically applied epinephrine and timolol on intraocular pressure and aqueous humor cyclic-AMP in the rabbit. Boas RO, et al. **Exp Eye Res** 1981 Jun;32(6):681-90

Effects of epinephrine on plasma fibrinogen levels in rats submitted to tissue injury. Palma JA, et al. **Experientia** 1981 Jul 15;37(7):780-2

Role of ovarian hormones in the long-term control of glucose homeostasis. Interaction with insulin, glucagon and epinephrine. Ahmed-Sorour H, et al. **Horm Res** 1980;13(6):396-403

In vitro methylation of chromosomal proteins of the brain of rats of various ages & its modulation by epinephrine. Das R, et al. **Indian J Biochem Biophys** 1980 Dec;17(6):429-31

Effects of epinephrine and norepinephrine infusion on lung fluid balance in sheep. Minnear FL, et al. **J Appl Physiol** 1981 Jun;50(6):1353-7

A new method of administering aqueous epinephrine: the EpiPen, an automatic syringe. Lockey SD. **J Asthma Res** 1980 Jul;17(4):153-5

The invagination complex in nerve endings on adrenomedullary adrenaline cells: quantitative ultrastructural description, and analysis of changes with time-of-day and their modification by sham-surgery and pinealectomy. Kachi T, et al. **J Auton Nerv Syst** 1980 Oct; 2(3):241-58

The relation of plasma norepinephrine and epinephrine levels over time in humans. Levin BE, et al. **J Auton Nerv Syst** 1980 Dec; 2(4):315-25

Further studies of hormone-sensitive sodium and potassium transport in red cells from developing chick embryos. Shanbaky NM, et al. **J Cell Physiol** 1981 May;107(2):303-8

Effect of gonadectomy on the concentrations of catecholamines in discrete areas of the diencephalon of the domestic fowl. Knight PG, et al. **J Endocrinol** 1981 Jun;89(3):389-97

Biochemical variability in a tem sports situation. Biersner RJ, et al. **J Human Stress** 1981 Sep;7(3):12-7

Catecholamine and cortisol excretion patterns in three-year-old children and their parents. Lundberg U, et al. **J Human Stress** 1981 Sep; 7(3):3-11

Mechanism of the age-related decrease of epinephrine-stimulated lipolysis in isolated rat adipocytes: beta-adrenergic receptor binding, adenylate cyclase activity, and cyclic AMP accumulation. Dax EM, et al. **J Lipid Res** 1981 Aug;22(6):934-43

Emergency treatment of insect sting reactions -- should adrenaline be available in schools and camps? Wray BB, et al. **J Med Assoc Ga** 1981 Aug;70(8):551-2

Inhibitors of phenylethanolamine N-methyltransferase and epinephrine biosynthesis. 3. Bis[tetrahydroisoquinoline]s. DeMarinis RM, et al. **J Med Chem** 1981 Jun;24(6):756-9

High-performance liquid chromatography with electrochemical detection as a highly efficient tool for studying catecholaminergic systems. I. Quantification of noradrenaline, adrenaline and dopamine in cultured adrenal medullary cells. Müller TH, et al. **J Neurosci Methods** 1981 Jun;4(1):39-52

A kinetic analysis of the effects of adrenaline on calcium distribution in isolated rat liver parenchymal cells. Barritt GJ, et al. **J Physiol (Lond)** 1981 Mar;312:29-55

The effect of adrenaline and noradrenaline on coronary vascular reserve in the dog. Creates MS, et al. **J Physiol (Lond)** 1980 Dec; 309:557-68

Note on estimating catecholamines in urine sampled after 75-min periods of mental work and inactivity. Forsman L. **J Psychosom Res** 1981; 25(3):223-5

The effect of catecholamines or sodium lactate on blood lactate distribution in the rat. Aragno R. **J Sports Med Phys Fitness** 1981 Mar; 21(1):7-14

Propranolol and epinephrine [letter] Stotter ML. **JAMA** 1981 Oct 16; 246(16):1772

Adrenaline activation of phosphofructokinase in rat heart mediated by alpha-receptor mechanism independent of cyclic AMP. Clark MG, et al. **Nature** 1981 Jul 30;292(5822):461-3

Two different biophases for adrenaline released by electrical stimulation or tyramine from the sympathetic nerve endings of the dog saphenous vein. Guimarães S, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun;316(3):200-4

Adrenal medullary secretory response to pontine and mesencephalic stimulation in the rat. Matsui H. **Neuroendocrinology** 1981 Aug; 33(2):84-7

Augmentation of thoracic duct lymph flow induced by adrenaline in the rabbits treated previously with propranolol. Toyosawa K, et al. **Nippon Seirigaku Zasshi** 1981;43(2):44-5

Carnitine optical isomers' action on the epinephrine stress induced in the isolated perfused rabbit heart. Fanelli O, et al. **Pharmacology** 1981; 22(6):371-7

Effect of epinephrine on prostaglandin E2 and cyclic AMP levels in gingiva of patients with chronic periodontitis. ElAttar TM, et al. **Prostaglandins Med** 1981 Jun;6(6):601-12

Low dose aspirin, platelet function and prostaglandin synthesis: influence of epinephrine and alpha adrenergic blockade. Rao GH, et al. **Prostaglandins Med** 1981 May;6(5):485-94

Relationships between sex-related psychological characteristics during adolescence and catecholamine excretion during achievement stress. Rauste-von Wright M, et al. **Psychophysiology** 1981 Jul;18(4):362-70

Epidurography using epinephrine and tomography. Easterbrook JS, et al. **Radiology** 1981 Sep;140(3):709-11

Changes of urinary kallikrein and kinin excretions induced by adrenalin infusion in conscious dogs. Olsen UB. **Scand J Clin Lab Invest** 1980 Apr;40(2):173-8

Effect of acetylcholine and catecholamines on the enterochromaffin-like cells of the stomach. Sano M, et al. **Surg Gynecol Obstet** 1981 Sep; 153(3):337-40

Responses of rabbit platelets to adrenaline induced by other agonists. Hallam TJ, et al. **Thromb Res** 1981 Feb-Mar;21(4-5):413-24

Effect of dexamethasone and epinephrine on metallothionein level in the perfused rat liver. Lee HS, et al. **Yonsei Med J** 1980;21(1):18-23

[Effect of pressure and local adrenaline application on carotid sinus on the perfusion pressure in the perfused hindlimb] Staak R. **Acta Biol Med Ger** 1981;40(2):189-99 (Eng. Abstr.) **(Ger)**

[Exercise-induced platelet aggregation: in vitro and ex-vivo aggregation of human platelets after administration of crystalline adrenaline and after ergometric exercise (author's transl)] Rieger H, et al. **Dtsch Med Wochenschr** 1981 Jul 17;106(29-30):942-5 (Eng. Abstr.) **(Ger)**

[Plasma catecholamines, metabolic substrates, aerobic and anaerobic capacity during graduated treadmill and bicycle ergometer exercise (author's transl)] Lehmann M, et al. **Klin Wochenschr** 1981 Jun 1; 59(11):553-9 (Eng. Abstr.) (Ger)

[The glycoregulatory response to glucagon and epinephrine infusions in chronic uremia] Perez G, et al. **Minerva Nefrol** 1979 Jul-Sep; 26(3):349-52 (Eng. Abstr.) (Ita)

[Effects of dipivalyl epinephrine and S-596, a new beta-adrenergic blocker, on human aqueous humor dynamics (author's transl)] Araie M, et al. **Nippon Ganka Gakkai Zasshi** 1981 May 10;85(5):349-54 (Eng. Abstr.) (Jpn)

[Effects of tetragastrin on catecholamines in gastric juice and gastric tissues in rats (author's transl)] Baba M, et al. **Nippon Shokakibyo Gakkai Zasshi** 1981 Jun;78(6):1191-7 (Eng. Abstr.) (Jpn)

[Adrenaline and noradrenaline levels before and after heart catheterization] Rumiński W, et al. **Pol Tyg Lek** 1981 Mar 30; 36(13):461-3 (Eng. Abstr.) (Pol)

[Plasma catecholamines of August and Wistar strain rats subjected to emotional stress] Kvetnanskii R, et al. **Fiziol Zh SSSR** 1981 Apr; 67(4):516-23 (Eng. Abstr.) (Rus)

ESCAPE REACTION

Social housing conditions influence escape deficits produced by uncontrollable stress: assessment of the contribution of norepinephrine. Anisman H, et al. **Behav Neural Biol** 1981 Aug;32(4):406-27

Cholinergic influences on escape deficits produced by uncontrollable stress. Anisman H, et al. **Psychopharmacology (Berlin)** 1981; 74(1):81-7

ESTRADIOL

Effect of oestrogen on the responsiveness of the pituitary gland to LRH: the role of corpora lutea. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1981 Sep;98(1):29-35

Effect of oestradiol-17 beta on the metabolism of noradrenaline in brain slices of ovariectomized rats. Köster G, et al. **Acta Endocrinol (Copenh)** 1981 Sep;98(1):1-7

A different distribution of corticotropin releasing factor and arginine vasopressin contents in the hypothalamic nuclei after estrogen administration. Hashimoto K, et al. **Acta Med Okayama** 1981 Feb; 35(1):37-43

Induction of pseudo-pregnancy in Saccobranchus fossilis and cytomorphological assay of anomalies. Saxena V, et al. **Biochem Exp Biol** 1980;16(3):257-60

Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Rivier C, et al. **Biol Reprod** 1981 Jun;24(5):1061-7

Effects of estradiol and progesterone on plasma gonadotropins, prolactin, and LHRH in specific brain areas of ovariectomized rats. Wise PM, et al. **Biol Reprod** 1981 May;24(4):820-30

Effects of ageing and gonadal steroid hormones on prolactin concentrations in the anterior pituitary of the chicken. Kono T, et al. **Br Poult Sci** 1980 Nov;21(6):431-6

Differential effects of gonadal steroids on dopamine metabolism in mesolimbic and nigro-striatal pathways of male rat brain. Alderson LM, et al. **Brain Res** 1981 Aug 10;218(1-2):189-206

Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Menniti FS, et al. **Brain Res** 1981 Jul 6; 216(1):89-107

The effects of stimulation and lesion of raphe nuclei on luteinizing hormone release in estrogen-progesterone-treated ovariectomized rats. Waloch M, et al. **Brain Res** 1981 Aug 3;217(2):305-13

Persistence of dihydrotestosterone inhibition of lordosis in estrogen-primed rats fed a tryptophan-deficient diet. Menniti FS, et al. **Brain Res Bull** 1981 Jul;7(1):1-4

Oestrogen-gonadotrophin feedback mechanisms in the puerperium. Glass MR, et al. **Clin Endocrinol (Oxf)** 1981 Mar;14(3):257-67

Electrical stimulation of mesencephalic noradrenergic pathway: effects on luteinizing hormone levels in blood of ovariectomized and ovariectomized, steroid-primed rats. Leung PC, et al. **Endocrinology** 1981 Sep;109(3):720-8

Estrogen facilitation of lordosis behavior in the female rat. Gorski RA, et al. **Exp Brain Res** 1981;Suppl 3:222-37

Estradiol concentration in dopamine-beta-hydroxylase containing neurons of lower brain stem demonstrated by combined autoradiography and immunohistochemistry. Sar M, et al. **Exp Brain Res** 1981; Suppl 3:29-36

Role of ovarian hormones in the long-term control of glucose homeostasis. Interaction with insulin, glucagon and epinephrine. Ahmed-Sorour H, et al. **Horm Res** 1980;13(6):396-403

Effects of oestradiol, hypothalamic extracts and luteinizing hormone releasing hormone on rat anterior pituitary gland gonadotrophin release in vitro before and after the preovulatory luteinizing hormone surge at pro-oestrus. Elias KA, et al. **J Endocrinol** 1981 Sep;90(3):345-54

2-hydroxyoestradiol inhibits prolactin release from the superfused rat pituitary gland. Linton EA, et al. **J Endocrinol** 1981 Sep; 90(3):315-22

The failure of prolactin to enhance the inhibitory effect of oestradiol-17 beta on LH synthesis and release in ewes. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):537-42

Effect of estradiol benzoate and clomiphene on tyrosine hydroxylase activity and on luteinizing hormone and prolactin levels in ovariectomized rats. Tobias H, et al. **Life Sci** 1981 Aug 17; 29(7):711-6

Uterine serotonin and receptor blockade during estrogen-induced uterine hyperemia. Van Orden DE, et al. **Proc Soc Exp Biol Med** 1981 Sep; 167(4):469-74

[Biological and immunological activity similar to digitalis glycosides of synthetic ACTH and some sex hormone 14-hydroxyderivatives (author's transl)] Schreiber V, et al. **Cas Lek Cesk** 1981 May 21; 120(20):616-8 (Eng. Abstr.) (Cze)

[Changes of hypothalamic LH-RH content induced by estradiol injection into female rats (author's transl)] Saito A. **Nippon Sanka Fujinka Gakkai Zasshi** 1981 Aug;33(8):1227-34 (Eng. Abstr.) (Jpn)

[Reaction between steroid hormones, the liver and its plasma membrane] Denisov IuP, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):722-5 (Eng. Abstr.) (Rus)

EUPHORIA

[Effect of euphorigenic drugs on emotionally-positive brain systems] Zvartau EE, et al. **Zh Vyssh Nerv Deiat** 1981;31(2):308-14 (Eng. Abstr.) (Rus)

EXPLORATORY BEHAVIOR

Comparison of the effects of beta-endorphin and morphine on exploratory and socio-sexual behaviour in the male rat. Meyerson BJ. **Eur J Pharmacol** 1981 Feb 19;69(4):453-63

Potentiation by Des-Tyr-gamma-endorphin on apomorphine-induced changes in rat open field behavior. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):77-81

Locomotor activity, defecation score and corticosterone levels during an openfield exposure: a comparison among individually and group-housed rats, and genetically selected rat lines. Gentsch C, et al. **Physiol Behav** 1981 Jul;27(1):183-6

The locomotor and exploratory activities in rats after lesion of hippocampal pyramidal cells with kainic acid. Kleinrok Z, et al. **Pol J Pharmacol Pharm** 1980;32(5):625-37

Effects of a piperazine derivative piribedil, on exploration, locomotor activity and social behaviour in the rat. File SE. **Prog Neuropsychopharmacol** 1981;5(3):245-55

EXTINCTION (PSYCHOLOGY)

The temporal structure of motivation IV: A reexamination of extinction effects in intracranial reward. Katz RJ. **Behav Neural Biol** 1981 Jun; 32(2):191-200

Extinction of a conditioned taste aversion in young, mid-aged, and aged C57/BL6 mice. Springer AD, et al. **Behav Neural Biol** 1981 Jul; 32(3):282-94

The partial reinforcement extinction effect: influence of chlordiazepoxide in septal lesioned rats. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 74(3):280-9

FEAR

Long-term effect of pentobarbital anesthesia on neophobia in the rat. McGee R, et al. **Behav Neural Biol** 1981 Jul;32(3):376-9

The acute effect of p-chloroamphetamine on the retention of fear conditioning in the rat: evidence for a role of serotonin in memory consolidation. Archer T, et al. **Neurosci Lett** 1981 Aug 7; 25(1):75-81

FENFLURAMINE

Different action of 5-hydroxytryptamine (5-HT) uptake inhibitors on fenfluramine- but not p-chloramphetamine-induced hyperthermia in rats. Pawlowski L. **J Pharm Pharmacol** 1981 Aug;33(8):538-40

FLUPHENAZINE

Daytime variation in serum prolactin level in patients receiving oral and depot antipsychotic medication. Goode DJ, et al. **Biol Psychiatry** 1981 Jul;16(7):653-62

Fluphenazine resistant psychosis. Brent R, et al. **Can J Psychiatry** 1981 Mar;26(2):118-9

Appropriate treatment of fibromyositis [letter] Labowitz RJ, et al. **Del Med J** 1981 Aug;53(8):389

Oral fluphenazine and tea and coffee drinking [letter] Wallace SM, et al. **Lancet** 1981 Sep 26;2(8248):691

Effects of fluphenazine hydrochloride on the bone-marrow cells of Swiss mice. Rao KP, et al. **Mutat Res** 1981 Jul;89(3):237-40

Flupenthixol versus combined fluphenazine-nortriptyline in depressive illness. Conway JF. **Practitioner** 1981 Mar;225(1353):400-4

The prolactin response in patients receiving neuroleptic therapy. The effect of fluphenazine decanoate. Dotti A, et al. **Prog Neuropsychopharmacol** 1981;5(1):69-77

[Flufenazine decanoate in the ambulatory treatment of schizophrenic patients] Populin M, et al. **Minerva Psichiatr** 1981 Apr-Jun; 22(2):85-92 (73 ref.) (Eng. Abstr.) **(Ita)**

FLURAZEPAM

Determination of the major urinary metabolite of flurazepam in man by high-performance liquid chromatography. Weinfeld RE, et al. **J Chromatogr** 1981 Apr 10;223(1):123-30

Regional specificity of benzodiazepine receptor down-regulation during chronic treatment of rats with flurazepam. Rosenberg HC, et al. **Neurosci Lett** 1981 Jun 12;24(1):49-52

Dose-related effects of flurazepam on human sleep-walking patterns. Karacan I, et al. **Psychopharmacology (Berlin)** 1981;73(4):332-9

FOOD DEPRIVATION

Rewarding effect of noradrenergic stimulation of the amygdala in food deprived rats. Jurkowlaniec E, et al. **Physiol Behav** 1981 Jul; 27(1):27-31

FSH

Direct effects of gonadotropin releasing hormone and its antagonist upon ovarian functions stimulated by FSH, prolactin, ans LH. Jones PB, et al. **Biol Reprod** 1981 May;24(4):747-59

Site of action of prolactin in the suppression of gonadotropin secretion during lactation in the rat: effect on pituitary responsiveness to LHRH. Smith MS. **Biol Reprod** 1981 Jun;24(5):967-76

The presence of two species of follicle-stimulating hormone within hamster anterior pituitary glands as disclosed by concanavalin A chromatography. Chappel SC. **Endocrinology** 1981 Sep;109(3):935-42

Frequency and amplitude of gonadotropin-releasing hormone stimulation and gonadotropin secretion in the rhesus monkey. Wildt L, et al. **Endocrinology** 1981 Aug;109(2):376-85

Influence of neonatal ovariectomy on the developmental patterns of serum gonadotropins, hypothalamic LH-RH concentration and organ weights in female rats. Döcke F, et al. **Endokrinologie** 1981 Mar; 77(3):273-85

Differential effects of testosterone and its metabolites on gonadotrophin secretion in the intact adult male rat. Reymond M, et al. **Horm Res** 1981;14(2):114-29

Multihormonal regulation of ornithine decarboxylase activity in highly differentiated porcine granulosa cells in vitro. Veldhuis JD, et al. **J Cell Physiol** 1981 Aug;108(2):213-20

Effects of oestradiol, hypothalamic extracts and luteinizing hormone releasing hormone on rat anterior pituitary gland gonadotrophin release in vitro before and after the preovulatory luteinizing hormone surge at pro-oestrus. Elias KA, et al. **J Endocrinol** 1981 Sep;90(3):345-54

Repetitive treatment with gonadotrophin releasing factor or a long-acting analogue upon gonadotrophin secretion in the ferret. Gledhill B, et al. **J Endocrinol** 1981 Aug;90(2):275-83

Time-related secretion of gonadotrophins after a single injection of steroid-free bovine follicular fluid in prepubertal and adult female rats. Hermans WP, et al. **J Endocrinol** 1981 Jul;90(1):69-76

Dissociation in the regulation of luteinizing hormone and follicle-stimulating hormone in a hyperprolactinaemic rat model: interrelationships between gonadotrophin and prolactin control. Tresguerres JA, et al. **J Endocrinol** 1981 Jul;90(1):41-51

Modulation of FSH-controlled steroidogenesis in rat granulosa cells: direct in-vitro effects of LHRH and ICI-118630. Hillier SG, et al. **Mol Cell Endocrinol** 1981 Aug;23(2):193-205

Hormonal regulation of cytodifferentiation and intercellular communication in cultured granulosa cells. Amsterdam A, et al. **Proc Natl Acad Sci USA** 1981 May;78(5):3000-4

[Intracellular mechanism for the action of inhibin on the secretion of the follicular-stimulating hormone and luteinizing hormone induced by LH-RH in vitro] Lecomte-Yerna MJ, et al. **C R Trav Lab Carlsberg** 1981;175(3):385-8 (Eng. Abstr.) **(Fre)**

[Effect of gonadotropin releasing hormone, clomide and L-dopa on the secretion of chorionic gonadotropins, follicle-stimulating hormone and prolactin in the first trimester of uncomplicated pregnancy] Rzempoluch J. **Ginekol Pol** 1981 Jan;52(2):211-4 **(Pol)**

GABA

Dextro-phenylalanine as inhibitor of the noradrenaline release from the isolated rat hypothalamus. Pardal JF, et al. **Acta Neurol Latinoam** 1979; 25(3-4):235-48

Role of GABA-ergic receptors for the synthesis of GABA in different compartments of the rat cerebellum. Carmona E, et al. **Acta Physiol Scand** 1981 May;112(1):109-10

Opposing actions of convulsants and anticonvulsants on GABA responses of crayfish stretch receptors. Adams PR, et al. **Adv Biochem Psychopharmacol** 1981;29:369-78

Opposite effects of 5,5-diphenylhydantoin and picrotoxin on GABAergic inhibition in crayfish stretch receptor. Aickin CC, et al. **Adv Biochem Psychopharmacol** 1981;29:301-7

Depolarizing postsynaptic actions of GABA in the rat dentate gyrus. Assaf SY, et al. **Adv Biochem Psychopharmacol** 1981;29:239-48

Actions of GABA on mammalian neurones, axons, and nerve terminals. Brown DA, et al. **Adv Biochem Psychopharmacol** 1981;29:321-6 (33 ref.)

Enzymology of the alternative reductive pathway of GABA catabolism leading to the biosynthesis of gamma-hydroxybutyrate. Cash CD, et al. **Adv Biochem Psychopharmacol** 1981;29:527-35 (31 ref.)

Development of GABA-accumulating neurons and glial cells in the rat visual cortex. Chronwall BM, et al. **Adv Biochem Psychopharmacol** 1981; 29:453-8

GABA and muscimol binding processes in CNS tissue culture preparations. DeFeudis FV, et al. **Adv Biochem Psychopharmacol** 1981; 29:405-10

Physiological study of amino acid uptake and receptor desensitization: the GABA system in dorsal root ganglia. Désarménien M, et al. **Adv Biochem Psychopharmacol** 1981;29:309-19

Effects of GABA metabolism on [3H]-GABA transport in synaptosomal preparations from rat cerebral cortex. Gardner CR, et al. **Adv Biochem Psychopharmacol** 1981;29:143-50

In vivo release of newly synthesized GABA in the basal ganglia of the cat. Gauchy C, et al. **Adv Biochem Psychopharmacol** 1981;29:183-91

GABA systems and behavior. Koella WP. **Adv Biochem Psychopharmacol** 1981;29:11-21 (32 ref.)

Comparison of the uptake processes of taurine, hypotaurine, and GABA. Kontro P. **Adv Biochem Psychopharmacol** 1981;29:161-7

Action of GABA on hippocampal neurons. Krnjević K. **Adv Biochem Psychopharmacol** 1981;29:231-7

THIP, isoguvacine, isoguvacine oxide, and related GABA agonists. Krogsgaard-Larsen P, et al. **Adv Biochem Psychopharmacol** 1981; 29:69-76 (31 ref.)

The neurohypophysial GABA system. Mathison RD, et al. **Adv Biochem Psychopharmacol** 1981;29:343-50 (23 ref.)

Autoradiographic and immunocytochemical evidence for the existence of GABAergic neurons in the nucleus raphe dorsalis--possible existence of neurons containing 5HT and glutamate decarboxylase. Nanopoulos D, et al. **Adv Biochem Psychopharmacol** 1981;29:519-25

Potassium-stimulated release of taurine, hypotaurine, and GABA from brain tissue in vitro. Oja SS, et al. **Adv Biochem Psychopharmacol** 1981; 29:175-81

Roles of GABA and glycine in the substantia nigra. Pycock CJ, et al. **Adv Biochem Psychopharmacol** 1981;29:77-87 (52 ref.)

GABA binding to dendrodendritic synaptosomal membranes from rat olfactory bulbs. Quinn MR, et al. **Adv Biochem Psychopharmacol** 1981; 29:421-8

GABA and its interaction with ACh in the rabbit retina. Redburn DA, et al. **Adv Biochem Psychopharmacol** 1981;29:169-74

Heterocyclic GABA analogues as selective inhibitors of astroglial GABA uptake. Schousboe A, et al. **Adv Biochem Psychopharmacol** 1981; 29:135-41 (28 ref.)

Release of endogenous GABA from the rat brain: methodological aspects and the effects of catecholamines. van der Heyden JA, et al. **Adv Biochem Psychopharmacol** 1981;29:193-203

Evidence for a dual role of GABA as a synaptic transmitter and a promoter of synaptogenesis. Wolff JR. **Adv Biochem Psychopharmacol** 1981;29:459-65 (29 ref.)

CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Gerner RH, et al. **Am J Psychiatry** 1981 Aug;138(8):1098-101

Effect of histamine H1- and H2-receptor agonists on gamma-aminobutyric acid (GABA) content in hypothalamus and striatum of the rat brain. Nowak JZ, et al. **Arch Immunol Ther Exp (Warsz)** 1980;28(6):917-20

Effects of gamma-acetylenic GABA and gamma-vinyl GABA on synaptosomal release and uptake of GABA. Abdul-Ghani AS, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1203-9

Pharmacological specificity of synaptosomal and synaptic membrane gamma-aminobutyric acid (GABA) transport processes. Early SL, et al. **Biochem Pharmacol** 1981 May 15;30(10):1105-13

Valproate induced changes in GABA metabolism at the subcellular level. Löscher W. **Biochem Pharmacol** 1981 Jun 1;30(11):1364-6

Efflux of gamma-aminobutyric acid by synaptic plasma membrane vesicles isolated from rat brain. Kanner BI, et al. **Biochemistry** 1981 Jun 9; 20(12):3354-8

Stimulation of benzodiazepine binding to rat brain membranes and solubilized receptor complex by avermectin B1a and gamma-aminobutyric acid. Pong SS, et al. **Biochim Biophys Acta** 1981 Aug 6;646(1):143-50

On the mechanism by which veratridine causes a calcium-independent release of gamma-aminobutyric acid from brain slices. Cunningham J, et al. **Br J Pharmacol** 1981 Jul;73(3):655-67

The effects of 4-aminopyridine on the isolated vas deferens and its effects on the inhibitory properties of adenosine, morphine, noradrenaline and gamma-aminobutyric acid. Stone TW. **Br J Pharmacol** 1981 Jul; 73(3):791-6

The dendritic response to GABA in CA1 of the hippocampal slice. Djørup A, et al. **Brain Res** 1981 Aug 24;219(1):196-201

Electrophysiological evidence favoring intracaudate axon collaterals of GABAergic caudate output neurons in the cat. Katayama Y, et al. **Brain Res** 1981 Jul 6;216(1):180-6

GABA and muscimol open ion channels of different lifetimes on cultured mouse spinal cord cells. Mathers DA, et al. **Brain Res** 1981 Jan 5; 204(1):242-7

Alteration of GABA system in frog retina following short light and dark adaptations - a quantitative comparison with retinal taurine. Nishimura C, et al. **Brain Res** 1981 Aug 31;219(2):433-8

Ultrastructure of GABA-neurons in cultures of rat neostriatum. Panula P, et al. **Brain Res** 1981 Aug 24;219(1):202-7

Ethyl beta-carboline-3-carboxylate antagonizes the action of GABA and benzodiazepines in the hippocampus. Polc P, et al. **Brain Res** 1981 Jul 27;217(1):216-20

Benzodiazepine binding and interactions with the GABA receptor complex in living cultures of rat cerebral cortex. White WF, et al. **Brain Res** 1981 Jun 29;215(1-2):162-76

Postnatal changes of GABAergic and glutamatergic parameters. Wong PT, et al. **Brain Res** 1981 Jul;227(4):519-29

Biochemical development of the human brain. II. Some parameters of the GABA-ergic system. Brooksbank BW, et al. **Dev Neurosci** 1981; 4(3):188-200

Developmental changes of the GABA and polyamine systems in isolated neurons in cell culture. Seiler N, et al. **Dev Neurosci** 1981; 4(3):181-7

Increases and decreases in local cerebral glucose utilization in response to GABA agonists. Palacios JM, et al. **Eur J Pharmacol** 1981 May 8; 71(2-3):333-6

[3H] Ethyl beta-carboline-3-carboxylate binding to the benzodiazepine receptor is not affected by GABA. Patel J, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):419-20

Effect of aminooxyacetic acid on endogenous GABA release from rat retina. Mizuno A, et al. **Exp Eye Res** 1981 Aug;33(2):197-202

Transport and metabolism of glutamate and GABA in neurons are glial cells. Schousboe A. **Int Rev Neurobiol** 1981;22:1-45 (419 ref.)

Gamma-aminobutyric acid system in rat oviduct. Martin del Rio R. **J Biol Chem** 1981 Oct 10;256(19):9816-9

GABAergic synapses in the goldfish retina: an autoradiographic study of 3H-muscimol and 3H-GABA binding. Yazulla S. **J Comp Neurol** 1981 Jul 20;200(1):83-93

Concurrent acetylcholinesterase staining and gamma-aminobutyric acid uptake of cortical neurons in culture. Mesulam MM, et al. **J Histochem Cytochem** 1981 Feb;29(2):306-8

Selective inhibition of L-glutamate and gammaaminobutyrate transport in nerve ending particles by aluminium, manganese, and cadmium chloride. Wong PC, et al. **J Inorg Biochem** 1981 Jun;14(3):253-60

Epimeric cis-decahydroquinoline-5-carboxylic acids: effects on gamma-aminobutyric acid uptake and receptor binding in vitro. Witiak DT, et al. **J Med Chem** 1981 Jul;24(7):788-94

Release of 3H-gamma-aminobutyric acid (GABA) by inhibitory neurons of the crayfish. Craelius W, et al. **J Neurobiol** 1981 May; 12(3):249-58

Enhancement of depolarization-induced release of gamma-aminobutyric acid from brain slices by antibodies to ganglioside. Frieder B, et al. **J Neurochem** 1981 Sep;37(3):634-9

Characterization of the binding of the GABA agonist [3H]piperidine-4-sulphonic acid to bovine brain synaptic membranes. Krogsgaard-Larsen P, et al. **J Neurochem** 1981 Aug;37(2):401-9

Effects of sodium and bicarbonate ions on gamma-aminobutyric acid receptor binding in synaptic membranes of rat brain. Kurioka S, et al. **J Neurochem** 1981 Aug;37(2):418-21

Characterization of gamma-aminobutyric acid binding sites on crude synaptic membranes. Kurioka S, et al. **J Neurochem** 1981 Aug; 37(2):283-8

Glutamate as a putative transmitter in the cerebellum: stimulation by GABA of glutamic acid release from specific pools. Levi G, et al. **J Neurochem** 1981 Jul;37(1):22-31

Effect of inhibitors of GABA aminotransferase on the metabolism of GABA in brain tissue and synaptosomal fractions. Löscher W. **J Neurochem** 1981 Apr;36(4):1521-7

gamma-Aminobutyric acid concentration in cerebrospinal fluid in schizophrenia. McCarthy BW, et al. **J Neurochem** 1981 Apr; 36(4):1406-8

GABA-benzodiazepine-barbiturate receptor interactions. Olsen RW. **J Neurochem** 1981 Jul;37(1):1-13 (146 ref.)

Elevation of brain GABA content by chronic low-dosage administration of hydrazine, a metabolite of isoniazid. Perry TL, et al. **J Neurochem** 1981 Jul;37(1):32-9

Sulfur amino acid metabolism in the developing rhesus monkey brain: subcellular studies of taurine, cysteinesulfinic acid decarboxylase, gamma-aminobutyric acid, and glutamic acid decarboxylase. Rassin DK, et al. **J Neurochem** 1981 Sep;37(3):740-8

Topographical distribution of gamma-aminobutyric acid within the cat thalamus in relation to the basal ganglia, as determined by mass fragmentometry. Yoshida M, et al. **J Neurochem** 1981 Sep; 37(3):670-6

Sizes and distributions of intrinsic neurons incorporating tritiated GABA in monkey sensory-motor cortex. Hendry SH, et al. **J Neurosci** 1981 Apr;1(4):390-408

Characterization of benzodiazepine and gamma-aminobutyric recognition sites and their endogenous modulators. Massotti M, et al. **J Neurosci** 1981 Apr;1(4):409-18

Different efficacies of d- and l-gamma-amino-beta-hydroxybutyric acids in GABA receptor and transport test systems. Roberts E, et al. **J Neurosci** 1981 Feb;1(2):132-40

Effect of GABAergic drugs on dopamine catabolism in the nigrostriatal and mesolimbic dopaminergic pathways of the rat. Gundlach AL, et al. **J Pharm Pharmacol** 1981 Jan;33(1):41-3

Reductions in retinal gamma-aminobutyric acid (GABA) content and in [3H]flunitrazepam binding after postnatal monosodium glutamate injections in rats. Regan JW, et al. **J Pharmacol Exp Ther** 1981 Sep; 218(3):791-6

Two kinds of recurrent inhibition of cat spinal alpha-motoneurones as differentiated pharmacologically. Cullheim S, et al. **J Physiol (Lond)** 1981 Mar;312:209-24

GABA-antagonists and spatial summation in Y-type cat retinal ganglion cells. Kirby AW, et al. **J Physiol (Lond)** 1981 Mar;312:335-44

The how of anxiety [editorial] **Lancet** 1981 Aug 1;2(8240):237-9

Neurochemical studies in the hypoxic brain: substance P, met-enkephalin, GABA and angiotensin converting enzyme. Arregui A, et al. **Life Sci** 1981 Jun 29;28(26):2925-9

Intracerebral injection of gamma vinyl GABA: method for measuring rates of GABA synthesis in specific brain regions in vivo. Casu M, et al. **Life Sci** 1981 Aug 17;29(7):681-8

Increased gamma-aminobutyric acid (GABA), homocarnosine and beta-alanine in cerebrospinal fluid of patients treated with gamma-vinyl GABA (4-amino-hex-5-enoic acid). Grove J, et al. **Life Sci** 1981 May 21;28(21):2431-9

Supersensitivity of substantia nigra pars reticulata neurons to GABAergic drugs after striatal lesions. Waszczak BL, et al. **Life Sci** 1981 May 21; 28(21):2411-20

GABA transport in the rat thyroid. Gebauer H. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):61-6

Comparison between (RS)-nipecotic acid and GABA transport in cultured astrocytes: coupling with two sodium ions. Larsson OM, et al. **Neurochem Res** 1981 Mar;6(3):257-66

Studies on the release of exogenous and endogenous GABA and glutamate from rat brain synaptosomes. Levi G, et al. **Neurochem Res** 1981 Mar; 6(3):275-85

Endogenous inhibitors of Na+-independent [3H]GABA binding to crude synaptic membranes. Massotti M, et al. **Neurochem Res** 1981 May; 6(5):551-65

Comparison of synaptosomal and glial uptake of pipecolic acid and GABA in rat brain. Nomura Y, et al. **Neurochem Res** 1981 Apr; 6(4):391-400

gamma-Aminobutyric acid system in isolated dorsal and ventral horn neurons from bovine spinal cord. Wakabayashi M, et al. **Neurochem Res** 1981 Jun;6(6):659-71

The in vitro iontophoretic release of radiolabelled histamine, N'-methylhistamine and GABA from 7-barrelled glass micropipettes. Roberts F. **Neuropharmacology** 1981 Jul;20(7):711-4

GABA receptors distribution in rat substantia nigra. De Montis GM, et al. **Neurosci Lett** 1981 May 29;23(3):257-61

Direct action of pentobarbitone in potentiating the responses to GABA of rat dorsal root ganglion neurones in vitro. Headley PM, et al. **Neurosci Lett** 1981 Jul 17;24(3):273-80

Autoradiographic localization of [3H]gamma-amino-butyric acid in the myenteric plexus of the guinea-pig small intestine. Krantis A, et al. **Neurosci Lett** 1981 May 29;23(3):263-8

Bilateral asymmetry in brain GABA function? Starr MS, et al. **Neurosci Lett** 1981 Sep 1;25(2):167-72

Septal driving of hippocampal theta rhythm: a role for gamma-aminobutyrate in the effects of minor tranquilizers? Mellanby J, et al. **Neuroscience** 1981;6(7):1412-21

Distribution of gamma-aminobutyrate in the rat thalamus: specific decreases in thalamic gamma-aminobutyrate following lesion or electrical stimulation of the substantia nigra. Starr MS, et al. **Neuroscience** 1981;6(6):1095-104

Effect of kainic acid on ultrastructure and gamma-aminobutyrate-related circuits in the optic tectum of the goldfish. Villani L, et al. **Neuroscience** 1981;6(7):1393-403

Effect of combined treatment with dopaminergic and GABA-ergic drugs on the threshold for maximal electroconvulsions in mice. Czuczwar SJ. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):25-35

Colonic bacteria: a source of gamma-aminobutyric acid in blood. Schafer

DF, et al. **Proc Soc Exp Biol Med** 1981 Jul;167(3):301-3

A dual role for GABA in quasi-morphine abstinence behavior induced by di-n-propylacetate involving both initiation and termination. Van der Laan JW, et al. **Psychopharmacology (Berlin)** 1981;74(2):143-8

Hindbrain GABA receptors influence parasympathetic outflow to the stomach. Williford DJ, et al. **Science** 1981 Oct 9;214(4517):193-4

[Influence of the GABAergic system on eating behavior induced by the tail pinching technic in rats] Bereksi B, et al. **C R Trav Lab Carlsberg** 1981;175(3):323-9 (Eng. Abstr.) **(Fre)**

[GABA containing neurons in the nucleus raphes dorsalis of the rat (author's transl)] Pfister C, et al. **Acta Histochem (Jena)** 1981; 68(1):117-24 (Eng. Abstr.) **(Ger)**

[GABA fluophore formation due to ninhydrin reaction in the octanolic milieu. Fluorescence histochemical investigation. 3. Information (author's transl)] Pfister C, et al. **Acta Histochem (Jena)** 1981; 68(2):231-7 (Eng. Abstr.) **(Ger)**

[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Preliminary results] Di Giorgio RM, et al. **Acta Neurol [Quad] (Napoli)** 1981;42:302-4 (Eng. Abstr.) **(Ita)**

[Pharmacological influences on the brain level and transport of GABA. II) Effect of various psychoactive drugs on brain level and uptake of GABA] Gabana MA, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30; 57(8):909-13 (Eng. Abstr.) **(Ita)**

[Pharmacological influences on the brain level and transport of GABA. I) Effect of various antipileptic drugs on brain levels of GABA] Varotto M, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30;57(8):904-8 (Eng. Abstr.) **(Ita)**

[Effect of GABA-negative preparations on the anxiolytic and sedative effects of diazepam] Andreev BV, et al. **Biull Eksp Biol Med** 1981 Jun; 91(6):685-7 (Eng. Abstr.) **(Rus)**

[Nipecotic acid, a competitive inhibitor of the net uptake of 3H-GABA by rat brain synaptosomes] Kovalev GI, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):692-4 (Eng. Abstr.) **(Rus)**

[GABA-ergic correlates of aggression and intraspecies sociability of mice subjected to isolation] Poshivalov VP. **Biull Eksp Biol Med** 1981 May; 91(5):584-7 (Eng. Abstr.) **(Rus)**

[New evidence for a GABA-ergic component in the mechanism of action of benzodiazepine tranquilizers] Zakusov VV, et al. **Biull Eksp Biol Med** 1981 May;91(5):571-4 (Eng. Abstr.) **(Rus)**

[A case of aminalon-induced disease] Bondarenko BB, et al. **Klin Med (Mosk)** 1981 Mar;59(3):109-10 **(Rus)**

GALVANIC SKIN RESPONSE

Bilateral skin conductance, finger pulse volume, and EEG orienting response to tones of differing intensities in chronic schizophrenics and controls. Bernstein AS, et al. **J Nerv Ment Dis** 1981 Aug; 169(8):513-28

Effects of exogenous stimuli and centrally acting drugs on galvanic skin responses in rats. Hata T, et al. **Jpn J Pharmacol** 1981 Feb; 31(1):23-31

GLUCURONIDASE

Comparative studies of asparagine-linked oligosaccharide structures of rat liver microsomal and lysosomal beta-glucuronidases. Mizuochi T, et al. **Arch Biochem Biophys** 1981 Jun;209(1):298-303

Disassociation of lysosomal enzyme secretion and macrophage-mediated bone resorption. Blair H, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):959-64

On the enzymatic hydrolysis of the sulfate conjugate of 3-methoxy-4-hydroxyphenylglycol (MHPG). Karoum F, et al. **Biochem Med** 1980 Dec;24(3):314-20

Beta-glucuronidase activity in Enterobacteriaceae. Massenti MF, et al. **Boll Ist Sieroter Milan** 1981;60(1):26-30

On-line cleavage of urinary estriol conjugates with immobilized beta-glucuronidase before liquid-chromatographic analysis. Bowers LD, et al. **Clin Chem** 1981 Sep;27(9):1554-7

Influence of age and sex on five human plasma lysosomal enzymes assayed by automated procedures. Lombardo A, et al. **Clin Chim Acta** 1981 Jun 18;113(2):141-52

The inhibition of PMN beta-glucuronidase release by Aroclor 1254. Lee TP. **Environ Res** 1981 Aug;25(2):386-90

The effects of testosterone and progestins on the rate of beta-glucuronidase synthesis in mouse kidney as studied with an immunoprecipitation assay. Gupta C, et al. **Int J Androl** 1981 Jun; 4(3):342-54

Acid hydrolases in the epididymis of normal, castrated, vasectomized, cryptorchid and cryptepididymal rats. Mayorga LS, et al. **Int J Androl** 1981 APr;4(2):208-19

Changes of sulfated mucopolysaccharides and mucopolysaccharidases during fetal development. Sampaio LO, et al. **J Biol Chem** 1981 Sep 10;256(17):9205-10

Turnover of two lysosomal enzymes in macrophages. Skudlarek MD, et al. **J Biol Chem** 1981 Oct 10;256(19):10137-44

Pulmonary alveolar macrophage lysosomal enzyme activity after sublethal rotational trauma. Starling JR, et al. **J Surg Res** 1981 Aug; 31(2):128-35

Increase of beta-glucuronidase activity in the serum of rats administered organophosphate and carbamate insecticides. Kikuchi H, et al. **J Toxicol Sci** 1981 Feb;6(1):27-35

Effect of organic thio-compounds on detoxication of glucuronyltransferase and beta-glucuronidase in the rat liver. Tamura S, et al. **J Toxicol Sci** 1981 Feb;6(1):19-16

Inhibitory effect of bile acids on the activity of human beta-glucuronidase at its optimal pH. Ho KJ, et al. **Proc Soc Exp Biol Med** 1981 Jul; 167(3):304-9

Circadian changes of lysosomal enzyme activities in rat hepatocytes using ultracytochemistry. Uchiyama Y, et al. **Prog Clin Biol Res** 1981; 59C(00):117-24

Histochemical evidence for radiation enhancement of lysosomal response following hyperthermia of tail cartilage in baby rat. Myers R, et al. **Radiat Res** 1981 Aug;87(2):329-40

[Histochemical demonstration of beta-glucuronidase and leucine aminopeptidase in cultivated aortic endothelial cells (author's transl)] Halle W, et al. **Acta Histochem (Jena)** 1981;68(2):188-92 (Eng. Abstr.) **(Ger)**

[Biochemical studies on acidic glycosaminoglycans in gingiva and dental pulp. 4. Beta-glucuronidase activity in dental pulp (author's transl)] Sakamoto N, et al. **Hiroshima Daigaku Shigaku Zasshi** 1980; 12(2):265-70 **(Jpn)**

GONADOTROPINS, PITUITARY

Gonadotrophin release by gonadotrophs incubated with gonadotrophin-releasing hormone is independent of intracellular cAMP accumulation. Benoist L, et al. **Acta Endocrinol (Copenh)** 1981; 97(3):329-37

Long lasting amplification and deformation of thyroid receptors after thyrotropin (TSH) and gonadotropin (GTH) treatment of chickens in the foetal period. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980; 56(3):303-7

On the correlation of luteinizing hormone-releasing hormone, luteinizing hormone, follicle-stimulating hormone, and prolactin levels in plasma of women with normal menstrual cycles. Aksel S. **Am J Obstet Gynecol** 1981 Oct 15;141(4):362-7

Effect of 20 alpha-dihydroprogesterone, progesterone, and their 5 alpha-reduced metabolites on serum gonadotropin levels and hypothalamic LHRH content. Gilies PA, et al. **Biol Reprod** 1981 Jun; 24(5):1088-97

Effects of estradiol and progesterone on plasma gonadotropins, prolactin, and LHRH in specific brain areas of ovariectomized rats. Wise PM, et al. **Biol Reprod** 1981 May;24(4):820-30

Oestrogen-gonadotrophin feedback mechanisms in the puerperium. Glass MR, et al. **Clin Endocrinol (Oxf)** 1981 Mar;14(3):257-67

Steroid effects on hypothalamic-gonadotropin interactions. McCann SM, et al. **Exp Brain Res** 1981;Suppl 3:142-50

Differences in negative and positive feedback of gonadal steroids on release of gonadotropins and prolactin in young and old rats. Meites J, et al. **Exp Brain Res** 1981;Suppl 3:151-7

GUANETHIDINE

Adrenergic blocking agents inadequate for nonsurgical male contraception. Alexander NJ, et al. **Fertil Steril** 1981 Jul; 36(1):119-21

[Effect of phenoxybenzamine on the adrenergic neurone blocking action of guanethidine in isolated guinea pig vas deferens (author's transl)] Kontani H. **Yakugaku Zasshi** 1980 Dec;100(12):1247-51 (Eng. Abstr.) **(Jpn)**

HABITUATION (PSYCHOPHYSIOLOGY)

Mathematical model of synaptic plasticity: II. Habituation. Lara R, et al. **Neurol Res** 1980;2(1):1-18

HALOPERIDOL

Hazards of mistaking haloperidol for diazepam [letter] Nininger JE, et al. **Am J Psychiatry** 1981 Aug;138(8):1130

An analysis of the effects of apomorphine and haloperidol on the release of [3H]-dopamine and [3H]-noradrenaline from rabbit brain slices. Kelly MJ. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):18-29

Effect of haloperidol withdrawal on motor activity and circadian rhythm of rats. Kumar A, et al. **Arzneimittelforsch** 1981;31(7):1096-8

Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Solomon PR, et al. **Biol Psychiatry** 1981 Jun; 16(6):519-37

Total and free serum haloperidol levels in schizophrenic patients and the effect of age thioridazine and fatty acid on haloperidol-serum protein binding in vitro. Rowell FJ, et al. **Br J Clin Pharmacol** 1981 Apr; 11(4):377-82

Increase in mesolimbic electrical self-stimulation after chronic

haloperidol: reversal by L-DOPA or lithium. Seeger TF, et al. **Brain Res** 1981 Jun 29;215(1-2):404-9
Promethazine and diazepam potantiate the haloperidol induced prolactin responses. Arató M. **Commun Psychopharmacol** 1980;4(4):317-22
In normal young men acute dopaminergic blockade does not impair free water excretion following a standard water load. Cohen M, et al. **Commun Psychopharmacol** 1980;4(4):323-6
Apomorphine, haloperidol and the average evoked potentials in normal human volunteers. Rey AC, et al. **Commun Psychopharmacol** 1980; 4(4):327-34
Apomorphine-induced stereotypy in matuse and senescent rats following cessation of chronic haloperidol treatment. Roffman M, et al. **Commun Psychopharmacol** 1980;4(4):283-6
Brain contribution to the haloperidol-induced increase in plasma homovanillic acid. Kendler KS, et al. **Eur J Pharmacol** 1981 May 8; 71(2-3):321-6
Antagonizing effects of haloperidol and bicuculline on inhibition of neurons of the substantia nigra, pars compacta. Nakamura S, et al. **Exp Neurol** 1981 Jul;73(1):304-9
Pituitary response to luteinizing hormone-releasing hormone during haloperidol-induced hyperprolactinemia. Del Carmen Díaz M, et al. **Fertil Steril** 1981 Jun;35(6):626-8
Isolation and identification of a metabolite of haloperidol. Pape BE. **J Anal Toxicol** 1981 May-Jun;5(3):113-7
High-performance liquid chromatographic determination of haloperidol in plasma. Miyazaki K, et al. **J Chromatogr** 1981 May 8; 223(2):449-53
Alterations of immune reactivity by haloperidol and delta-9-tetrahydrocannabinol. Levy JA, et al. **J Immunopharmacol** 1981; 3(1):93-109
Identification and distribution of neuroleptic binding sites in the rat spinal cord. Demenge P, et al. **J Neurochem** 1981 Jul;37(1):53-9
Haloperidol-induced reduction of nigral substance P-like immunoreactivity: a probe for the interactions between dopamine and substance P neuronal systems. Hanson GR, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):568-74
Effects of haloperidol and pimozide on classical conditioning of the rabbit nictitating membrane response. Harvey JA, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):712-9
Effects of short- and long-term neuroleptic treatment on brain serotonin synthesis and turnover: focus on the serotonin hypothesis of schizophrenia. Rastogi RB, et al. **Life Sci** 1981 Aug 17;29(7):735-41
Prolonged adverse effects of haloperidol in normal subjects [letter] Anderson BG, et al. **N Engl J Med** 1981 Sep 10;305(11):643-4
Illicit haldol [letter] Kruesi M, et al. **N Engl J Med** 1981 Sep 24; 305(13):769
Modulation by dopamine antagonists of DNA synthesis in the pituitary gland of the male rat. Jacobi JM, et al. **Neuroendocrinology** 1981 Aug; 33(2):97-100
A double-blind comparison of bromperidol and haloperidol in newly admitted schizophrenic patients. Brannen JO, et al. **Pharmacopsychiatria** 1981 Jul;14(4):139-40
A multicenter controlled trial in phobic-obsessive psychoneurosis. The effect of chlorimipramine and of its combinations with haloperidol and diazepam. Cassano GB, et al. **Prog Neuropsychopharmacol** 1981; 5(2):129-38
Chronic haloperidol treatment fails to alter the anorexic actions of dopaminergic agonists and cholinergic drugs. Hynes MD, et al. **Prog Neuropsychopharmacol** 1981;5(3):271-5
Enduring behavioural and biochemical effects in the adult rat after prolonged postnatal administration of haloperidol. Cuomo V, et al. **Psychopharmacology (Berlin)** 1981;74(2):166-9
Effects of chronic haloperidol treatment on ingestive behaviour and body weight regulation in the rat. Uguru-Okorie DC. **Psychopharmacology (Berlin)** 1981;73(4):384-7
The effects of haloperidol on the EEG spectrum. Wieneke GH, et al. **Psychopharmacology (Berlin)** 1981;74(1):33-4
[Toxicity of organic phosphates under the influence of neuroleptics] Andreas K, et al. **Acta Biol Med Ger** 1980;39(8-9):987-9 **(Ger)**
[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Preliminary results] Di Giorgio RM, et al. **Acta Neurol [Quad] (Napoli)** 1981;42:302-4 (Eng. Abstr.) **(Ita)**
[Pharmacological influences on the brain level and transport of GABA. II) Effect of various psychoactive drugs on brain level and uptake of GABA] Gabana MA, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30; 57(8):909-13 (Eng. Abstr.) **(Ita)**

HANDLING (PSYCHOLOGY)

Stressor effects of handling on the immature fowl. Freeman BM, et al. **Res Vet Sci** 1979 Mar;26(2):223-6

HEXOBARBITAL

Effect of diethyldithiocarbamate on the metabolic elimination of hexobarbital, phenazone, tolbutamide and four halogenated hydrocarbons. Siegers CP, et al. **Eur J Drug Metab Pharmacokinet** 1981; 6(2):141-8
Heme enhances hexobarbital metabolism in perfused rat liver after drug-mediated destruction of cytochrome P-450. Farrell GC, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):363-7
Interaction of lithium and disulfiram in hexobarbital hypnosis: possible role of the 5-HT system. Minegishi A, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):481-7
[The effect of noise on the biotransformation of hexobarbital in the rat] Loertzer HJ, et al. **Z Gesamte Hyg** 1981;27(6):438-40 (Eng. Abstr.) **(Ger)**
[Development of hexobarbital radiometry and its application (author's transl)] Inoue K, et al. **Eisei Shikenjo Hokoku** 1980;98:56-62 (Eng. Abstr.) **(Jpn)**
[Inhibition of bacterial luminescence by cytochrome P-450 substrates] Ismailov AD, et al. **Biokhimiia** 1981 Feb;46(2):234-9 (Eng. Abstr.) **(Rus)**
[Mechanism of pantogam potentiation of certain effects of hexobarbital and sodium barbital and inhibition of phenamine hyperactivity] Avakumov VM, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):30-4 (Eng. Abstr.) **(Rus)**

HISTAMINE

Pharmacological investigations into the effects of histamine and histamine analogs on guinea pig and rat uterus. Goyal RK, et al. **Agents Actions** 1981 Jul;11(4):312-7
The importance of human intestinal diamine oxidase in the oxidation of histamine and/or putrescine. Biegański T, et al. **Arch Immunol Ther Exp (Warsz)** 1980;28(6):901-6
Influence of oxotremorine on histamine level and histamine synthesis in the rat brain. Bielkiewicz B, et al. **Arch Immunol Ther Exp (Warsz)** 1980;28(6):921-5
Effects of mianserin, desipramine and maprotiline on blood pressure responses evoked by acetylcholine, histamine and 5-hydroxytryptamine in rats. Cavero I, et al. **Br J Pharmacol** 1981 Sep;74(1):143-8
Reactivity of isolated trachea, bronchus and lung strip of cats of carbachol, 5-hydroxytryptamine and histamine: evidence for the existence of methysergide-sensitive receptors. Chand N. **Br J Pharmacol** 1981 Aug; 73(4):853-7
Effects of chemical transmitters on function of isolated canine parietal cells. Soll AH, et al. **Fed Proc** 1981 Aug;40(10):2519-23
Mechanism of histamine-induced excitation of the cat pylorus. Biancani P, et al. **J Clin Invest** 1981 Sep;68(3):582-8
Snake alpha-toxin effects on cholinergic and noncholinergic responses of Aplysia californica neurons. Ono JK, et al. **J Neurosci** 1981 Mar; 1(3):259-70
Cholinergic and alpha adrenergic augmentation of histamine-induced contraction of canine airway smooth muscle. Leff AR, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):582-7
The in vitro iontophoretic release of radiolabelled histamine, N'-methylhistamine and GABA from 7-barrelled glass micropipettes. Roberts F. **Neuropharmacology** 1981 Jul;20(7):711-4
[Blood and skin histamine and serotonin levels in rats following second degree burns] Nowik-Jurek M, et al. **Pol Tyg Lek** 1981 May 4; 36(18):631-5 (Eng. Abstr.) **(Pol)**
[Effect of various pharmacologic preparations on the viability of Chinese hamster fibroblasts in vitro] Beuverova EI, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):739-40 (Eng. Abstr.) **(Rus)**
[Effect of disturbance of the liver and myocardium innervation on the histamine and serotonin contents in their tissues] Aksenova VM. **Ukr Biokhim Zh** 1980 Sep-Oct;52(5):569-72 (Eng. Abstr.) **(Rus)**

HOSTILITY

Changes in the hostility of schizophrenic patients during treatment. Tsiantis J, et al. **Br J Med Psychol** 1981 Sep;54(Pt 3):251-8
Hostility conflict and the effect of chlordiazepoxide on change in hostility level. Downing RW, et al. **Compr Psychiatry** 1981 Jul-Aug; 22(4):362-7

HYDANTOINS

Induction of drug-metabolizing enzymes by the enantiomers of normephenytoin in the rat. James R, et al. **Drug Metab Dispos** 1981 May-Jun;9(3):297-302
Mesantoin (methoin) [letter] Buckroyd JE. **Med J Aust** 1981 Apr 18; 1(8):431

HYDRAZINES

Effects of benserazide and carbidopa on the metabolism of L-tryptophan by isolated rat liver cells. Smith SA, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):623-8
Toxic and teratogenic effects of hydrazine on fathead minnow (pimephales promelas) embryos. Henderson V, et al. **Arch Environ Contam Toxicol** 1981 Jun;26(6):807-12
Elevation of brain GABA content by chronic low-dosage administration

of hydrazine, a metabolite of isoniazid. Perry TL, et al. **J Neurochem** 1981 Jul;37(1):32–9

Metabolism of isoniazid and free hydrazine formation in isolated rat hepatocytes. Hirata M, et al. **J Pharmacobiodyn** 1981 Feb;4(2):145–7

[Effect of hydrazine sulfate on lipid composition in rat liver homogenates and plasma membranes] Nechiporuk TS, et al. **Ukr Biokhim Zh** 1980 Sep–Oct;52(5):636–42 (Eng. Abstr.) **(Rus)**

HYDRAZONES

Identification of hydrazone of norethindrone, a metabolic product resulting from the interaction between isoniazid and norethindrone. Watanabe H, et al. **Res Commun Chem Pathol Pharmacol** 1981 Mar; 31(3):435–42

[Research on substances with antiviral activity. XVIII. Bis–amidinohydrazones of N–heterocyclic aromatic dialdehydes] Garuti L, et al. **Farmaco [Sci]** 1981 Jun;36(6):393–9 (Eng. Abstr.) **(Ita)**

HYDROXYBUTYRATES

Enzymology of the alternative reductive pathway of GABA catabolism leading to the biosynthesis of gamma–hydroxybutyrate. Cash CD, et al. **Adv Biochem Psychopharmacol** 1981;29:527–35 (31 ref.)

Influence of ration composition and energy balance on blood beta–hydroxybutyrate (ketone) and plasma glucose concentrations of dairy cows in early lactation. Herdt TH, et al. **Am J Vet Res** 1981 Jul;42(7):1177–80

The influence of sodium gamma–hydroxybutyrate on GABA receptors and catecholamine effect potentiation. Kozhechkin SN. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):242–53

Metabolism of L–and D–3–hydroxybutyrate by rat liver during development. Swiatek KR, et al. **Biochem Med** 1981 Apr; 25(2):160–7

Ontogeny of gamma–hydroxybutyric acid. I. Regional concentration in developing rat, monkey and human brain. Snead OC 3d, et al. **Brain Res** 1981 Jul;227(4):579–89

Glucose and 3–hydroxybutyrate utilization by chick telencephalon during postnatal development. Nehlig A, et al. **Experientia** 1981 Jun; 37(6):553–5

Electrocorticographic activity induced by gamma hydroxybutyrate in the rat during ontogenesis. Rokyta R, et al. **Experientia** 1981 Jul 15; 37(7):750–2

Blood concentration and disappearance of injected alanine and beta–hydroxybutyrate in surgical patients. Swaminathan R, et al. **Horm Metab Res** 1981 Jul;13(7):383–6

Energy metabolism in rat brain: inhibition of pyruvate decarboxylation by 3–hydroxybutyrate in neonatal mitochondria. Booth RF, et al. **J Neurochem** 1981 Jul;37(1):179–85

Regional and subcellular localization in rat brain of the enzymes that can synthesize gamma–hydroxybutyric acid. Rumigny JF, et al. **J Neurochem** 1981 Apr;36(4):1433–8

Gamma–hydroxybutyrate treatment of schizophrenia: a pilot study. Schulz SC, et al. **Pharmacopsychiatria** 1981 Jul;14(4):129–34

[Effect of sodium hydroxybutyrate on mitochondrial oxidative phosphorylation and myocardial pentose cycle enzymes during high altitude hypoxia] Chotoev ZhA, et al. **Farmakol Toksikol** 1981 Mar–Apr; 44(2):159–62 (Eng. Abstr.) **(Rus)**

[Effect of certain GABA–ergic substances on dopamine metabolism in the rat brain] Malikova LA, et al. **Farmakol Toksikol** 1981 Jan–Feb; 44(1):37–40 (Eng. Abstr.) **(Rus)**

HYDROXYDOPAMINES

Effect of neonatal administrations of 6–OHDA on the brain development. I. Alteration in the striatum. Imamoto K, et al. **Arch Histol Jpn** 1980 Oct;43(4):347–64

Conspecific odor preferences of male albino rats are reversed by intracerebral 6–hydroxydopamine. Cornwell–Jones CA. **Brain Res** 1981 Jun 1;213(2):379–85

Behavioural recovery following transplantation of substantia nigra in rats subjected to 6–OHDA lesions of the nigrostriatal pathway. I. Unilateral lesions. Dunnett SB, et al. **Brain Res** 1981 Jun 29;215(1–2):147–61

Presynaptic alpha–adrenergic mediation of self–stimulation in locus coeruleus in rats treated neonatally with 6–hydroxydopamine. Umemoto M, et al. **Brain Res** 1981 Aug 24;219(1):107–19

Changes in brain norepinephrine content in mice following neonatal 6–hydroxydopamine. Lovell KL. **Brain Res Bull** 1981 Jul;7(1):41–4

Effect of dopamine agonists and antagonists on the electrical activity of substantia nigra neurons transplanted into the lateral ventricle of the rat. Wuerthele SM, et al. **Exp Brain Res** 1981;44(1):1–10

6–Hydroxydopamine and radiofrequency lesions of the lateral entorhinal cortex facilitate an operant appetitive conditioning task in mice. Gauthier M, et al. **Neurosci Lett** 1981 Jul 2;24(2):193–7

Effects of 6–hydroxydopamine lesions of locus coeruleus on startle in rats. Adams LM, et al. **Psychopharmacology (Berlin)** 1981; 73(4):394–8

HYDROXYINDOLEACETIC ACID

Cerebrospinal fluid amine metabolites, tryptophan and clinical parameters in depression. Part 1. Background variables. Banki CM, et al. **J Affective Disord** 1981 Jun;3(2):81–9

Postmortem changes of 5–hydroxytryptamine and 5–hydroxyindoleacetic acid in mouse brain and their prevention by pargyline and microwave irradiation. Van Wijk M, et al. **Neurochem Res** 1981 Apr; 6(4):425–30

[Metabolism of peripheral catecholamines and indole amines in healthy persons. Clinico–biochemical correlates] Krzyżowski J, et al. **Pol Tyg Lek** 1981 Mar 16;36(11):417–21 (Eng. Abstr.) **(Pol)**

[Interstrain differences in the serotonin and 5–hydroxyindoleacetic acid levels in the postnatal ontogeny of C57BL/6J and BALB/cLac strain mice] Lobacheva II, et al. **Ontogenez** 1981;12(3):306–10 (Eng. Abstr.) **(Rus)**

HYDROXYTRYPTOPHAN

Effect of 5–hydroxytryptophan on electrocortical activity and breathing movements of fetal sheep. Quilligan EJ, et al. **Am J Obstet Gynecol** 1981 Oct 1;141(3):271–5

Inverse relation of substance P–like immunoreactivity in dorsal raphe nucleus to serotonin levels in pons–medulla following administration of cocaine and 5–hydroxytryptophan. Pradhan S, et al. **Biochem Pharmacol** 1981 May 15;30(10):1071–6

Rapid and simple analysis of DOPA and 5–HTP using high performance liquid chromatography with electrochemical detection. Arnerić SP, et al. **Brain Res Bull** 1981 May;6(5):407–11

Monoamine precursor uptake in ganglia of a mollusc Anodonta cygnea L. (Bivalvia) An autoradiographic and ultrastructural study. Elekes K. **Cell Tissue Res** 1981;219(2):403–15

Elevation of 3,4–dihydroxyphenylacetic acid concentration by L–5–hydroxytryptophan in control and fluoxetine–pretreated rats. Fuller RW, et al. **J Pharm Pharmacol** 1981 Jun;33(6):406–7

Backward walking induced by L–5–hydroxytryptophan in mice. Shimomura K, et al. **Jpn J Pharmacol** 1981 Feb;31(1):39–46

Radioautographic study of uptake and storage of indoleamines in the rabbit enterochromaffin cells. Mourre C, et al. **Neurosci Lett** 1981 May 29;23(3):251–6

Effects of serotonin and L–5–hydroxytryptophan on plasma renin activity in rats. Barney CC, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):895–900

Peripheral conversion of L–5–hydroxytryptophan to serotonin induces drinking in rats. Kikta DC, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):889–93

Supersensitivity to L–5–hydroxytryptophan after 5,7–dihydroxytryptamine injections in desmethylimipramine– and nomifensine–pretreated rats: behavioral evidence for postsynaptic supersensitivity. Ortmann R, et al. **Psychopharmacology (Berlin)** 1981; 74(2):109–14

HYDROXYZINE

Simultaneous determination of hydroxyzine hydrochloride and benzyl alcohol in injection solutions by high–performance liquid chromatography. Menon GN, et al. **J Pharm Sci** 1981 Jun; 70(6):697–8

HYPERKINESIS

Suction lesions of the frontal cerebral cortex in the rat induce asymmetrical behavioral and catecholaminergic responses. Pearlson GD, et al. **Brain Res** 1981 Aug 10;218(1–2):233–42

HYPERKINETIC SYNDROME

L–dopa and treatment of hyperactive children. Knobel M, et al. **Acta Paedopsychiatr (Basel)** 1981 May;47(1):27–31

Tryptophan metabolism in children with attentional deficit disorder. Irwin M, et al. **Am J Psychiatry** 1981 Aug;138(8):1082–5

Treatment alternatives for hyperactive children – a comment on 'problem children' and stimulant drug treatment. Glow RA. **Aust NZ J Psychiatry** 1981 Jun;15(2):123–8

'Problem children' and stimulant drug treatment. Prior M. **Aust NZ J Psychiatry** 1981 Jun;15(2):117–21

Saccades of hyperactive and normal boys during ocular pursuit. Bala SP, et al. **Dev Med Child Neurol** 1981 Jun;23(3):323–36

The hyperactive child in adolescence: some pharmacologic approaches. White JH. **J Adolesc** 1981 Mar;4(1):79–86

Optimal dosages of methylphenidate for improving the learning and behavior of hyperactive children. Charles L, et al. **JDBP** 1981 Sep; 2(3):78–81

HYSTERIA

[Feasibility of pathogenetic therapy for hysteria] Semke VIa.

Zh Nevropatol Psikhiatr 1981;81(3):420-5 (Eng. Abstr.) (Rus)

IMIPRAMINE

A comparison of phenelzine and imipramine in an obsessive-compulsive patient. Isberg RS. **Am J Psychiatry** 1981 Sep;138(9):1250-1

Cognitive dysfunction and imipramine in outpatient depressive. Glass RM, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1048-51

Prophylactic lithium carbonate with and without imipramine for bipolar I patients. A double-blind study. Quitkin FM, et al. **Arch Gen Psychiatry** 1981 Aug;38(8):902-7

Interaction of imipramine with the ionic channel of the acetylcholine receptor of motor endplate and electric organ. Eldefrawi ME, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1391-4

Plasma concentration monitoring of hydroxylated metabolites of imipramine and desipramine. DeVane CL, et al. **Drug Intell Clin Pharm** 1981 Apr;15(4):263-6

Species and dose differences in the accumulation of imipramine by mammalian lungs. Drew R, et al. **Drug Metab Dispos** 1981 Jul-Aug; 9(4):322-6

Sodium dependency of [3H]imipramine binding in rat cerebral cortex. Briley M, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):377-80

Absence of high-ffinity [3H]imipramine binding in platelets and cerebral cortex of fawn-hooded rats. Dumbrille-Ross A, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):137-8

Differential sensitivity to the effects of psychotropic drugs: psychotics vs normals; Asian vs Western populations. Okuma T. **Folia Psychiatr Neurol Jpn** 1981;35(1):79-87

Selective inhibitory effects of chlorpromazine and imipramine on platelet aggregation. Ishigooka J, et al. **Int Pharmacopsychiatry** 1980; 15(5):270-80

Differential effects of cognitive therapy and pharmacotherapy on depressive symptoms. Rush AJ, et al. **J Affective Disord** 1981 Sep; 3(3):221-9

Distribution of specific high-affinity binding sites for [3H]imipramine in human brain. Langer SZ, et al. **J Neurochem** 1981 Aug;37(2):267-71

Localisation of tricyclic antidepressant binding sites on serotonin nerve terminals. Sette M, et al. **J Neurochem** 1981 Jul;37(1):40-2

Simultaneous determination of imipramine, desipramine, and their 2-hydroxy metabolites in plasma by ion-pair reversed-phase high-performance liquid chromatography with amperometric detection. Suckow RF, et al. **J Pharm Sci** 1981 Mar;70(3):257-61

The effect of single and chronic administration of imipramine on clonidine-induced hypothermia in the rat. Górka Z, et al. **Life Sci** 1981 Jun 22;28(25):2847-54

Does high affinity [3H] imipramine binding label serotonin reuptake sites in brain and platelet? Paul SM, et al. **Life Sci** 1981 Jun 15; 28(24):2753-60

CSF-MHPG in depressive syndromes: basal values and imipramine-induced modifications. Roccatagliata G, et al. **Neuropsychobiology** 1981;7(4):169-71

Further studies on a novel animal model of depression: therapeutic effects of a tricyclic antidepressant. Roth KA, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):253-8

The effect of imipramine and mianserin on the behavior and EEG afterdischarges induced by single electric stimulation of the rabbit amygdala. Ossowska K, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug; 32(4):513-22

The effect of multiple imipramine administration on monoaminergic systems of the rat brain. Vetulani J, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):523-30

The effect of multiple rising doses of Ro 11-2465 (serotonin uptake inhibitor) on serotonin content of human platelets. Lenehan T, et al. **Psychopharmacology (Berlin)** 1981;74(1):1-3

Effect of imipramine on high potassium evoked 3H-dopamine release in the rat striatum. Kamiya H, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):49-60

INHIBITION (PSYCHOLOGY)

Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Solomon PR, et al. **Biol Psychiatry** 1981 Jun; 16(6):519-37

[Physiopathology of inhibition and proposals for an original therapeutic response] Laborit H. **Agressologie** 1981;22(2):45-53 (90 ref.) (Eng. Abstr.) **(Fre)**

LACTATES

Stimulation of rat renal phosphoenolpyruvate carboxykinase activity after an intravenous lactic acid load. Vargas AM, et al. **FEBS Lett** 1981 May 5;127(1):121-4

The effect of catecholamines or sodium lactate on blood lactate distribution in the rat. Aragno R. **J Sports Med Phys Fitness** 1981 Mar; 21(1):7-14

LEARNING

Modifications of the dopaminergic receptors sensitivity and learning of normoxic or hypobaric hypoxic rats. Saligaut C, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):80-7

A new approach to the role of noradrenaline in learning: problem-solving in the marmoset after alpha-noradrenergic receptor blockade. Ridley RM, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):849-55

The influence of fragments of the LPH chains on learning, memory and attention in animals and man. Sandman CA, et al. **Pharmacol Ther [B]** 1981;13(1):39-60 (76 ref.)

Post-learning paradoxical sleep, reticular activation and noradrenergic activity. Leconte P, et al. **Physiol Behav** 1981 Apr;26(4):587-94

[Improvement of post-training performance 4 weeks after stimulation of the locus coeruleus in rats : absence of an effect of a lesion of the dorsal noradrenergic bundle] Velley L, et al. **C R Acad Sci [D] (paris)** 1981 May 4;292(16):943-6 (Eng. Abstr.) **(Fre)**

LEVODOPA

L-dopa and treatment of hyperactive children. Knobel M, et al. **Acta Paedopsychiatr (Basel)** 1981 May;47(1):27-31

Decrease of vascular angiotensin sensitivity by L-dopa during human pregnancy. Kaulhausen H, et al. **Am J Obstet Gynecol** 1981 Jul 15; 140(6):671-5

Striatal dopamine turnover and L-dopa treatment after short-term exposure of rats to manganese. Shukla GS, et al. **Arch Toxicol** 1981 Jun;47(3):191-6

Aromatic L-amino acid decarboxylase activity in central and peripheral tissues and serum of rats with L-DOPA and L-5-hydroxytryptophan as substrates. Rahman MK, et al. **Biochem Pharmacol** 1981 Mar 15; 30(6):645-9

L-DOPA (L-3,4-dihydroxyphenylalanine) uptake by human red blood cells. Floud A, et al. **Biochim Biophys Acta** 1981 Jul 20; 645(2):165-9

Increase in mesolimbic electrical self-stimulation after chronic haloperidol: reversal by L-DOPA or lithium. Seeger TF, et al. **Brain Res** 1981 Jun 29;215(1-2):404-9

Induction of swimming in the high spinal stingray by L-DOPA. Williams BJ, et al. **Brain Res** 1981 Sep 7;220(1):208-13

Inhibition of the renin-angiotensin-aldosterone system by L-dopa with and without inhibition of extracerebral dopa decarboxylase in man. Barbieri C, et al. **Clin Sci** 1981 Aug;61(2):187-90

Effects of L-dopa on dopamine and norepinephrine concentrations in rat brain assessed by gas chromatography. Doshi PS, et al. **J Chromatogr** 1981 Jun 19;210(3):505-11

Dosage form design for improvement of bioavailability of levodopa IV: Possible causes of low bioavailability of oral levodopa in dogs. Sasahara K, et al. **J Pharm Sci** 1981 Jul;70(7):730-3

Antagonism of KW-5338 (domperidone) against emesis and depression of intestinal motility induced by L-DOPA. Shuto K, et al. **J Pharmacobiodyn** 1980 Dec;3(12):709-14

Pharmacological difference of L-dopa, apomorphine, and bromocriptine against metoclopramide. Fang VS. **Life Sci** 1981 May 11; 28(19):2143-9

Effect of L-dopa treatment on cerebral amino acid levels in rats after portocaval anastomosis. Zanchin G, et al. **Neurochem Res** 1981 Jun; 6(6):649-58

Synergistic induction of pineal gland N-acetyltransferase activity by amphetamine and L-DOPA. Altar A, et al. **Proc West Pharmacol Soc** 1981;24:101-4

[Effect of gonadotropin releasing hormone, clomide and L-dopa on the secretion of chorionic gonadotropins, follicle-stimulating hormone and prolactin in the first trimester of uncomplicated pregnancy] Rzempoluch J. **Ginekol Pol** 1981 Jan;52(2):211-4 **(Pol)**

[Effect of certain neuromediators on segmental mechanisms of vasomotor regulation] Zaitsev AA, et al. **Farmakol Toksikol** 1981 Mar-Apr; 44(2):178-81 (Eng. Abstr.) **(Rus)**

LH

Dopaminergic and adrenergic effects on plasma LH levels in rats with hypothalamic islands. van Dieten JA, et al. **Acta Endocrinol (Copenh)** 1981;97(3):289-96

Potentiation of prostaglandin E2-induced release of LH by the prostaglandin analogue, 7-oxa-13-prostynoic acid. Warberg J. **Acta Endocrinol (Copenh)** 1981;97(3):297-304

Hypothalamic-pituitary function in normal ewes and ewes which grazed oestrogenic subterranean clover for several years. Chamley WA, et al. **Aust J Biol Sci** 1981;34(2):239-44

Melatonin effect on the hamster pituitary response to LHRH. Bacon A, et al. **Biol Reprod** 1981 Jun;24(5):993-9

Direct effects of gonadotropin releasing hormone and its antagonist upon ovarian functions stimulated by FSH, prolactin, ans LH. Jones PB, et al. **Biol Reprod** 1981 May;24(4):747-59

Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Rivier C, et al. **Biol Reprod** 1981

Jun;24(5):1061-7

Site of action of prolactin in the suppression of gonadotropin secretion during lactation in the rat: effect on pituitary responsiveness to LHRH. Smith MS. **Biol Reprod** 1981 Jun;24(5):967-76

Lack of a relationship between concentrations of plasma luteinising hormone, thyroxine and prolactin at nine week's of age and subsequent egg production in the domestic hen. Sharp PJ, et al. **Br Poult Sci** 1981 Jan;22(1):53-8

Effects of an epinephrine synthesis inhibitor, SKF64139, on the secretion of luteinizing hormone in ovariectomized female rats. Crowley WR, et al. **Brain Res** 1981 Jan 5;204(1):231-5

Effect of manipulating central catecholamines on puberty and the surge of luteinizing hormone and gonadotropin releasing hormone induced by pregnant mare serum gonadotropin in female rats. Sarkar DK, et al. **Brain Res** 1981 Jun 1;213(2):335-49

The effects of stimulation and lesion of raphe nuclei on luteinizing hormone release in estrogen-progesterone-treated ovariectomized rats. Waloch M, et al. **Brain Res** 1981 Aug 3;217(2):305-13

Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Huhtaniemi IT, et al. **Endocrinology** 1981 Aug; 109(2):483-90

Electrical stimulation of mesencephalic noradrenergic pathway: effects on luteinizing hormone levels in blood of ovariectomized and ovariectomized, steroid-primed rats. Leung PC, et al. **Endocrinology** 1981 Sep;109(3):720-8

Endocrine correlates of sexual development in the male monkey, Macaca fascicularis. Steiner RA, et al. **Endocrinology** 1981 Sep;109(3):914-9

Frequency and amplitude of gonadotropin-releasing hormone stimulation and gonadotropin secretion in the rhesus monkey. Wildt L, et al. **Endocrinology** 1981 Aug;109(2):376-85

Influence of neonatal ovariectomy on the developmental patterns of serum gonadotropins, hypothalamic LH-RH concentration and organ weights in female rats. Döcke F, et al. **Endokrinologie** 1981 Mar; 77(3):273-85

Differential effects of testosterone and its metabolites on gonadotrophin secretion in the intact adult male rat. Reymond M, et al. **Horm Res** 1981;14(2):114-29

Role of thyroxine & gonadotropins on the mobilization of ovarian cholesterol in a teleost Anabas testudineus (Bloch). Sen S, et al. **Indian J Exp Biol** 1981 May;19(5):408-12

Multihormonal regulation of ornithine decarboxylase activity in highly differentiated porcine granulosa cells in vitro. Veldhuis JD, et al. **J Cell Physiol** 1981 Aug;108(2):213-20

Effects of oestradiol, hypothalamic extracts and luteinizing hormone releasing hormone on rat anterior pituitary gland gonadotrophin release in vitro before and after the preovulatory luteinizing hormone surge at pro-oestrus. Elias KA, et al. **J Endocrinol** 1981 Sep;90(3):345-54

Repetitive treatment with gonadotrophin releasing factor or a long-acting analogue upon gonadotrophin secretion in the ferret. Gledhill B, et al. **J Endocrinol** 1981 Aug;90(2):275-83

Time-related secretion of gonadotrophins after a single injection of steroid-free bovine follicular fluid in prepubertal and adult female rats. Hermans WP, et al. **J Endocrinol** 1981 Jul;90(1):69-76

Effect of gonadectomy on the concentrations of catecholamines in discrete areas of the diencephalon of the domestic fowl. Knight PG, et al. **J Endocrinol** 1981 Jun;89(3):389-97

Evidence that changes in luteinizing hormone secretion regulate the growth of the preovulatory follicle in the ewe. McNatty KP, et al. **J Endocrinol** 1981 Sep;90(3):375-89

Dissociation in the regulation of luteinizing hormone and follicle-stimulating hormone in a hyperprolactinaemic rat model: interrelationships between gonadotrophin and prolactin control. Tresguerres JA, et al. **J Endocrinol** 1981 Jul;90(1):41-51

Development of a quotidian increase in pituitary responsiveness to GnRH in prepubertal female rats. Wilkinson M, et al. **J Reprod Fertil** 1981 Jul;62(2):393-8

Prolactin and LH release in response to LH-RH and TRH in ewes during dioestrus, pregnancy and post partum. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):447-53

The failure of prolactin to enhance the inhibitory effect of oestradiol-17 beta on LH synthesis and release in ewes. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):537-42

Neuroendocrine effects of D,L-propranolol [letter] Malas KL, et al. **Lancet** 1981 Aug 22;2(8243):424

Effect of estradiol benzoate and clomiphene on tyrosine hydroxylase activity and on luteinizing hormone and prolactin levels in ovariectomized rats. Tobias H, et al. **Life Sci** 1981 Aug 17; 29(7):711-6

[Intracellular mechanism for the action of inhibin on the secretion of the follicular-stimulating hormone and luteinizing hormone induced by LH-RH in vitro] Lecomte-Yerna MJ, et al. **C R Trav Lab Carlsberg** 1981;175(3):385-8 (Eng. Abstr.) **(Fre)**

[Changes of hypothalamic LH-RH content induced by estradiol injection into female rats (author's transl)] Saito A. **Nippon Sanka Fujinka Gakkai Zasshi** 1981 Aug;33(8):1227-34 (Eng. Abstr.) **(Jpn)**

[Role of noradrenaline in luteinizing hormone secretion] Adamskaia El, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):730-3 (Eng. Abstr.) **(Rus)**

[Role of noradrenaline-sensitive neurons of the preoptic area in regulating luteinizing hormone release] Babichev VN, et al. **Fiziol Zh SSSR** 198 Jun;67(6):809-15 (Eng. Abstr.) **(Rus)**

LH-FSH RELEASING HORMONE

Effect of oestrogen on the responsiveness of the pituitary gland to LRH: the role of corpora lutea. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1981 Sep;98(1):29-35

Effect of a synthetic LH-RH agonist on the endocrine function of the testis, adrenocortex and thyroid gland in cocks. Pethes G, et al. **Acta Physiol Acad Sci Hung** 1980;56(3):281-7

On the correlation of luteinizing hormone-releasing hormone, luteinizing hormone, follicle-stimulating hormone, and prolactin levels in plasma of women with normal menstrual cycles. Aksel S. **Am J Obstet Gynecol** 1981 Oct 15;141(4):362-7

Handling of luteinizing hormone-releasing hormone by renal proximal tubular segments in vitro. Stetler-Stevenson MA, et al. **Am J Physiol** 1981 Aug;241(2):F117-22

D-tryptophan-6-LH-RH-at los doses in the treatment of male subfertility. Levalle O, et al. **Andrologia** 1981 May-Jun;13(3):207-11

Luteinizing hormone-releasing hormone analogs with increased anti-ovulatory activity. Erchegyi J, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):915-20

Degradation of luteinizing hormone - releasing hormone and analogs by adenohypophyseal peptidases. Horsthemke B, et al. **Biochem Biophys Res Commun** 1981 May 29;100(2):753-9

Synthesis and degradation of cyclic nucleotides in the pituitary gland, ovary and testis of rats treated with D-Trp6-luteinizing hormone-releasing hormone. Hierowski MT, et al. **Biochim Biophys Acta** 1981 Jul;675(2):232-8

Melatonin effect on the hamster pituitary response to LHRH. Bacon A, et al. **Biol Reprod** 1981 Jun;24(5):993-9

Effect of 20 alpha-dihydroprogesterone, progesterone, and their 5 alpha-reduced metabolites on serum gonadotropin levels and hypothalamic LHRH content. Gilles PA, et al. **Biol Reprod** 1981 Jun; 24(5):1088-97

Direct effects of gonadotropin releasing hormone and its antagonist upon ovarian functions stimulated by FSH, prolactin, ans LH. Jones PB, et al. **Biol Reprod** 1981 May;24(4):747-59

Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Rivier C, et al. **Biol Reprod** 1981 Jun;24(5):1061-7

Relative importance of the adenohypophyseal and gonadal sites in inhibitory action of LHRH agonists. Séguin C, et al. **Biol Reprod** 1981 May;24(4):889-901

Site of action of prolactin in the suppression of gonadotropin secretion during lactation in the rat: effect on pituitary responsiveness to LHRH. Smith MS. **Biol Reprod** 1981 Jun;24(5):967-76

Effects of estradiol and progesterone on plasma gonadotropins, prolactin, and LHRH in specific brain areas of ovariectomized rats. Wise PM, et al. **Biol Reprod** 1981 May;24(4):820-30

LHRH systems in brain of platyfish. Münz H, et al. **Brain Res** 1981 Sep 21;221(1):1-13

Effect of manipulating central catecholamines on puberty and the surge of luteinizing hormone and gonadotropin releasing hormone induced by pregnant mare serum gonadotropin in female rats. Sarkar DK, et al. **Brain Res** 1981 Jun 1;213(2):335-49

The fetal development of the luteinizing hormone-releasing hormone (LHRH) neuronal systems of the guinea pig brain. Schwanzel-Fukuda M, et al. **Brain Res Bull** 1981 Sep;7(3):293-315

Ultrastructural immunocytochemical evidence of the presence of a peptide related to ACTH in granules of LHRH nerve terminals in the median eminence of the guinea pig. Beauvillain JC, et al. **Cell Tissue Res** 1981; 218(1):1-6

Immunocytochemistry of luteinizing hormone-releasing hormone, vasopressin, and corticotropin following deafferentation of the basal hypothalamus of the male rat brain. Scott PM, et al. **Cell Tissue Res** 1981;219(2):393-402

The in-vivo effect of Lithospermum ruderale on LHRH activity in the chick. Zeller FJ, et al. **Contraception** 1981 Jul;24(1):77-81

Endocrine and behavioral effects of continuous exposure of male rats to a potent luteinizing hormone-releasing hormone (LHRH) agonist: evidence for central nervous system actions of LHRH. Dorsa DM, et al. **Endocrinology** 1981 Sep;109(3):729-35

Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Huhtaniemi IT, et al. **Endocrinology** 1981 Aug; 109(2):483-90

Direct inhibitory effect of GnRH on androgen secretion by ovarian interstitial cells. Magoffin DA, et al. **Endocrinology** 1981 Aug; 109(2):661-3

Frequency and amplitude of gonadotropin-releasing hormone stimulation and gonadotropin secretion in the rhesus monkey. Wildt L, et al. **Endocrinology** 1981 Aug;109(2):376-85

Influence of neonatal ovariectomy on the developmental patterns of serum gonadotropins, hypothalamic LH-RH concentration and organ weights in female rats. Döcke F, et al. **Endokrinologie** 1981 Mar; 77(3):273-85

Estrogen effects on LH-RH degrading brain and pituitary enzymes. Bauer K, et al. **Exp Brain Res** 1981;Suppl 3:93-107

The morphology of LRH and oxytocin neurons. Weindl A, et al. **Exp Brain Res** 1981;Suppl 3:1-17 (37 ref.)

Photo-affinity inactivation of gonadotropin releasing hormone receptors. Hazum E. **FEBS Lett** 1981 Jun 1;128(1):111-3

Slow cholinergic and peptidergic transmission in sympathetic ganglia. Brown DA, et al. **Fed Proc** 1981 Sep;40(11):2625-30

Role of an LHRH-like peptide as a neurotransmitter is sympathetic ganglia of the frog. Jan LY, et al. **Fed Proc** 1981 Sep;40(11):2560-4

Pituitary response to luteinizing hormone-releasing hormone during haloperidol-induced hyperprolactinemia. Del Carmen Díaz M, et al. **Fertil Steril** 1981 Jun;35(6):626-8

Failure to interrupt established pregnancy in humans by D-tryptophan-6-luteinizing hormone-releasing hormone. Tolis G, et al. **Fertil Steril** 1981 Aug;36(2):241-2

Effect of LH-RH treatment on hypothalamo-pituitary-gonadal axis and Leydig cell ultrastructure in cryptorchid boys. Hadziselimovic F, et al. **Horm Res** 1980;13(6):358-66

The fate of conceptuses in rats receiving an intrauterine injection of luteinizing hormone-releasing hormone (LRH) prior to implantation. Jones RC. **Int J Fertil** 1981;26(2):120-3

Suppression of androgen production by D-tryptophan-6-luteinizing hormone-releasing hormone in man. Tolis G, et al. **J Clin Invest** 1981 Sep;68(3):819-22

Effects of oestradiol, hypothalamic extracts and luteinizing hormone releasing hormone on rat anterior pituitary gland gonadotrophin release in vitro before and after the preovulatory luteinizing hormone surge at pro-oestrus. Elias KA, et al. **J Endocrinol** 1981 Sep;90(3):345-54

Repetitive treatment with gonadotrophin releasing factor or a long-acting analogue upon gonadotrophin secretion in the ferret. Gledhill B, et al. **J Endocrinol** 1981 Aug;90(2):275-83

Time-related secretion of gonadotrophins after a single injection of steroid-free bovine follicular fluid in prepubertal and adult female rats. Hermans WP, et al. **J Endocrinol** 1981 Jul;90(1):69-76

Immunocytochemical localization of luteinizing hormone-releasing hormone (LHRH) in Vibratome-sectioned brain. Joseph SA, et al. **J Histochem Cytochem** 1981 Feb;29(2):247-54

Immunocytochemical analysis of the rat pineal gland using antisera generated against luteinizing hormone-releasing hormone (LHRH). Piekut DT, et al. **J Histochem Cytochem** 1981 May;29(5):616-22

An approach to the elucidation of metabolic breakdown products of the luteinizing hormone-releasing hormone. Stetler-Stevenson MA, et al. **J Med Chem** 1981 Jun;24(6):688-92

Inadequate corpus luteum function after the induction of ovulation in anoestrous ewes by LH-RH or an LH-RH agonist. McNeilly AS, et al. **J Reprod Fertil** 1981 Sep;63(1):137-44

Stimulation of pituitary and testicular functions with LH-RH agonist or pulsatile LH-RH treatment in the rhesus monkey during the non-breeding season. Wickings EJ, et al. **J Reprod Fertil** 1981 Sep; 63(1):129-36

Development of a quotidian increase in pituitary responsiveness to GnRH in prepubertal female rats. Wilkinson M, et al. **J Reprod Fertil** 1981 Jul;62(2):393-8

Prolactin and LH release in response to LH-RH and TRH in ewes during dioestrus, pregnancy and post partum. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):447-53

Control of gonadotrophic hormone release in trout: influence of synthetic LH-RH and LH-RH analogues in vivo and in vitro. Crim LW, et al. **Life Sci** 1981 Jan 12;28(2):129-35

Binding of luteinizing hormone-releasing hormone analogues to dispersed rat pituitary cells. Meidan R, et al. **Life Sci** 1981 Apr 27; 28(17):1961-7

Modulation of FSH-controlled steroidogenesis in rat granulosa cells: direct in-vitro effects of LHRH and ICI-118630. Hillier SG, et al. **Mol Cell Endocrinol** 1981 Aug;23(2):193-205

Reversible inhibition of testicular steroidogenesis and spermatogenesis by a potent gonadotropin-releasing hormone agonist in normal men: an approach toward the development of a male contraceptive. Linde R, et al. **N Engl J Med** 1981 Sep 17;305(12):663-7

Gonadotropin releasing hormone stimulates calmodulin redistribution in rat pituitary. Conn PM, et al. **Nature** 1981 Jul 16;292(5820):264-5

Age-related changes in dopamine, LHRH and somatostatin in the rat hypothalamus. Hoffman GE, et al. **Neurobiol Aging** 1980 Summer; 1(1):27-37

Inhibin-like activity in extracts of rabbit placentae. Hochberg Z, et al. **Placenta** 1981 Jul-Sep;2(3):259-64

Hormonal regulation of cytodifferentiation and intercellular communication in cultured granulosa cells. Amsterdam A, et al. **Proc Natl Acad Sci USA** 1981 May;78(5):3000-4

Increased pituitary sensitivity to luteinizing hormone releasing hormone at puberty: an event of proestrus. Johnson JH, et al. **Proc Soc Exp Biol Med** 1981 Jul;167(3):434-7

Continuous infusion of luteinizing hormone releasing hormone (LHRH) in patients with anorexia nervosa. Beumont PJ, et al. **Psychol Med** 1981 Aug;11(3):477-84

Facilitation of mounting behavior in male rats by intracranial injections of luteinizing hormone-releasing hormone. Dorsa DM, et al. **Regul Pept** 1980 Oct;1(2):147-55

Degradation of luteinizing hormone-releasing hormone by serum and plasma in vitro. McDermott JR, et al. **Regul Pept** 1981 May; 2(2):69-79

Vasoactive intestinal peptide stimulates luteinizing hormone-releasing hormone release from median eminence synaptosomes. Samson WK, et al. **Regul Pept** 1981 Aug;2(4):253-64

Studies on mechanism of action of luteinizing releasing hormone (LH-RH) in ovulation of fish—intracellular distribution of LH-RH-A in pituitary gonadotrophs as revealed by electron-microscopic autoradiography. Pan XG, et al. **Sci Sin** 1981 Jul;24(7):982-8

Immunohistochemical demonstration of a testicular substance related to luteinizing hormone-releasing hormone. Paull WK, et al. **Science** 1981 Sep 11;213(4513):1263-4

[Regulation of the endocrine function of the placenta] Presl J. **Cesk Gynekol** 1981 Jul;46(6):466-7 **(Cze)**

[Intermittent liberation of gonadoliberin (GnRH) by the rat hypothalamus in vitro] Bourguignon JP, et al. **C R Trav Lab Carlsberg** 1981; 175(3):389-96 (Eng. Abstr.) **(Fre)**

[Gonadocrinin-like activity of the peritoneal fluid during the menstrual cycle in the normal female] Demoulin A, et al. **C R Trav Lab Carlsberg** 1981;175(3):377-84 (Eng. Abstr.) **(Fre)**

[Intracellular mechanism for the action of inhibin on the secretion of the follicular-stimulating hormone and luteinizing hormone induced by LH-RH in vitro] Lecomte-Yerna MJ, et al. **C R Trav Lab Carlsberg** 1981;175(3):385-8 (Eng. Abstr.) **(Fre)**

[Changes of hypothalamic LH-RH content induced by estradiol injection into female rats (author's transl)] Saito A. **Nippon Sanka Fujinka Gakkai Zasshi** 1981 Aug;33(8):1227-34 (Eng. Abstr.) **(Jpn)**

[Indirect effects of synthetic LHRH on cervical mucus characteristics] Meden-Vrtovec H. **Jugosl Ginekol Opstet** 1980 May-Aug; 20(3-4):236-42 (Eng. Abstr.) **(Scr)**

LIPOTROPIN

beta-Adrenergic stimulation of the release of ACTH- and LPH-related peptides from the pars intermedia of the rat pituitary gland. Tilders FJ, et al. **Acta Endocrinol (Copenh)** 1981;97(3):343-51

Conformational properties of central nervous system myelin basic protein, beta-endorphin, and beta-lipotropin in water and in the presence of anionic lipids. Mattice WL, et al. **Biopolymers** 1981 Jul; 20(7):1421-34

beta-lipotrophin and beta-endorphin plasma levels during pregnancy. Genazzani AR, et al. **Clin Endocrinol (Oxf)** 1981 Apr;14(4):409-18

Effects of beta-lipotropin and beta-lipotropin-derived peptides on aldosterone production in the rat adrenal gland. Matsuoka H, et al. **J Clin Invest** 1981 Sep;68(3):752-9

Parallel stimulation of ACTH, beta-LPH + beta-endorphin and alpha-MSH release by alpha-adrenergic agents in rat anterior pituitary cells in culture. Raymond V, et al. **Mol Cell Endocrinol** 1981 Jun; 22(3):295-303

Physical conditioning facilitates the exercise-induced secretion of beta-endorphin and beta-lipotropin in women. Carr DB, et al. **N Engl J Med** 1981 Sep 3;305(10):560-3

Vasopressin stimulates release of beta-lipotropin and beta-endorphin in conscious rats as measured by radioimmunoassay of unextracted plasma. Anhut H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb; 316(1):59-63

The influence of fragments of the LPH chains on learning, memory and attention in animals and man. Sandman CA, et al. **Pharmacol Ther [B]** 1981;13(1):39-60 (76 ref.)

LITHIUM

Mechanism for exoelectron emission mainly from LiF. Samuelsson LI. **Acta Radiol [Suppl] (Stockh)** 1979;359:1-93

Thermoluminescence dosimetry in the muGy range. Theoretical and experimental investigations of the optimum performance of a LiF-TLD system. Spanne P. **Acta Radiol [Suppl] (Stockh)** 1979;360:1-118

Lithium capsule. Holland PJ. **Am Fam Physician** 1981 Sep;24(3):147-8

Physostigmine and lithium response in the schizophrenias. Edelstein P, et al. **Am J Psychiatry** 1981 Aug;138(8):1078-81

Inaccurate creatinine clearance tests [letter] Pulier M. **Am J Psychiatry** 1981 Sep;138(9):1258-9

Determination of lithium in small-animal tissues at physiological levels by flame emission photometry. Pickett EE, et al. **Anal Biochem** 1981 Apr;112(2):213-8

Prophylactic lithium carbonate with and without imipramine for bipolar 1 patients. A double-blind study. Quitkin FM, et al. **Arch Gen Psychiatry** 1981 Aug;38(8):902-7

Regulation of lithium in cerebrospinal fluid of the cat by the choroid plexus isolated in situ. Yen MH, et al. **Arch Int Pharmacodyn Ther** 1981 Jun;251(2):217-27

Toxicity and renal elimination of lithium in rats of different ages. Kersten L. **Arch Toxicol** 1981 Apr;47(2):135-44

Olfactory discrimination of lithium chloride by the coyote (Canis latrans). Ellins SR, et al. **Behav Neural Biol** 1981 Feb;31(2):214-24

Failure of albino guinea pigs to exhibit Lavin's poisoned partner effect. Revusky S, et al. **Behav Neural Biol** 1981 May;32(1):111-3

Current perspectives in lithium prophylaxis. International symposium, Vienna, October 19-20, 1979. **Bibl Psychiatr** 1981;(161):1-248 (Eng, Mul)

Practical guide-lines of lithium prophylaxis. Kerry RJ. **Bibl Psychiatr** 1981;(161):197-205

Lithium carbonate in the treatment of acute depressive illness. Khan MC. **Bibl Psychiatr** 1981;(161):244-8

Responders and non-responders to lithium therapy. Some potential biological indicators. Mendlewicz J. **Bibl Psychiatr** 1981;(161):63-8 (39 ref.)

Prophylactic and therapeutic profile of lithium. Peselow E, et al. **Bibl Psychiatr** 1981;(161):1-31 (158 ref.)

Kidney morphology and function in lithium-treated patients. Vestergaard P, et al. **Bibl Psychiatr** 1981;(161):104-14 (17 ref.)

Memory performances in depressed patients during prophylactic treatment with lithium salts. Zerbi F, et al. **Bibl Psychiatr** 1981;(161):190-6

The hamster adipocyte adenylate cyclase system. II. Regulation of enzyme stimulation and inhibition by monovalent cations. Aktories K, et al. **Biochim Biophys Acta** 1981 Aug 5;676(1):59-67

Binding constants of Li+, K+, and Tl+ in the gramicidin channel determined from water permeability measurements. Dani JA, et al. **Biophys J** 1981 Aug;35(2):485-99

Lithium intoxication treated by peritoneal dialysis. Brown EA, et al. **Br J Clin Pract** 1981 Feb;35(2):90-1

Lithium induces rapid relief of depression in tricyclic antidepressant drug non-responders. Dé Montigny C, et al. **Br J Psychiatry** 1981 Mar; 138:252-6

Increase in mesolimbic electrical self-stimulation after chronic haloperidol: reversal by L-DOPA or lithium. Seeger TF, et al. **Brain Res** 1981 Jun 29;215(1-2):404-9

Does lithium prevent neutropenia caused by antidepressants? [letter] Vasconcelos JA, et al. **Can Med Assoc J** 1981 Jul 1;125(1):20

Nephrotic syndrome associated with lithium therapy. Alexander F, et al. **Clin Nephrol** 1981 May;15(5):267-71

Effects of diclofenac on lithium kinetics. Reimann IW, et al. **Clin Pharmacol Ther** 1981 Sep;30(3):348-52

Severe lithium poisoning. Marshall SM, et al. **Drug Intell Clin Pharm** 1981 Jul-Aug;15(7-8):598-9

Effect of chronic lithium treatment on isolation-induced behavioral and biochemical effects in mice. Frances H, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):337-41

Phototransfer, sensitization and re-estimation of dose in lithium fluoride TLD. Jain VK. **Health Phys** 1981 Aug;41(2):363-70

Lithium excretion and therapeutic response in mania. Sampath G, et al. **Indian J Med Res** 1981 May;73:768-71

Kidney function in patients with affective disorders with and without lithium therapy. Wahlin A, et al. **Int Pharmacopsychiatry** 1980; 15(4):253-9

Lithium prophylaxis and the kidney. Bakris GL, et al. **J Affective Disord** 1981 Mar;3(1):37-42

Bipolar affective disorder, lithium carbonate and Ca++ ATPase. Choi SJ, et al. **J Affective Disord** 1981 Jun;3(2):77-9

A longitudinal record study of renal function in patients treated with lithium. Hwu HG, et al. **J Affective Disord** 1981 Jun;3(2):101-9

The activity of the lithium--sodium countertransport system in erythrocytes in depression and mania. Rybakowski J, et al. **J Affective Disord** 1981 Mar;3(1):59-64

Antinuclear antibodies and histocompatibility antigens in patients on long-term lithium therapy. Whalley LJ, et al. **J Affective Disord** 1981 Jun;3(2):123-30

Effects of fluoride, lithium and strontium on extracellular polysaccharide production by Streptococcus mutans and Actinomyces viscosus. Treasure P. **J Dent Res** 1981 Aug;60 Spec No C:1601-10

Dependence of water movement on sodium transport in kidney proximal tubule: a microperfusion study substituting lithium for sodium. Corman B, et al. **J Membr Biol** 1981;62(1-2):105-11

Action of lithium on the adrenergic nerve ending. Beaty O 3d, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):309-17

Interaction of lithium and disulfiram in hexobarbital hypnosis: possible role of the 5-HT system. Minegishi A, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):481-7

The effect of lithium on electrolyte transport by the in situ choroid plexus of the cat. Reed DJ, et al. **J Physiol (Lond)** 1980 Dec;309:329-39

Determination of lithium-induced impairment of distal water reabsorption. Thomsen K, et al. **J Psychiatr Res** 1981;16(2):79-85

Lithium carbonate for recurrent fever and neutropenia. Gerner RH, et al. **JAMA** 1981 Oct 2;246(14):1584-6

Renal toxicity of lithium and its implications. DePaulo JR Jr, et al. **Johns Hopkins Med J** 1981 Jul;149(1):15-21

Further studies on the potentiating effect of lithium chloride on methamphetamine-induced stereotypy in mice. Miyauchi T, et al. **Jpn J Pharmacol** 1981 Feb;31(1):61-8

Chromosome studies of patients on long-term lithium therapy for psychiatric disorders. Garson OM, et al. **Med J Aust** 1981 Jul 11; 2(1):37-9

Case 17-1981: chronic interstitial nephritis from lithium therapy [letter] Wahlin A, et al. **N Engl J Med** 1981 Aug 13;305(7):408

Post-amphetamine depression of self-stimulation behavior in rats: prophylactic effects of lithium. Predy PA, et al. **Neurosci Lett** 1981 May 29;23(3):343-7

Leukocytosis during long-term lithium treatment. Yassa R. **NY State J Med** 1981 Sep;81(10):1479-80

John F.J. Cade, 1912 to 1980: a reminiscence. Johnson FN. **Pharmacopsychiatria** 1981 Jul;14(4):148-9

Thermal quenching by phototransfer in LiF TLD-100. Kathuria SP, et al. **Phys Med Biol** 1981 Jul;26(4):707-10

Effect of lithium intake on sodium and lithium appetite in sodium deficient cattle. Sly J, et al. **Physiol Behav** 1981 Jul;27(1):147-52

Lithium promotes entrainment of rats to long circadian light-dark cycles. McEachron DL, et al. **Psychiatry Res** 1981 Aug;5(1):1-9

Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. van Kammen DP, et al. **Psychiatry Res** 1981 Jun;4(3):313-25

Continuation therapy with lithium and amitriptyline in unipolar depressive illness: a controlled clinical trial. A report by the Medical Research Council Drug Trials Subcommittee. **Psychol Med** 1981 May; 11(2):409-16

Lithium increases serotonin release and decreases serotonin receptors in the hippocampus. Treiser SL, et al. **Science** 1981 Sep 25; 213(4515):1529-31

Lithium inhibits adenylate cyclase of human platelets. Imandt L, et al. **Thromb Haemost** 1981 Apr 30;45(2):142-5

[Clinical experience with the preparation lithium carbonicum retard in psychiatry (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Apr;77(2):110-5 (Eng. Abstr.) (Cze)

[Clinical significance of the erythro-plasmatic ratio of lithium (author's transl)] Braccini T, et al. **Acta Psychiatr Belg** 1980 Jul-Aug; 80(4):413-9 (Eng. Abstr.) (Fre)

[Manic-depressive psychosis. Efficacy of lithium in various disorders of carbohydrate metabolism (letter)] Gisselmann A, et al. **Nouv Presse Med** 1981 Jun 6;10(25):2121 (Fre)

[Lithium] Lemoine JM, et al. **Soins Psychiatr** 1981 Jan;(7):37-42 (Fre)

[Unsolved problems in the indications for lithium prophylaxis in affective and schizoaffective disorders] Angst J. **Bibl Psychiatr** 1981; (161):32-44 (Eng. Abstr.) (Ger)

[Lithium prophylaxis in neurologic practice] Baumhackl U, et al. **Bibl Psychiatr** 1981;(161):221-3 (Ger)

[Pharmacokinetics and toxicology of lithium] Greil W. **Bibl Psychiatr** 1981;(161):69-103 (147 ref.) (Eng. Abstr.) (Ger)

[Status of lithium therapy in Austria] König P, et al. **Bibl Psychiatr** 1981; (161):206-220 (Eng. Abstr.) (Ger)

[Effects of lithium on normal psychic functions as a restriction on prophylactic use] Kropf D. **Bibl Psychiatr** 1981;(161):141-51 (Eng. Abstr.) (Ger)

[Lithium prophylaxis in schizoaffective psychoses] Lenz G, et al. **Bibl Psychiatr** 1981;(161):45-57 (54 ref.) (Ger)

[Motor reactivity during lithium prophylaxis] Opgenoorth E, et al. **Bibl Psychiatr** 1981;(161):152-69 (Eng. Abstr.) (Ger)

[Maximal motor nerve conduction rate with lithium] Presslich O, et al. **Bibl Psychiatr** 1981;(161):121-8 (Eng. Abstr.) (Ger)

[Metabolic studies on lithium] Rittmannsberger H, et al. **Bibl Psychiatr** 1981;(161):129-33 (Ger)

[Enduring structure of the 'depressive personality' in lithium prophylaxis. With special reference to the social partners] Schuster P, et al. **Bibl Psychiatr** 1981;(161):170-8 (Eng. Abstr.) (Ger)

[Clinico-psychopathologic research on prophylactic lithium therapy] Teufel S, et al. **Bibl Psychiatr** 1981;(161):58-62 (Ger)

[A study on the prevention of recurrences of affective diseases using lithium] Felber W. **Psychiatr Neurol Med Psychol (Leipz)** 1981 Jun; 33(6):330-2 (Ger)

[Lithium therapy in congenital neutropenia (author's transl)] Kuratsuji T, et al. **Rinsho Ketsueki** 1981 Mar;22(3):317-24 (Eng. Abstr.) (Jpn)

[Morphofunctional changes in the thyroid glands of rats following lithium chloride administration] Semenov VV, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):754-7 (Eng. Abstr.) (Rus)

[Comparative characteristics of the preventive properties of short-acting and delayed-action lithium carbonate in endogenous affective psychoses] Panteleeva GP, et al. **Zh Nevropatol Psikhiatr** 1981; 81(3):406-12 (Eng. Abstr.) (Rus)

[Mechanisms of the central action of lithium] Sinitskii VN, et al. **Zh Nevropatol Psikhiatr** 1981;81(4):567-75 (Eng. Abstr.) (Rus)

[Slow-release lithium carbonate versus standard preparation in bipolar affective disorders (author's transl)] Bohaček N, et al. **Lijec Vjesn** 1980 Oct;102(10):575-9 (Eng. Abstr.) (Ser)

[Effect of lithium chloride on carbohydrate metabolism in mice] Espósito Avella M, et al. **Rev Med Panama** 1981 May;6(2):183-92 (Eng. Abstr.) **(Spa)**

MEMORY

Differential effect of REM stimulating and REM inhibiting drugs (reserpine and amitriptylin) on memory. Faber J, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):169-71

Alterations in human memory following acute maprotiline, diazepam and codeine administration. Liljequist R, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Feb;48(2):190-2

Veratridine as an amnestic agent in the domestic chick. Clifton PG. **Behav Neural Biol** 1981 Jul;32(3):295-307

The involvement of the locus coeruleus in memory. Prado de Carvalho L, et al. **Behav Neural Biol** 1981 Feb;31(2):173-86

Methylphenidate impairs learning and memory in normal adults. Wetzel CD, et al. **Behav Neural Biol** 1981 Apr;31(4):413-24

Memory performances in depressed patients during prophylactic treatment with lithium salts. Zerbi F, et al. **Bibl Psychiatr** 1981;(161):190-6

Cholinergic receptor interactions and their effects on long-term memory processing. Flood JF, et al. **Brain Res** 1981 Jun 29;215(1-2):177-85

Plasma catecholamines: effects of footshock level and hormonal modulators of memory storage. McCarty R, et al. **Horm Behav** 1981 Jun;15(2):168-82

Brain cholinergic dysfunction and memory in aged rats. Lippa AS, et al. **Neurobiol Aging** 1980 Summer;1(1):13-9

The acute effect of p-chloroamphetamine on the retention of fear conditioning in the rat: evidence for a role of serotonin in memory consolidation. Archer T, et al. **Neurosci Lett** 1981 Aug 7; 25(1):75-81

The influence of fragments of the LPH chains on learning, memory and attention in animals and man. Sandman CA, et al. **Pharmacol Ther [B]** 1981;13(1):39-60 (76 ref.)

[Participation of hypothalamic noradrenergic structures in the reproduction of conditioned 'passive' avoidance reactions] Tolochko ZS. **Zh Vyssh Nerv Deiat** 1981;31(2):267-70 (Eng. Abstr.) **(Rus)**

MEMORY DISORDERS

Effects of an ACTH short chain neuropeptide in man. Dornbush RL, et al. **Am J Psychiatry** 1981 Jul;138(7):962-4

MEMORY, SHORT-TERM

Plasma catecholamines and pituitary adrenal hormones related to mental task demand under quiet and noise conditions. Brandenberger G, et al. **Biol Psychol** 1980 Jun;10(4):239-52

MENTAL DISORDERS

Psychotropic drug use in the elderly: an overview. Levenson AJ. **Am Fam Physician** 1981 Aug;24(2):194-9

Prolactin and psychiatry. Meltzer HY. **Am J Psychiatry** 1981 Sep; 138(9):1203-6

Pharmacotherapy as an intervention during the stages of psychotherapy. Beitman BD. **Am J Psychother** 1981 Apr;35(2):206-14

Mortality among psychiatric inpatients. Age-adjusted comparison of populations before and after psychotropic drug era. Craig TJ, et al. **Arch Gen Psychiatry** 1981 Aug;38(8):935-8

Current perspectives in lithium prophylaxis. International symposium, Vienna, October 19-20, 1979. **Bibl Psychiatr** 1981;(161):1-248 **(Eng, Mul)**

Thyrotropic hormone and psychiatric symptoms. Beumont PJ, et al. **Biol Psychiatry** 1981 Jul;16(7):671-7

Management of the acutely disturbed patient on the general ward. Pfeffer JM. **Br J Hosp Med** 1981 Jul;26(1):73-8

Drug histories obtained by pharmacists from psychiatric inpatients. Dobbs JH. **Hosp Community Psychiatry** 1981 Sep;32(9):639-40

Differential therapeutics: a guide to treatment selection. Frances A, et al. **Hosp Community Psychiatry** 1981 Aug;32(8):537-46

Enhancing medication compliance in coffee groups. Olarte SW, et al. **Hosp Community Psychiatry** 1981 Jun;32(6):417-9

On being a necessary evil at a mental health center. Peterson LG. **Hosp Community Psychiatry** 1981 Sep;32(9):644

The significance of secondary depression. Clayton PJ, et al. **J Affective Disord** 1981 Mar;3(1):25-35

Improving drug knowledge in psychiatric patients. Smith JE. **J Psychiatr Nurs** 1981 Apr;19(4):16-8

Law for the nurse manager: forced medication of mental patients. Creighton H. **Nurs Manage** 1981 Sep;12(9):72-3

Guidelines for the evaluation of drugs in the elderly neuropsychiatric patient (demented and non-demented). **Pharmacopsychiatria** 1981 Jul; 14(4):150-4 contd

Double-blind assessment of the activity of minaprine (30038-CB) in child psychiatry. Maffla AG. **Pharmatherapeutica** 1981;2(9):601-6

The problem of psychopharmacotherapy in the medically ill. Siris SG, et al. **Psychiatr Clin North Am** 1981 Aug;4(2):379-90 (48 ref.)

On predicting therapeutic usefulness of psychotropic drugs from experiments in health persons. Spiegel R. **Rev Pure Appl Pharmacol Sci** 1980 Jul-Sep;1(3):215-91 (163 ref.)

[Mechanism of action and indications for psychopharmaceutic agents; possibilities and limitations in the elderly] Verhoeven WM. **Gerontologie** 1981 Aug;12(3):126-38 (Eng. Abstr.) **(Dut)**

[Endorphins in psychiatry] Rimón R. **Duodecim** 1980;96(21):1387-9 **(Fin)**

[Nursing care and chemotherapy] Larney E. **Soins Psychiatr** 1981 Jan; (7):47-51 **(Fre)**

[Psychotropic agents in emergencies] Troillard AM. **Soins Psychiatr** 1980 Apr 30;(2):33-8 **(Fre)**

[Lithium prophylaxis in neurologic practice] Baumhackl U, et al. **Bibl Psychiatr** 1981;(161):221-3 **(Ger)**

[Effectiveness of drug testing with the help of psychometric methods. Possibilities and problems] Oswald WD. **Med Welt** 1981 Aug 21; 32(34):1225-31 **(Ger)**

[Use of transformation in ridits for the evaluation of the activity of psychotropic drugs] Rovida S, et al. **Arch E Maragliano Patol Clin** 1979; 35:41-6 **(Ita)**

[Peptides as carriers of information in psychiatric diseases] Reichelt KL. **Nord Med** 1980 Nov;95(11):283-6 **(Nor)**

MENTAL PROCESSES

Note on estimating catecholamines in urine sampled after 75-min periods of mental work and inactivity. Forsman L. **J Psychosom Res** 1981; 25(3):223-5

[Effects of lithium on normal psychic functions as a restriction on prophylactic use] Kropf D. **Bibl Psychiatr** 1981;(161):141-51 (Eng. Abstr.) **(Ger)**

MEPROBAMATE

Meprobamate [news] Gomolin I. **Clin Toxicol** 1981 Jun 18(6):757-60

[Interference of meprobamate with adrenal hormone assays (author's transl)] Jambart S, et al. **Nouv Presse Med** 1981 May 2; 10(20):1643-4 (Eng. Abstr.) **(Fre)**

METHOTRIMEPRAZINE

[Pharmacological influences on the brain level and transport of GABA. II) Effect of various psychoactive drugs on brain level and uptake of GABA] Gabana MA, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30; 57(8):909-13 (Eng. Abstr.) **(Ita)**

METHYLPHENIDATE

Use of stimulant medication in treating pervasive developmental disorder [letter] Sporn A, et al. **Am J Psychiatry** 1981 Jul;138(7):997

Pharmacokinetics and behavioral effects of methylphenidate in Thoroughbred horses. Shults T, et al. **Am J Vet Res** 1981 May; 42(5):722-6

Methylphenidate impairs learning and memory in normal adults. Wetzel CD, et al. **Behav Neural Biol** 1981 Apr;31(4):413-24

Liquid-chromatographic analysis for methylphenidate (Ritalin) in serum. Soldin SJ, et al. **Clin Chem** 1979 Mar;25(3):401-4

Behavioral and neurochemical interactions of dextroamphetamine and methylphenidate in rats. Reigle TG, et al. **J Pharm Sci** 1981 Jul; 70(7):816-8

Optimal dosages of methylphenidate for improving the learning and behavior of hyperactive children. Charles L, et al. **JDBP** 1981 Sep; 2(3):78-81

Intracerebral des-tyrosine-gamma-endorphin inhibits methylphenidate induced locomotor activity. Davis KL, et al. **Life Sci** 1981 May 21; 28(21):2421-4

Antagonism of methylphenidate-induced behavior by neostigmine or hemicholinium-3. Ward HE Jr, et al. **Neuropharmacology** 1981 Jul; 20(7):705-9

Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Leith NJ, et al. **Psychopharmacology (Berlin)** 1981;74(1):23-8

METHYSERGIDE

Reactivity of isolated trachea, bronchus and lung strip of cats of carbachol, 5-hydroxytryptamine and histamine: evidence for the existence of methysergide-sensitive receptors. Chand N. **Br J Pharmacol** 1981 Aug; 73(4):853-7

Effects of methysergide or phenoxybenzamine on the renal and cardiovascular responses to endotoxin in rats. Keeler R. **Circ Shock** 1981;8(3):361-8

A pre-junctional action of 5-hydroxytryptamine and methysergide on noradrenergic nerves in dog isolated saphenous vein. Watts AD, et al. **J Pharm Pharmacol** 1981 Aug;33(8):515-20

Effect of lergotrile mesylate and methysergide on morphine induced increase in prolactin release. Ratner A, et al.

Proc West Pharmacol Soc 1981;24:335-9

MOTIVATION

The temporal structure of motivation IV: A reexamination of extinction effects in intracranial reward. Katz RJ. **Behav Neural Biol** 1981 Jun; 32(2):191-200

Effect of injury to the serotoninergic and noradrenergic brain systems on food and defensive conditioned reflexes in rats. Gromova EA, et al. **Neurosci Behav Physiol** 1981 Jan-Feb;11(1):10-5

MOTOR ACTIVITY

Kainic acid induced lesion of ventral tegmental area: locomotor effect of apomorphine. Morgenstern R. **Acta Biol Med Ger** 1980; 39(8-9):911-5

The influence of microinjections of cholinomimetics into hypothalamus on the locomotor activity of rats. Plech A. **Agressologie** 1979; 20(D):279-82

Effect of haloperidol withdrawal on motor activity and circadian rhythm of rats. Kumar A, et al. **Arzneimittelforsch** 1981;31(7):1096-8

Effects of 60-Hz electric fields on avoidance behavior and activity of rats. Hjeresen DL, et al. **Bioelectromagnetics** 1980;1(3):299-312

Effect of short electromagnetic pulses on brain acetylcholine content and spontaneous motor activity of mice. Modak AT, et al. **Bioelectromagnetics** 1981;2(1):89-92

Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Menniti FS, et al. **Brain Res** 1981 Jul 6; 216(1):89-107

Role of dorsal mesencephalic reticular formation and deep layers of superior colliculus in turning behaviour elicited from the striatum. Morelli M, et al. **Brain Res** 1981 Jun 29;215(1-2):337-41

Disproportionate increases in locomotor activity in response to hormonal and photic stimuli following regional neurochemical depletions of serotonin. Waldbillig RJ, et al. **Brain Res** 1981 Jul 27;217(1):79-91

Behavioural effects of cathinone, an amine obtained from Catha edulis Forsk.: comparisons with amphetamine, norpseudoephedrine, apomorphine and nomifensine. Zelger JL, et al. **Bull Narc** 1980; 32(3):67-81

Supersensitivity of nigral serotonin receptors and rat rotational behaviour. Blackburn TP, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):343-6

Pharmacological studies with several analogs of mazindol: correlation between effects on dopamine uptake and various in vivo responses. Heikkila RE, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):277-86

Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice. Joshi VV, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):499-502

Involvement of dopamine in circling responses to muscimol depends on intranigral site of injection. Kilpatrick IC, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):407-19

Potentiation by Des-Tyr-gamma-endorphin on apomorphine-induced changes in rat open field behavior. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):77-81

Detailed analysis of the effects of apomorphine and d-amphetamine on spontaneous locomotor behaviour of rats as measured in a TV-based, automated open-field system. Nickolson VJ. **Eur J Pharmacol** 1981 Jun 10;72(1):45-56

Involvement of noradrenergic and dopaminergic neurons in shock-induced jumping in rats. Nishikawa T, et al. **Eur J Pharmacol** 1981 May 22;71(4):429-36

Injection of low doses of apomorphine into the nucleus accumbens of rats reduces locomotor activity. Van Ree JM, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):107-11

Effects of microinjection of 2-chloro-11 (2-dimethylaminoethoxy)-dibenzo[b,f]-thiepine (zotepine), thioridazine and haloperidol into the striatum and nucleus accumbens on stereotypic behaviour and motor activity. Lai H, et al. **J Pharm Pharmacol** 1981 Apr;33(4):252-4

Age-related changes in the central catecholaminergic function and its interaction with methamphetamine during postnatal life in the rat. Nomura Y, et al. **J Pharm Pharmacol** 1981 Apr;33(4):264-6

Backward walking induced by L-5-hydroxytryptophan in mice. Shimomura K, et al. **Jpn J Pharmacol** 1981 Feb;31(1):39-46

Induction of behavioral supersensitivity to apomorphine by DFP treatment. Davis KL, et al. **Life Sci** 1981 Apr 27;28(17):1953-9

Intracerebral des-tyrosine-gamma-endorphin inhibits methylphenidate induced locomotor activity. Davis KL, et al. **Life Sci** 1981 May 21; 28(21):2421-4

Differential effects of several dopamine uptake inhibitors and releasing agents on locomotor activity in normal and in reserpinized mice. Heikkila RE. **Life Sci** 1981 Apr 27;28(17):1867-73

Dopamine independent rotational response to unilateral intranigral injection of serotonin. Oberlander C, et al. **Life Sci** 1981 Jun 8; 28(23):2595-601

Single or repeated administration of small doses of apomorphine on water intake and activity in water-deprived rats. Dourish CT, et al. **Neuropharmacology** 1981 Mar;20(3):257-60

Multi-dimensional analyses of behavior in mice treated with alpha-endorphin. Kameyama T, et al. **Neuropharmacology** 1981 Mar; 20(3):247-50

Brain levels of noradrenalin, dopamine, and serotonin in rats with different levels of motor activity. Semenova TP, et al. **Neurosci Behav Physiol** 1981 Mar-Apr;11(2):153-5

Locomotor activity, defecation score and corticosterone levels during an openfield · exposure: a comparison among individually and group-housed rats, and genetically selected rat lines. Gentsch C, et al. **Physiol Behav** 1981 Jul;27(1):183-6

The locomotor and exploratory activities in rats after lesion of hippocampal pyramidal cells with kainic acid. Kleinrok Z, et al. **Pol J Pharmacol Pharm** 1980;32(5):625-37

Effects of a piperazine derivative piribedil, on exploration; locomotor activity and social behaviour in the rat. File SE. **Prog Neuropsychopharmacol** 1981;5(3):245-55

Neuroanatomical dissociation of thyrotropin-releasing hormone induced shaking behavior and thermogenic mechanisms. Kalivas PW, et al. **Regul Pept** 1981 Feb;1(5):335-45

[Central depletion of transmitters by reserpine and motor behavior in the rat (author's transl)] Funk KF, et al. **Acta Biol Med Ger** 1980; 39(8-9):923-7 (Eng. Abstr.) (Ger)

[Mechanism of pantogam potentiation of certain effects of hexobarbital and sodium barbital and inhibition of phenamine hyperactivity] Avakumov VM, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):30-4 (Eng. Abstr.) (Rus)

MOTOR SKILLS

Diazepam and driving ability. Landauer AA. **Med J Aust** 1981 Jun 13; 1(12):624-6

The effects of amoxapine and ethanol on psychomotor skills related to driving: a placebo and standard controlled study. Wilson WH, et al. **Prog Neuropsychopharmacol** 1981;5(3):263-70

[Motor reactivity during lithium prophylaxis] Opgenoorth E, et al. **Bibl Psychiatr** 1981;(161):152-69 (Eng. Abstr.) (Ger)

[Influence of thioridazine on cognitive, psychomotor, and reaction performance in patients with dysthymic-depressive syndrome (author's transl)] Meyer FP, et al. **Pharmacopsychiatria** 1981 May;14(3):94-9 (Ger)

MSH

Processing, turnover and release of corticotropins, endorphins and melanotropin in the toad pituitary intermediate lobe. Loh YP. **Ciba Found Symp** 1981;(81):55-78

Functions of alpha-melanotropin and other opiomelanocortin peptides in labour, intrauterine growth and brain development. Swaab DF, et al. **Ciba Found Symp** 1981;(81):196-217

Endogenous alpha-melanotropin and central dopamine systems in physical and psychological stress. Monnet F, et al. **Exp Brain Res** 1981; 42(2):203-11

Parallel stimulation of ACTH, beta-LPH + beta-endorphin and alpha-MSH release by alpha-adrenergic agents in rat anterior pituitary cells in culture. Raymond V, et al. **Mol Cell Endocrinol** 1981 Jun; 22(3):295-303

alpha-MSH, MIF-I and melatonin: effects on novelty-induced defecation, plasma 11-OHCS and central catecholamines in rats. Datta PC, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:143-54

Effects of alpha-MSH and beta-endorphin on startle reflex in rat. Hoehler FK, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:137-41

Stimulatory effect of prostaglandin E1 on thyroliberin-induced alpha-melanotropin release from perifused neuro-intermediate lobes of frog pituitary gland. Leroux P, et al. **Prostaglandins** 1981 Apr; 21(4):599-608

NEUROREGULATORS

The insect neuropeptide proctolin can affect the CNS and the smooth=muscle of mammals. Schulz H, et al. **Acta Biol Med Ger** 1981; 40(2):K1-5

Neurotransmitters in the cochlea and the cochlear nucleus. Klinke R. **Acta Otolaryngol (Stockh)** 1981 May-Jun;91(5-6):541-54 (88 ref.)

Effect of electroconvulsive treatment on brain monoamine content, pituitary-adrenal function and plasma prolactin. Arató M, et al. **Acta Physiol Acad Sci Hung** 1980;56(2):163-71

Amino acid neurotransmitters. **Adv Biochem Psychopharmacol** 1981; 29:1-572

Neuron-glia interactions in the biosynthesis and release of transmitter amino acids. Hamberger A, et al. **Adv Biochem Psychopharmacol** 1981; 29:509-18 (29 ref.)

Glutamate as a transmitter of the hippocampal commissural system. Nitsch C. **Adv Biochem Psychopharmacol** 1981;29:97-104

Pharmacology of excitatory amino acid transmitters. Watkins JC. **Adv Biochem Psychopharmacol** 1981;29:205-12 (31 ref.)

Evidence for a dual role of GABA as a synaptic transmitter and a promoter of synaptogenesis. Wolff JR. **Adv Biochem Psychopharmacol** 1981;29:459–65 (29 ref.)

General characteristics, localization, and adaptative responsiveness of neurotransmitter–sensitive adenylate cyclases in the central nervous system. Bockaert J. **Adv Cyclic Nucleotide Res** 1981;14:611–28

Inhibition of adenylate cyclase by hormones and neurotransmitters. Jakobs KH, et al. **Adv Cyclic Nucleotide Res** 1981;14:173–87

Transport models of the neurotransmitter–receptor interaction. Vieth WR, et al. **Ann NY Acad Sci** 1981;369:99–111

Dual action of meperidine on the frog neuromuscular junction: a prejunctional, opiate receptor–mediated depression of transmitter release and a postjunctional, nonopiate receptor effect on the endplate. Durham HD, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):150–65

Changes in brain biogenic amines in cats performing a symmetrically reinforced go–nogo visual discrimination task. Kitsikis A, et al. **Behav Neural Biol** 1981 Jun;32(2):133–47

Divalent cations and transmitter release at low concentration of tetrodotoxin. Dascal N, et al. **Biophys J** 1981 Sep;35(3):573–86

Tests of an electrostatic screening hypothesis of the inhibition of neurotransmitter release by cations at the frog neuromuscular junction. Misler S, et al. **Biophys J** 1980 Jul;31(1):9–30

Diet, neurotransmitters and brain function. Anderson GH. **Br Med Bull** 1981 Jan;37(1):95–100 (69 ref.)

The neuropeptide proctolin acts directly on Limulus cardiac muscle to increase the amplitude of contraction. Benson JA, et al. **Brain Res** 1981 Jun 1;213(2):449–54

Evidence for glutamate as the neurotransmitter of corticothalamic and corticorubral pathways. Bromberg MB, et al. **Brain Res** 1981 Jun 29; 215(1–2):369–74

Patterns of endogenous amino acid release from slices of rat and guinea–pig olfactory cortex. Collins GG, et al. **Brain Res** 1981 Jan 5; 204(1):103–20

Fourth ventricular tanycytes: a possible relationship with monoaminergic nuclei. Felten DL, et al. **Brain Res Bull** 1981 May;6(5):427–36

Immunocytochemical identification of proctolinlike immunoreactivity in the terminal ganglion and hindgut of the cockroach Periplaneta americana (L.). Eckert M, et al. **Cell Tissue Res** 1981;217(3):633–45

Diamide, temperature and spontaneous transmitter release at the neuromuscular junction: stimulation of exocytosis by a direct effect on membrane fusion? Pubiicover SJ, et al. **Eur J Pharmacol** 1981 Mar 12; 70(2):203–11

Electrical responses of pineal cells to melatonin and putative transmitters. Evidence for circadian changes in sensitivity. Semm P, et al. **Exp Brain Res** 1981;43(3–4):361–70

Role of neurotransmitter release and cyclic AMP–dependent membrane phosphorylation in low voltage myocardial automaticity. Saxon ME, et al. **Experientia** 1981 Jul 15;37(7):731–4

Biophysical aspects of transmitter action. Adams PR. **Fed Proc** 1981 Sep; 40(11):2611–3

Neuroendocrine involvement in regulation of isocitrate & glucose–6–phosphate dehydrogenase activities in the fresh water field crab Oziotelphusa senex senex. Purushotham KR, et al. **Indian J Exp Biol** 1981 Apr;19(4):399–400

Neurotransmitter receptors: neuroanatomical localization through autoradiography. Murrin LC. **Int Rev Neurobiol** 1981;22:111–71 (379 ref.)

Mechanisms of synaptic modulation. Shain W, et al. **Int Rev Neurobiol** 1981;22:205–50 (254 ref.)

On the structural and phyletic origin of the aminergic nerves of the hypophysis of frog tadpoles (Rana temporaria) with special reference to pars distalis. Aronsson S, et al. **J Comp Neurol** 1981 Aug 10; 200(3):315–21

Respiratory depression by GABA–ergic drugs in the preterm rabbit. Hedner J, et al. **J Dev Physiol** 1980 Dec;2(6):401–7

Cyclic AMP, 5–HT, and the modulation of transmitter release at the crayfish neuromuscular junction. Enyeart J. **J Neurobiol** 1981 Sep; 12(5):505–13

The effect of anti–synaptosomal membrane antibodies of neurotransmitter uptake. Hofstein R, et al. **J Neurochem** 1981 Jul;37(1):14–21

Aspartate and glutamate as possible neurotransmitters in the visual cortex. Baughman RW, et al. **J Neurosci** 1981 Apr;1(4):427–39

Transmitter release properties along regenerated nerve processes at the frog neuromuscular junction. Decino P. **J Neurosci** 1981 Mar; 1(3):308–17

Synaptic transmission within the central nervous system. Neatherlin JS, et al. **J Neurosurg Nurs** 1981 Jun;13(3):146–9

A smooth muscle inhibitory material from the bovine retractor penis and rat anococcygeus muscles. Gillespie JS, et al. **J Physiol (Lond)** 1980 Dec;309:55–64

Transmitter control of voltage–dependent currents. Pellmer TC. **Life Sci** 1981 May 18;28(20):2199–205 (36 ref.)

The status of glycine as a supraspinal neurotransmitter. Pycock CJ, et al. **Life Sci** 1981 Jun 15;28(24):2679–86 (81 ref.)

An opiate system in the goldfish retina. Djamgoz MB, et al. **Nature** 1981 Aug 13;292(5824):620–3

Tetanus toxin and botulinum A toxin inhibit release and uptake of various transmitters, as studied with particulate preparations from rat brain and spinal cord. Bigalke H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun;316(3):244–51

Age and neurochemical correlates of radial maze performance in rats. Ingram DK, et al. **Neurobiol Aging** 1981 Spring;2(1):41–7

Age–related alterations in neurotransmitter receptors: an electrophysiological and biochemical analysis. Lippa AS, et al. **Neurobiol Aging** 1981 Spring;2(1):3–8

Recovery cycles of visual cortical primary responses during pharmacological and electrical intervention on monoaminergic systems of the rat brain. Vorob'ev VV, et al. **Neurosci Behav Physiol** 1981 Mar–Apr;11(2):129–33

Peptides as neurotransmitters: focus on the enkephalins and endorphins. Miller RJ. **Pharmacol Ther [B]** 1981;12(1):73–108 (214 ref.)

Sleep deprivation: effects on circadian rhythms of rat brain neurotransmitter receptors. Wirz–Justice A, et al. **Psychiatry Res** 1981 Aug;5(1):67–76

Effect of chronic methylmercury exposure on activities of neurotransmitter enzymes in rat cerebellum. Tsuzuki Y. **Toxicol Appl Pharmacol** 1981 Sep 15;60(2):379–81

[Diet, neurotransmitters and brain function (editorial)] **S Afr Med J** 1981 Aug 8;60(6):221 **(Afr)**

[Clinical implications of present knowledge respecting neuropharmacologic control of antipituitary hormones] Martin–Du Pan R, et al. **Schweiz Med Wochenschr** 1980 Nov 29;110(48):1784–1814 (346 ref.) (Eng. Abstr.) **(Fre)**

[Hypophyseal hormones––neurotransmitters? (editorial)] Korczyn A. **Harefuah** 1980 Dec 15;99(12):441–2 **(Heb)**

[Effect of monocrotophos on the neurotransmitter system in the central nervous system] Borkowska J, et al. **Rocz Panstw Zakl Hig** 1980; 31(6):605–10 (Eng. Abstr.) **(Pol)**

[Role of dopamine receptors in regulating glutamatergic synaptic transmission in the rat neostriatum] Godukhin OV, et al. **Fiziol Zh SSSR** 1981 Mar;67(3):384–9 (Eng. Abstr.) **(Rus)**

[Neurohumoral regulation of the microcirculation in vibration–related disorders] Kostiuk IF, et al. **Vrach Delo** 1981;(6):100–2 **(Rus)**

[Mechanisms of the central action of lithium] Sinitskil VN, et al. **Zh Nevropatol Psikhiatr** 1981;81(4):567–75 (Eng. Abstr.) **(Rus)**

NEUROTENSIN

The regional distribution of somatostatin, substance P and neurotensin in human brain. Cooper PE, et al. **Brain Res** 1981 Aug 10; 218(1–2):219–32

Immunocytochemical localization of neurotensin–containing neurons in the hypothalamus of the Japanese quail, Coturnix coturnix japonica. Yamada S, et al. **Cell Tissue Res** 1981;218(1):29–39

Neurotensin–like immunoreactivity in the nervous system of hydra. Grimmelikhuijzen CJ, et al. **Histochemistry** 1981;72(2):199–209

Neurotensin–induced contractions in venous smooth muscle. Helle KB, et al. **J Auton Nerv Syst** 1980 Jul;2(2):143–55

Synthesis of peptides by the solid–phase method. 6. Neurotensin, fragments, and analogues. St–Pierre S, et al. **J Med Chem** 1981 Apr; 24(4):370–6

Mechanism of neurotensin–induced pressor effect and tachycardia in guinea pigs. Kérouac R, et al. **Life Sci** 1981 Jun 1;28(22):2477–87

Effects of intraventricular administration of neurotensin and somatostatin on thermoregulation in the rat. Chandra A, et al. **Neuropharmacology** 1981 Jul;20(7):715–8

Neurotensin–like and somatostatin–like immunoreactivity within amacrine cells of the retina. Brecha N, et al. **Neuroscience** 1981;6(7):1329–40

Neurotensin: first report of a cortical pathway. Roberts GW, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:37–43

Electrophysiological actions of neurotensin in rat cerebellum. Marwaha J, et al. **Regul Pept** 1980 Oct;1(2):115–25

Neurotensin and substance P: differential effects on plasma cholesterol levels in conscious ovariectomized rats. Raju K, et al. **Regul Pept** 1981 Aug;2(4):265–74

Effect of neurotensin on regional intestinal blood flow in the dog. Baća I, et al. **Res Exp Med (Berl)** 1981;179(1):53–8

NEUROTIC DISORDERS

[Theoretical assessment and personal experience with the combination of psychotropic drugs and psychotherapy] Seidler C. **Z Arztl Fortbild (Jena)** 1981 May 1;75(9):412–5 **(Ger)**

NIALAMIDE

Comparisons of rotamer populations of nialamide, azaperone, and chloroquine in solid state and in solution. Migliaccio GP, et al. **J Pharm Sci** 1981 Mar;70(3):284–7

NITRAZEPAM

[Pharmaceutical use of some activated bentonites (author's transl)] Grecu I, et al. **Ann Pharm Fr** 1980;38(6):501–6 (Eng. Abstr.) **(Fre)**

NOREPINEPHRINE

Interaction at the synaptic level of fusaric acid with neurotransmitters. Fischer HD, et al. **Acta Biol Med Ger** 1980;39(8–9):935–40
Effect of oestradiol-17 beta on the metabolism of noradrenaline in brain slices of ovariectomized rats. Köster G, et al. **Acta Endocrinol (Copenh)** 1981 Sep;98(1):1–7
Dextro-phenylalanine as inhibitor of the noradrenaline release from the isolated rat hypothalamus. Pardal JF, et al. **Acta Neurol Latinoam** 1979; 25(3–4):235–48
Noradrenaline release and uptake in isolated small dense cored vesicles from rat seminal ducts. Fried G. **Acta Physiol Scand** 1981 May; 112(1):41–6
Neuronal and extraneuronal uptake of 3H-noradrenaline in rat portal vein in vitro. Hedner J, et al. **Acta Physiol Scand** 1981 Feb;111(2):171–7
Responses to catecholamines and nerve stimulation of the perfused rete tibiotarsale and associated blood vessels in the hind limb of the Mallard (Anas platyrhynchos). Midtgård U, et al. **Acta Physiol Scand** 1981 May; 112(1):77–81
Stimulatory and inhibitory effects of catecholamines and of prostaglandin E2 on human fat cell adenylate cyclase. Kather H, et al. **Adv Cyclic Nucleotide Res** 1981;14:555–62
Bradykinin effects on adrenergic transmission in the canine kidney: relation to prostaglandins. Sušić H, et al. **Am J Physiol** 1981 Sep; 241(3):R146–51
Endogenous norepinephrine release induced by tyramine modulates intestinal ion transport. Tapper EJ, et al. **Am J Physiol** 1981 Sep; 241(3):G264–9
Functional properties of noradrenergic nervous system in rat colonic mucosa: uptake of [3H]norepinephrine. Wu ZC, et al. **Am J Physiol** 1981 Aug;241(2):G137–42
The effect of pimozide on CSF norepineparine in schizophrenia. Sternberg DE, et al. **Am J Psychiatry** 1981 Aug;138(8):1045–50
Reverse-phase high-performance liquid chromatographic separation and electrochemical detection of norepinephrine, dopamine, serotonin, and related major metabolites. Kempf E, et al. **Anal Biochem** 1981 Apr; 112(2):223–31
Application of high-performance liquid chromatography with a chemiluminescence detection system to determine catecholamines in urine. Kobayashi S, et al. **Anal Biochem** 1981 Mar 15;112(1):99–104
Catecholamine excretion rates in relation to life-styles in the male population of Otmoor, Oxfordshire. Reynolds V, et al. **Ann Hum Biol** 1981 May–Jun;8(3):197–209
An analysis of the effects of apomorphine and haloperidol on the release of [3H]-dopamine and [3H]-noradrenaline from rabbit brain slices. Kelly MJ. **Arch Int Pharmacodyn Ther** 1981 Mar;250(1):18–29
Social housing conditions influence escape deficits produced by uncontrollable stress: assessment of the contribution of norepinephrine. Anisman H, et al. **Behav Neural Biol** 1981 Aug;32(4):406–27
The involvement of the locus coeruleus in memory. Prado de Carvalho L, et al. **Behav Neural Biol** 1981 Feb;31(2):173–86
Effects on fluorine analogs of norepinephrine on stimulation of cyclic adenosine 3',5'-monophosphate and binding to beta-adrenergic receptors in intact pinealocytes. Auerbach DA, et al. **Biochem Pharmacol** 1981 May 15;30(10):1085–9
No evidence for reverse trans-synaptic regulation of neuronal uptake by beta-adrenoceptors in kitten atria. Cornish EJ, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1439–42
Amfonelic acid antagonism of dopamine and norepinephrine depletion by alpha-methyl-m-tyrosine in rat brain. Fuller RW, et al. **Biochem Pharmacol** 1981 Jul 15;30(14):2025–6
Na+, K+-ATPase activity and noradrenaline turnover in brown adipose tissue of rats exhibiting diet-induced thermogenesis. Rothwell NJ, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1709–12
Adrenocortical function and plasma norepinephrine in normal human subjects. Sotsky SM, et al. **Biol Psychiatry** 1981 Jul;16(7):643–51
Habitual catecholamine excretion and its relation to habitual distress. Forsman L. **Biol Psychol** 1980 Sep;11(2):83–97
Changes in plasma catecholamine concentrations during endotracheal intubation. Russell WJ, et al. **Br J Anaesth** 1981 Aug;53(8):837–9
Isoprenaline- and noradrenaline-induced hyperpolarization of guinea-pig liver cells. Karashima T. **Br J Pharmacol** 1981 Aug;73(4):867–77
The effects of 4-aminopyridine on the isolated vas deferens and its effects on the inhibitory properties of adenosine, morphine, noradrenaline and gamma-aminobutyric acid. Stone TW. **Br J Pharmacol** 1981 Jul; 73(3):791–6
Noradrenergic innervation of serotonergic neurons in the dorsal raphe: demonstration by electron microscopic autoradiography. Baraban JM, et al. **Brain Res** 1981 Jan 5;204(1):1–11
Insulin-induced elevation of hypothalamic norepinephrine turnover persists after glucorestoration unless feeding occurs. Bellin SI, et al. **Brain Res** 1981 Aug 3;217(2):327–37
The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Coote JH, et al. **Brain Res** 1981 Jun 29;215(1–2):135–45
Noradrenaline stimulates somatostatin release from incubated slices of the amygdala and the hypothalamic preoptic area. Epelbaum J, et al. **Brain Res** 1981 Jun 29;215(1–2):393–7
Release of endogenous catecholamines from slices of hypothalamus of rats. Hamlet MA, et al. **Brain Res** 1981 Aug 3;217(2):315–25
Norepinephrine reduces excitability of single cutaneous primary afferent C-fibers in the cat spinal cord. Jeftinija S, et al. **Brain Res** 1981 Aug 31;219(2):456–63
Norepinephrine depletion alters cerebral oxidative metabolism in the 'active' state. LaManna JC, et al. **Brain Res** 1981 Jan 5; 204(1):87–101
Chemical deafferentation of the olfactory bulb: plasticity of the levels of tyrosine hydroxylase, dopamine and norepinephrine. Nadi NS, et al. **Brain Res** 1981 Jun 1;213(2):365–77
Suction lesions of the frontal cerebral cortex in the rat induce asymmetrical behavioral and catecholaminergic responses. Pearlson GD, et al. **Brain Res** 1981 Aug 10;218(1–2):233–42
Cyclic AMP-generating systems in rat hippocampal slices. Segal M, et al. **Brain Res** 1981 Jun 1;213(2):351–64
Effects of ventral tegmental area stimulation and microiontophoretic application of dopamine and norepinephrine on hypothalamic neurons. Barone FC, et al. **Brain Res Bull** 1981 Aug;7(2):181–93
Interaction between central gray and nucleus raphe magnus: role of norepinephrine. Behbehani MM, et al. **Brain Res Bull** 1981 May; 6(5):361–4
Forebrain norepinephrine and serotonin concentrations and cardiac conditioning in normal rabbits and rabbits with septal lesions. Hernández LL, et al. **Brain Res Bull** 1981 Jun;6(6):479–86
Changes in brain norepinephrine content in mice following neonatal 6-hydroxydopamine. Lovell KL. **Brain Res Bull** 1981 Jul;7(1):41–4
Regional changes in brain norepinephrine content in relation to mouse-killing behavior by rats. Yoshimura H, et al. **Brain Res Bull** 1981 Aug;7(2):151–5
Catecholamines and 5-hydroxytryptamine in photophores of Porichthys notatus. Radioenzymatic detection and radioautographic localization. Anctil M, et al. **Cell Tissue Res** 1981;219(3):557–66
Correlative light-, fluorescence- and electron-microscopic studies of catecholamine-storing cells in the adrenal medulla of the domestic fowl. Chungsamarnyart N, et al. **Cell Tissue Res** 1981;217(3):471–7
Catecholamine-storing cells in the adrenal medulla of the pre- and postnatal rat. Acetylcholinesterase as a means for early discrimination of cell types. Millar TJ, et al. **Cell Tissue Res** 1981;217(1):155–70
Prejunctional inhibition of norepinephrine release caused by acetylcholine in the human saphenous vein. Rorie DK, et al. **Circ Res** 1981 Aug; 49(2):337–41
Spread of contraction in rabbit ear artery preparations in response to stimulation by norepinephrine. Vonderlage M. **Circ Res** 1981 Sep; 49(3):600–8
Studies of diurnal changes in plasma renin activity, and plasma noradrenaline, aldosterone and cortisol concentrations in man. Lightman SL, et al. **Clin Endocrinol (Oxf)** 1981 Mar;14(3):213–23
Intraventricular administration of vasopressin and oxytocin effects the steady-state levels of serotonin, dopamine and norepinephrine in rat brain. Schwarzberg H, et al. **Endocrinol Exp (Bratisl)** 1981; 15(2):75–80
Effects of diltiazem hydrochloride on pressor and steroidogenic actions of angiotensins and norepinephrine in man. Ikeda F, et al. **Endocrinol Jpn** 1980 Dec;27(6):779–84
Electrical stimulation of mesencephalic noradrenergic pathway: effects on luteinizing hormone levels in blood of ovariectomized and ovariectomized, steroid-primed rats. Leung PC, et al. **Endocrinology** 1981 Sep;109(3):720–8
Norepinephrine and thyrotropin effects on the thyroid in vitro: simultaneous stimulation of iodide organification and antagonism of thyroxine release. Maayan ML, et al. **Endocrinology** 1981 Sep; 109(3):930–4
pH-dependence of the ATP-driven uptake of noradrenaline by bovine chromaffin-granule ghosts. Scherman D, et al. **Eur J Biochem** 1981 Jun 1;116(3):535–9
Lack of modulation by presynaptic alpha 2-adrenoceptors of adrenergic transmitters release evoked by activation of 5-hydroxytryptamine and nicotine receptors. Carr SR, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):27–34
High-affinity [3H] DMI binding is associated with neuronal noradrenaline uptake in the periphery and the central nervous system. Langer SZ, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):423–4
An interaction between prejunctional alpha-adrenoceptors and prejunctional beta-adrenoceptors. Majewski H, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):493–8
Involvement of noradrenergic and dopaminergic neurons in shock-induced jumping in rats. Nishikawa T, et al. **Eur J Pharmacol** 1981 May 22;71(4):429–36
Differential actions of mianserin and iprindole on the sensitivity of cortical neurons to noradrenaline: effect of chronic treatment. Olpe HR, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):381–5
Norepinephrine produces tension through electromechanical coupling in rabbit ear artery. Trapani A, et al. **Eur J Pharmacol** 1981 Jun 10;

72(1):87-91

The effect of noradrenaline on Na-K transport in rat cerebral cortical slices. Wu PH, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):529-31

Effect of chlorphentermine on the pulmonary disposition of norepinephrine in the isolated perfused rabbit lung. Angevine LS, et al. **Exp Lung Res** 1981 May;2(2):71-84

Inhibitory action of bradykinin on release of the adrenergic transmitter in the isolated lapine kidney. Malik KU, et al. **Experientia** 1981 May 15;37(5):496-7

Thermogenic response as the function of extravascular influx of infused noradrenaline. Mejsnar J, et al. **Experientia** 1981 May 15;37(5):482-3

The effect of drugs on accumulation of exogenous norepinephrine in nervous tissue cultured in vitro. IV. The effect of clonidine. Szydłowska H, et al. **Folia Histochem Cytochem (Krakow)** 1981;19(2):93-8

Differential transmural constrictor response to norepinephrine in rabbit carotid artery. Flaim SF, et al. **Gen Pharmacol** 1981;12(4):295-301

Thyrotropin-releasing hormone increases plasma norepinephrine in man. Morley JE, et al. **Horm Res** 1981;14(1):18-23

Effects of exposure to trichloroethylene and tetrachloroethylene on the contents of acetylcholine, dopamine, norepinephrine and serotonin in rat brain. Honma T, et al. **Ind Health** 1980;18(4):171-8

The effect of light exercise on the plasma superoxide dismutase activity and on the plasma noradrenaline concentration. Minami M, et al. **Ind Health** 1981;19(2):133-8

Reduced norepinephrine response to dynamic exercise in human subjects during O2 breathing. Hesse B, et al. **J Appl Physiol** 1981 Jul; 51(1):176-8

Effects of epinephrine and norepinephrine infusion on lung fluid balance in sheep. Minnear FL, et al. **J Appl Physiol** 1981 Jun;50(6):1353-7

Effects of noradrenergic and serotonergic neurons on blood pressure, heart rate and baroreceptor-heart rate reflex of the conscious rabbit. Korner PI, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):511-23

The relation of plasma norepinephrine and epinephrine levels over time in humans. Levin BE, et al. **J Auton Nerv Syst** 1980 Dec; 2(4):315-25

Noradrenergic innervation of the villi of rat jejunum. Thomas EM, et al. **J Auton Nerv Syst** 1981 Feb;3(1):25-9

Effects of L-dopa on dopamine and norepinephrine concentrations in rat brain assessed by gas chromatography. Doshi PS, et al. **J Chromatogr** 1981 Jun 19;210(3):505-11

Some observations on the catecholaminergic innervation of the intermediate zone of the thoracolumbar spinal cord of the cat. McLachlan EM, et al. **J Comp Neurol** 1981 Aug 20;200(4):529-44

An ultrastructural and biochemical analysis of norepinephrine-containing varicosities in the cerebral cortex of the turtle Pseudemys. Ouimet CC, et al. **J Comp Neurol** 1981 Jan 10;195(2):289-304

Effect of gonadectomy on the concentrations of catecholamines in discrete areas of the diencephalon of the domestic fowl. Knight PG, et al. **J Endocrinol** 1981 Jun;89(3):389-97

Ultrastructural demonstration of noradrenergic synapses in the rat central nervous system by dopamine-beta-hydroxylase immunocytochemistry. Olschowka JA, et al. **J Histochem Cytochem** 1981 Feb;29(2):271-80

Biochemical variability in a tem sports situation. Biersner RJ, et al. **J Human Stress** 1981 Sep;7(3):12-7

Catecholamine and cortisol excretion patterns in three-year-old children and their parents. Lundberg U, et al. **J Human Stress** 1981 Sep; 7(3):3-11

Involvement of brain monoamines in the delta-9-tetrahydrocannabinol-induced reduction of hippocampal choline uptake. Lindamood C 3d, et al. **J Neurochem** 1981 Sep; 37(3):788-91

Diurnal variations in monoamine contents in discrete brain regions of the mongolian gerbil (Meriones unguiculatus). Matsumoto M, et al. **J Neurochem** 1981 Sep;37(3):792-4

The development of pre- and postsynaptic components of the noradrenergic system in the rat cerebellum. Waddington G, et al. **J Neurochem** 1981 Sep;37(3):576-81

Neuronal responses of the globus pallidus to systemic administration of d-amphetamine: investigation of the involvement of dopamine, norepinephrine, and serotonin. Bergstrom DA, et al. **J Neurosci** 1981 Mar;1(3):292-9

High-performance liquid chromatography with electrochemical detection as a highly efficient tool for studying catecholaminergic systems. I. Quantification of noradrenaline, adrenaline and dopamine in cultured adrenal medullary cells. Müller TH, et al. **J Neurosci Methods** 1981 Jun;4(1):39-52

Effect of cocaine on contractile responses to noradrenaline of canine isolated mesenteric vein. O'Connor PC, et al. **J Pharm Pharmacol** 1981 Jan;33(1):55-8

Effect of cocaine on noradrenaline contractions of mesenteric vein: pre or postjunctional mechanism? O'Connor PC, et al. **J Pharm Pharmacol** 1981 Jan;33(1):58-60

Effects of norepinephrine on pineal tryptophan hydroxylase, using an improved [14C]CO2-trapping microtechnique. Chan A, et al. **J Pharmacol Methods** 1981 Aug;6(1):13-20

Site(s) and ionic basis of alpha-autoinhibition and facilitation of '3H'noradrenaline secretion in guinea-pig vas deferens. Alberts P, et al. **J Physiol (Lond)** 1981 Mar;312:297-334

The effect of adrenaline and noradrenaline on coronary vascular reserve in the dog. Creates MS, et al. **J Physiol (Lond)** 1980 Dec; 309:557-68

The influence of the infusion of noradrenaline on plasma cortisol levels in man. Few JD, et al. **J Physiol (Lond)** 1980 Dec;309:375-89

The release of adenosine and inosine from canine subcutaneous adipose tissue by nerve stimulation and noradrenaline. Fredholm BB, et al. **J Physiol (Lond)** 1981;313:351-67

Localization of specialized noradrenaline receptors at neuromuscular junctions on arterioles of the guinea-pig. Hirst GD, et al. **J Physiol (Lond)** 1981;313:343-50

Note on estimating catecholamines in urine sampled after 75-min periods of mental work and inactivity. Forsman L. **J Psychosom Res** 1981; 25(3):223-5

The effect of catecholamines or sodium lactate on blood lactate distribution in the rat. Aragno R. **J Sports Med Phys Fitness** 1981 Mar; 21(1):7-14

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633-9

Stimulation of prostaglandin E2-synthesis by noradrenaline in primary cell cultures from rabbit splenic pulpa is mediated by atypical alpha-adrenoceptors. Brückner-Schmidt R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):1-7

The positive inotropic effect of (-)-noradrenaline and (+/-)-isoprenaline after chemical sympathectomy: evidence in favour of differences at a postsynaptic site. Ebner F, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):8-18

In vitro studies on 6-fluoronoradrenaline at several peripheral sympathetic neuroeffector junctions. Shepperson NB, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):1-4

Enhancement of 3H-noradrenaline overflow from cardiac sympathetic nerves by low Ca and tetraethylammonium. Wakade AR, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jul;316(4):273-7

Norepinephrine uptake in aging adrenergic nerve terminals. Hoffman DW, et al. **Neurobiol Aging** 1980 Summer;1(1):65-8

The effect of hypoxia on monoamine levels in discrete regions of aged rat brain. Roubein IF, et al. **Neurobiol Aging** 1981 Spring;2(1):37-40

Importance of norepinephrine alpha 2-receptor activation for morphine-induced rat growth hormone secretion. Eriksson E, et al. **Neuroendocrinology** 1981 Aug;33(2):91-6

Adrenal medullary secretory response to pontine and mesencephalic stimulation in the rat. Matsui H. **Neuroendocrinology** 1981 Aug; 33(2):84-7

Effect of injury to the serotoninergic and noradrenergic brain systems on food and defensive conditioned reflexes in rats. Gromova EA, et al. **Neurosci Behav Physiol** 1981 Jan-Feb;11(1):10-5

Brain levels of noradrenalin, dopamine, and serotonin in rats with different levels of motor activity. Semenova TP, et al. **Neurosci Behav Physiol** 1981 Mar-Apr;11(2):153-5

Recovery cycles of visual cortical primary responses during pharmacological and electrical intervention on monoaminergic systems of the rat brain. Vorob'ev VV, et al. **Neurosci Behav Physiol** 1981 Mar-Apr;11(2):129-33

The effects of lesions of lateral tegmental noradrenergic neurons on components of sexual behavior and pseudopregnancy in female rats. Hansen S, et al. **Neuroscience** 1981;6(6):1105-17

Behavioral assessment of norepinephrine and serotonin function and interaction in the hippocampal formation. Gage FH, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):815-21

A new approach to the role of noradrenaline in learning: problem-solving in the marmoset after alpha-noradrenergic receptor blockade. Ridley RM, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):849-55

Diltiazem and verapamil inhibit norepinephrine-stimulated 45Ca uptake in rabbit aorta. Flaim SF, et al. **Pharmacology** 1981;22(5):286-93

Compartmental analysis of tyramine-induced norepinephrine depletion. Rapoport RM, et al. **Pharmacology** 1981;22(4):235-42

Rewarding effect of noradrenergic stimulation of the amygdala in food deprived rats. Jurkowlaniec E, et al. **Physiol Behav** 1981 Jul; 27(1):27-31

The central noradrenergic transmission and the locus coeruleus: a review of the data, and their implications for neurotransmission and neuromodulation. van Dongen PA. **Prog Neurobiol** 1981; 16(2):117-43 (303 ref.)

Effects of 6-hydroxydopamine lesions of locus coeruleus on startle in rats. Adams LM, et al. **Psychopharmacology (Berlin)** 1981; 73(4):394-8

Noradrenergic and dopaminergic interactions in escape behavior: analysis of uncontrollable stress effects. Anisman H, et al. **Psychopharmacology (Berlin)** 1981;74(3):263-8

Differences in presynaptic alpha-blockade, noradrenaline uptake inhibition, and potential antidepressant activity between (+)- and (-)mianserin. Schoemaker H, et al. **Psychopharmacology (Berlin)** 1981; 74(2):137-42

Relationships between sex-related psychological characteristics during adolescence and catecholamine excretion during achievement stress. Rauste-von Wright M, et al. **Psychophysiology** 1981 Jul;18(4):362-70

MK-771 enhances the turnover of norepinephrine in brain. Rastogi RB, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):187-90

Biosynthesis of biopterin: adrenergic cyclic adenosine monophosphate-dependent inhibition in the pineal gland. Kapatos G, et al. **Science** 1981 Sep 4;213(4512):1129-31

Cerebroventricular propranolol elevates cerebrospinal fluid norepinephrine and lowers blood pressure. Tackett RL, et al. **Science** 1981 Aug 21;213(4510):911-3

Effect of acetylcholine and catecholamines on the enterochromaffin-like cells of the stomach. Sano M, et al. **Surg Gynecol Obstet** 1981 Sep; 153(3):337-40

Similar regulatory mechanism underlying 3H-noradrenaline release from isolated hypothalamus and perfused tail artery or the rat by Latrodectus antheratus (black widow spider) venom gland extract and by potassium. Pardal JF, et al. **Toxicon** 1981;19(2):249-54

[Plasma catecholamines, metabolic substrates, aerobic and anaerobic capacity during graduated treadmill and bicycle ergometer exercise (author's transl)] Lehmann M, et al. **Klin Wochenschr** 1981 Jun 1; 59(11):553-9 (Eng. Abstr.) **(Ger)**

[Metabolic effects of intravenous noradrenaline in metabolically healthy humans] Möricke R, et al. **Z Gesamte Inn Med** 1981 Jul 1; 36(13):433-43 (Eng. Abstr.) **(Ger)**

[Urinary excretion of MHPG in endogenous depression. Clinico-therapeutic index] Roccatagliata G, et al. **Minerva Psichiatr** 1981 Apr-Jun;22(2):75-8 (Eng. Abstr.) **(Ita)**

[Norepinephrine content in the inferior turbinate of the patients with nasal allergy (author's transl)] Fujitani T, et al. **Nippon Jibiinkoka Gakkai Kaiho** 1981 Feb;84(2):168-73 (Eng. Abstr.) **(Jpn)**

[Effects of tetragastrin on catecholamines in gastric juice and gastric tissues in rats (author's transl)] Baba M, et al. **Nippon Shokakibyo Gakkai Zasshi** 1981 Jun;78(6):1191-7 (Eng. Abstr.) **(Jpn)**

[Adrenaline and noradrenaline levels before and after heart catheterization] Rumiński W, et al. **Pol Tyg Lek** 1981 Mar 30; 36(13):461-3 (Eng. Abstr.) **(Pol)**

[Role of noradrenaline in luteinizing hormone secretion] Adamskaia EI, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):730-3 (Eng. Abstr.) **(Rus)**

[Technic for simultaneous recording of the uptake and secretion of 14C-noradrenaline by rat brain synaptosomes] Bazian AS, et al. **Biull Eksp Biol Med** 1981 Mar;91(3):377-9 (Eng. Abstr.) **(Rus)**

[Regulation of the functioning of molluscan neuron cholinoreceptors by succinate and noradrenaline] Andreev AA, et al. **Dokl Akad Nauk SSSR** 1981;258(6):1466-9 **(Rus)**

[Role of noradrenaline-sensitive neurons of the preoptic area in regulating luteinizing hormone release] Babichev VN, et al. **Fiziol Zh SSSR** 1981 Jun;67(6):809-15 (Eng. Abstr.) **(Rus)**

[Plasma catecholamines of August and Wistar strain rats subjected to emotional stress] Kvetnanskiĭ R, et al. **Fiziol Zh SSSR** 1981 Apr; 67(4):516-23 (Eng. Abstr.) **(Rus)**

[Effects of certain biologically active compounds and bivalent cations on lactate and malate dehydrogenase activities in cerebral cellular fractions] Bdovichenko LM. **Ukr Biokhim Zh** 1981 May-Jun; 53(3):66-70 (Eng. Abstr.) **(Rus)**

[Effect of scopolamine on temporary connection formation and fixation in rats with altered brain noradrenaline content] Orlova NV. **Zh Vyssh Nerv Deiat** 1981 May-Jun;31(3):571-6 (Eng. Abstr.) **(Rus)**

[Participation of hypothalamic noradrenergic structures in the reproduction of conditioned 'passive' avoidance reactions] Tolochko ZS. **Zh Vyssh Nerv Deiat** 1981;31(2):267-70 (Eng. Abstr.) **(Rus)**

NORMETANEPHRINE

A radioenzymatic method for determination of normetanephrine in blood plasma. Nagel-Hiemke M, et al. **J Biochem Biophys Methods** 1981 Jun; 4(5-6):255-9

Concomitant analysis of normetanephrine and 3-methoxytyramine in brain: a new gas-liquid chromatography procedure. LeGatt DF, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):61-8

NORTRIPTYLINE

Fatal nortriptyline overdose, plasma levels, and in vivo methylation of tricyclic antidepressants. Rudorfer MV, et al. **Am J Psychiatry** 1981 Jul;138(7):982-3

The pharmacokinetics of nortriptyline in patients with chronic renal failure. Dawling S, et al. **Br J Clin Pharmacol** 1981 Jul;12(1):39-45

E- and Z-10-hydroxylation of nortriptyline: relationship to polymorphic debrisoquine hydroxylation. Mellström B, et al. **Clin Pharmacol Ther** 1981 Aug;30(2):189-93

Amitriptyline and nortriptyline plasma levels monitoring. Perspective in clinical practice. Corona GL, et al. **Commun Psychopharmacol** 1980; 4(4):309-16

Reliability of tricyclic antidepressant levels — further questions [letter] Bank RL, et al. **J Clin Psychiatry** 1981 Sep;42(9):364

Effects of nortriptyline treatment on learned helplessness in the rat. Telner JI, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):823-6

Flupenthixol versus combined fluphenazine-nortriptyline in depressive illness.. Conway JF. **Practitioner** 1981 Mar;225(1353):400-4

Amitriptyline pharmacokinetics. A crossover study with single doses of amitriptyline and nortriptyline. Burch JE, et al. **Psychopharmacology (Berlin)** 1981;74(1):35-42

OBSESSIVE-COMPULSIVE DISORDER

A comparison of phenelzine and imipramine in an obsessive-compulsive patient. Isberg RS. **Am J Psychiatry** 1981 Sep;138(9):1250-1

Rapid response of severe obsessive-compulsive disorder to tranylcypromine. Jenike MA. **Am J Psychiatry** 1981 Sep; 138(9):1249-50

Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. Ananth J, et al. **Prog Neuropsychopharmacol** 1981; 5(3):257-62

ORGANIC MENTAL DISORDERS, PSYCHOTIC

[Role of psychopharmacotherapy in the treatment of late middle-aged and elderly patients with organic psychotic syndromes] Saarma IuM, et al. **Vestn Akad Med Nauk SSSR** 1980;(12):50-3 (Eng. Abstr.) **(Rus)**

OXALATES

[Prevention effect of some substances on experimental oxalic calculosis in the frog] Sorrentino F, et al. **Minerva Nefrol** 1979 Jul-Sep; 26(3):329-31 (Eng. Abstr.) **(Ita)**

OXAZEPAM

Specific binding of racemic oxazepam esters to rat brain synaptosomes and the influence of bioactivation by esterases. Maksay G, et al. **Arzneimittelforsch** 1981;31(6):979-81

Benzodiazepine structure versus reactivity with EMIT oxazepam antibody. Budd RD. **Clin Toxicol** 1981 May;18(5):643-55

Disposition of oxazepam in relation to age, sex, and cigarette smoking. Ochs HR, et al. **Klin Wochenschr** 1981 Aug 17;59(16):899-903

[Pharmaceutical use of some activated bentonites (author's transl)] Grecu I, et al. **Ann Pharm Fr** 1980;38(6):501-6 (Eng. Abstr.) **(Fre)**

PAIRED-ASSOCIATE LEARNING

Methylphenidate impairs learning and memory in normal adults. Wetzel CD, et al. **Behav Neural Biol** 1981 Apr;31(4):413-24

PARASYMPATHOMIMETICS

The influence of microinjections of cholinomimetics into hypothalamus on the locomotor activity of rats. Plech A. **Agressologie** 1979; 20(D):279-82

Influence of castration upon the seminal vesicle response to parasympathomimetic drugs. Porto CS, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):204-11

Evidence of overadditive interaction between fenoterol and ipratropium bromide in the counteraction of cholinomimetic-induced tracheobronchial contractions. Bongrani S, et al. **Arzneimittelforsch** 1981;31(6):970-3

Effect of antimuscarinic agents on the contractile responses to cholinomimetics in the rat anococcygeus muscle. Doggrell SA. **Br J Pharmacol** 1981 Aug;73(4):829-35

Cholinergic receptor interactions and their effects on long-term memory processing. Flood JF, et al. **Brain Res** 1981 Jun 29;215(1-2):177-85

Vasoconstriction produced by intracoronary cholinomimetic drugs in isolated donor-perfused hearts of rhesus monkeys: comparison with pig, dog, and rabbit hearts. Sakai K. **J Cardiovasc Pharmacol** 1981 May-Jun; 3(3):500-9

Disruption and facilitation of cue discrimination in the rat by cholinergic agents. Rick JT, et al. **Neuropharmacology** 1981 Aug;20(8):747-52

Chronic haloperidol treatment fails to alter the anorexic actions of dopaminergic agonists and cholinergic drugs. Hynes MD, et al. **Prog Neuropsychopharmacol** 1981;5(3):271-5

[Cholinergics and anticholinergics] Advenier C, et al. **Rev Prat** 1981 Aug; 31(37):2663-8 (Eng. Abstr.) **(Fre)**

PARGYLINE

Influence of harmaline on the ability of pargyline to alter catecholamine metabolism in rats. Fuller RW, et al. **Biochem Pharmacol** 1981 Jun 1; 30(11):1295-8

Differences in the structure of A and B forms of human monoamine oxidase. Cawthon RM, et al. **J Neurochem** 1981 Aug;37(2):363-72

The acetylenic monoamine oxidase inhibitors clorgyline, deprenyl, pargyline and J-508: their properties and applications. Fowler CJ, et al. **J Pharm Pharmacol** 1981 Jun;33(6):341–7 (83 ref.)

Postmortem changes of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in mouse brain and their prevention by pargyline and microwave irradiation. Van Wijk M, et al. **Neurochem Res** 1981 Apr; 6(4):425–30

PEMOLINE

Effects of Mg-pemoline on the central catecholaminergic system. Molina VA, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):66–79

PENTOBARBITAL

Cimetidine hydrochloride compatibility with preoperative medications. Yuhas EM, et al. **Am J Hosp Pharm** 1981 Aug;38(8):1173–4

Canine cerebral metabolic tolerance during 24 hours deep pentobarbital anesthesia. Gronert GA, et al. **Anesthesiology** 1981 Aug;55(2):110–3

Long-term effect of pentobarbital anesthesia on neophobia in the rat. McGee R, et al. **Behav Neural Biol** 1981 Jul;32(3):376–9

Effects of pentobarbital on delayed alternation performance. Terry WS, et al. **Behav Neural Biol** 1981 Jul;32(3):380–5

Effects of chronic administration of pentobarbital or morphine on the brain microsomal cytochrome P-450 system. Nabeshima T, et al. **Biochem Pharmacol** 1981 May 15;30(10):1142–5

The effects of thyrotropin releasing hormone on pentobarbital tolerance. Bhargava HN. **Eur J Pharmacol** 1981 Jun 10;72(1):63–8

Effect of monoamine oxidase inhibitors on codeine disposition and pentobarbitone sleep-times in the rat. Findlay JW, et al. **J Pharm Pharmacol** 1981 Jan;33(1):45–7

Pentobarbital enhances [3H]diazepam binding to soluble receptors at the benzodiazepine--GABA-receptor-ionophore complex. Davis WC, et al. **Neurosci Lett** 1981 May 6;23(2):209–13

Direct action of pentobarbitone in potentiating the responses to GABA of rat dorsal root ganglion neurones in vitro. Headley PM, et al. **Neurosci Lett** 1981 Jul 17;24(3):273–80

Effect of acute or chronic pentobarbital administration on the steady state levels and the turnover rates of catecholamines in discrete brain areas of mice. Nabeshima T, et al. **Prog Neuropsychopharmacol** 1981; 5(2):121–8

Use of simple tasks to test for impairment of complex skills by a sedative. Ellinwood EH Jr, et al. **Psychopharmacology (Berlin)** 1981; 73(4):350–4

[Age and the effects of barbiturates on rat liver microsome oxidative enzymes] Paramonova GI. **Farmakol Toksikol** 1981 Jan–Feb; 44(1):98–101 (Eng. Abstr.) **(Rus)**

PEPTIDES

beta-Adrenergic stimulation of the release of ACTH- and LPH-related peptides from the pars intermedia of the rat pituitary gland. Tilders FJ, et al. **Acta Endocrinol (Copenh)** 1981;97(3):343–51

Stimulation of gastrin and somatostatin secretion from the isolated rat stomach by bombesin. DuVal JW, et al. **Am J Physiol** 1981 Sep; 241(3):G242–7

Nanosecond fluorometry and the luminescence of biological macromolecules. Brand L, et al. **Ann NY Acad Sci** 1981; 366:197–207

Comparative histochemistry as a springboard for the discovery of biogenic amines and active peptides in molluscan tissues and amphibian skin. Erspamer V. **Basic Appl Histochem** 1981;25(1):3–14

Epidermal growth factor stimulates monovalent cation transport in isolated rat hepatocytes. Fehlmann M, et al. **Biochem Biophys Res Commun** 1981 May 15;100(1):254–60

Laser chemically induced dynamic nuclear polarization study of the reaction between photoexcited flavins and tryptophan derivatives at 360 MHz. McCord EF, et al. **Biochemistry** 1981 May;20(10):2880–8

Systematic variation in bond lengths of peptides. Chakrabarti P, et al. **Biochim Biophys Acta** 1981 Aug 28;670(1):134–7

Excitatory effect of a new polypeptide (anthopleurin-B) from sea anemone on the guinea-pig vas deferens. Norton TR, et al. **Br J Pharmacol** 1981 Sep;74(1):23–8

Thermoregulatory effects of centrally administered bombesin, bradykinin, and methionine-enkephalin. Francesconi R, et al. **Brain Res Bull** 1981 Jul;7(1):63–8

Epidermal growth factor induces rapid tyrosine phosphorylation of proteins in A431 human tumor cells. Hunter T, et al. **Cell** 1981 Jun; 24(3):741–52

Immunohistochemical localization of polypeptide hormones in endocrine cells of the digestive tract of Branchiostoma lanceolatum. Reinecke M. **Cell Tissue Res** 1981;219(3):445–56

Isolation of peptides from uremic plasma that inhibit phenytoin binding to normal plasma proteins. Kinniburgh DW, et al. **Clin Pharmacol Ther** 1981 Aug;30(2):276–80

Inhibition of pituitary-testicular axis response to gonadotropin releasing hormone by pineal treatment. Damian E, et al. **Endocrinologie** 1981 Apr–Jun;19(2):93–6

Hormonal regulation of epidermal growth factor and protease in the submandibular gland of the adult mouse. Gresik EW, et al. **Endocrinology** 1981 Sep;109(3):924–9

Effect of thyroxine, testosterone, and corticosterone on nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations in adult female mouse submaxillary gland: dissociation of NGF and EGF responses. Walker P, et al. **Endocrinology** 1981 Aug;109(2):582–7

The contractile effect of bombesin on the rat isolated urinary bladder. Abdel-Hakim AM, et al. **Eur J Pharmacol** 1981 Mar 12; 70(2):167–73

Bombesin, calcitonin and leu-enkephalin immunoreactivity in endocrine cells of human lung. Cutz E, et al. **Experientia** 1981 Jul 15; 37(7):765–7

Hypothalamic peptides: central nervous system control of visceral functions. Brown M, et al. **Fed Proc** 1981 Sep;40(11):2565–9 (32 ref.)

Systematic separation of medium-sized biologically active peptides by high-performance liquid chromatography. Mabuchi H, et al. **J Chromatogr** 1981 Aug 28;213(2):275–86

The distribution of nine peptides in rat spinal cord with special emphasis on the substantia gelatinosa and on the area around the central canal (lamina X). Gibson SJ, et al. **J Comp Neurol** 1981 Sep 1; 201(1):65–79

Hypothalamic hypophysiotrophic peptides, known and unknown. The Sir Henry Dale lecture for 1980. Guillemin R. **J Endocrinol** 1981 Jul; 90(1):3p–10p (38 ref.)

The expression of anti-poly(LGlu60, LPhe40) idiotypic determinants dictated by the gene products in the major histocompatibility complex. Babu UM, et al. **J Exp Med** 1981 Sep 1;154(3):649–58

Structure of murine Ia antigens. Two dimensional electrophoretic analyses and high pressure liquid chromatography tryptic peptide maps of products of the I-A and I-E subregions and of an associated invariant polypeptide. McMillan M, et al. **J Exp Med** 1981 Apr 1; 153(4):936–50

Synthesis of peptides by the solid-phase method. 6. Neurotensin, fragments, and analogues. St-Pierre S, et al. **J Med Chem** 1981 Apr; 24(4):370–6

Behavioral and neurochemical effects of the new opioid peptide dynorphin--(1–13): comparison with other neuropeptides. Zwiers H, et al. **Life Sci** 1981 Jun 1;28(22):2545–51

Human transforming growth factors induce tyrosine phosphorylation of EGF receptors. Reynolds FH Jr, et al. **Nature** 1981 Jul 16; 292(5820):259–62

Somatostatin-like immunoreactivity in the facial, glossopharyngeal and vagal lobes of the carp. Tohyama M, et al. **Neurosci Lett** 1981 Jul 17; 24(3):233–6

Neurotensin-like and somatostatin-like immunoreactivity within amacrine cells of the retina. Brecha N, et al. **Neuroscience** 1981;6(7):1329–40

Neuropeptides and brain cAMP and phosphoproteins. Wiegant VM, et al. **Pharmacol Ther** 1981;12(3):463–90

Peptides as neurotransmitters: focus on the enkephalins and endorphins. Miller RJ. **Pharmacol Ther [B]** 1981;12(1):73–108 (214 ref.)

The effect of somatostatin and 16,16-dimethyl-prostaglandin E2 on bombesin-stimulated canine gastric acid, plasma gastrin and pancreatic polypeptide secretion. Materia A, et al. **Regul Pept** 1981 Jan; 1(4):297–305

Stimulation of canine pancreatic polypeptide, gastrin, and gastric acid secretion by ranatensin, litorin, bombesin nonapeptide and substance P. Modlin IM, et al. **Regul Pept** 1981 Jan;1(4):279–88

Effect of bombesin upon plasma somatostatin-like immunoreactivity, insulin and glucagon in normal and chemically sympathectomized dogs. Schusdziarra V, et al. **Regul Pept** 1980 Oct;1(2):89–96

[Immunohistochemical localization of neuropeptides in mammalian brain (author's transl)] Zhang ZX, et al. **Sheng Li Ko Hsueh Chin Chan** 1980 Apr;11(4):342–7 **(Chi)**

[The relation between nerves and gastrointestinal peptides] Zhu WY. **Sheng Li Ko Hsueh Chin Chan** 1980 Mar;11(3):259–62 **(Chi)**

[Present status of studies on peptides with biological activity] Suzuki T. **Nippon Rinsho** 1980 Oct;38(10):4230–7 (42 ref.) **(Jpn)**

[Peptides as carriers of information in psychiatric diseases] Reichelt KL. **Nord Med** 1980 Nov;95(11):283–6 **(Nor)**

[Effects of cerebral, hypothalamic and hypophyseal peptides on the central nervous system] Comaru-Schally AM, et al. **Medicina (B Aires)** 1981; 41(2):244–56 (108 ref.) **(Spa)**

PERCEPTUAL DISORDERS

Span of apprehension deficits during the postpsychotic stages of schizophrenia. A replication and extension. Asarnow RF, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1006–11

PERPHENAZINE

[On the question of differences between therapeutic responses after particular neuroleptics in comparison to perphenazine in schizophrenics (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981 Feb; 77(1):25–30 (Eng. Abstr.) **(Cze)**

PERSONALITY INVENTORY

[Effect of phenobarbital on self-ratings of healthy subjects in comparison to the objective impairment of their performance] Walther H, et al. **Acta Biol Med Ger** 1980;39(8-9):949-60 (Eng. Abstr.) **(Ger)**

PHENCYCLIDINE

Color test for detection of 1-piperidinocyclohexanecarbonitrile (PCC) in illicit phencyclidine. Dulik DM, et al. **Clin Toxicol** 1981 Jun; 18(6):737-42

The metabolism of phencyclidine by rabbit liver preparations. Kammerer RC, et al. **Drug Metab Dispos** 1981 May-Jun;9(3):274-8

Stimulation of synaptosomal tyrosine hydroxylation by phencyclidine in vitro. Vickroy TW, et al. **Eur J Pharmacol** 1981 May 22; 71(4):463-73

Simultaneous determination of phencyclidine and monohydroxylated metabolites in urine of man by gas chromatography-mass fragmentography with methane chemical ionization. Cone EJ, et al. **J Chromatogr** 1981 May 8;223(2):331-9

Detection of phencyclidine in hair. Baumgartner AM, et al. **J Forensic Sci** 1981 Jul;26(3):576-81

Mammalian metabolism of phencyclidine. Baker JK, et al. **J Med Chem** 1981 Jun;24(6):666-9

Electrophysiological effects of phencyclidine on rat hippocampal pyramidal neurons. Bickford PC, et al. **Neuropharmacology** 1981 Aug; 20(8):733-42

Behavioral effects of phencyclidine in the developing cat. Levine MS, et al. **Neuropharmacology** 1981 Aug;20(8):743-5

Chronic phencyclidine induced changes in rat central cholinergic receptor regulation. Ward DP, et al. **Proc West Pharmacol Soc** 1981;24:3-4

Doxylamine: a cause for false-positive gas chromatographic assay for phencyclidine. Schaldenbrand JD, et al. **Ther Drug Monit** 1981; 3(2):181-3

PHENELZINE

A comparison of phenelzine and imipramine in an obsessive-compulsive patient. Isberg RS. **Am J Psychiatry** 1981 Sep;138(9):1250-1

PHENETHYLAMINES

Physico-chemical properties of phenethylamines and their uptake into synaptic vesicles of the caudate nucleus. Lentzen H, et al. **Biochem Pharmacol** 1981 Jul 1;30(13):1759-64

The formation of azoxy-2-phenylethane during the biological oxidation of phenylethylamine by rabbit liver microsomes. Fiala ES, et al. **Carcinogenesis** 1981;2(3):165-73

Studies on phenethylamine hallucinogens. 2. Conformations of arylmethoxyl groups using 13C NMR. Knittel JJ, et al. **J Med Chem** 1981 Jul;24(7):906-9

Alteration of dopamine synthesis in rat striatum subsequent to selective type A monoamine oxidase inhibition. Schoepp DD, et al. **J Neurochem** 1981 Aug;37(2):527-30

Substrate- and stereoselective inhibitor of human brain monoamine oxidase by 4-dimethylamino-alpha, 2-dimethylphenethylamine (FLA 336). Fowler CJ, et al. **J Pharm Pharmacol** 1981 Jun;33(6):403-6

The acetylenic monoamine oxidase inhibitors clorgyline, deprenyl, pargyline and J-508: their properties and applications. Fowler CJ, et al. **J Pharm Pharmacol** 1981 Jun;33(6):341-7 (83 ref.)

GLC analysis of phenylalkyl amines using nitrogen detector. Javaid JI, et al. **J Pharm Sci** 1981 Jul;70(7):813-5

Studies on beta-phenylethylamine deamination by human placental monoamine oxidase. Oguchi K, et al. **Jpn J Pharmacol** 1981 Feb; 31(1):7-14

Central action of phenylethylamine in rats. Jagiello-Wójtowicz E. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):59-71

[Hemodynamic effects of Praxinor on the peripheral circulation (author's transl)] Oliva I, et al. **Sem Hop Paris** 1981 May 18-25; 57(19-20):1034-8 (Eng. Abstr.) **(Fre)**

[Effect of pyrazidole and deprenyl on monoamine oxidase in the rat intestine] Mashkovskiĭ MD, et al. **Biull Eksp Biol Med** 1981 Mar; 91(3):309-11 (Eng. Abstr.) **(Rus)**

PHENOBARBITAL

Enzyme inducer effects after liver denervation in the rat. Frenkl R, et al. **Acta Physiol Acad Sci Hung** 1981;57(1):47-50

Adverse effects of phenobarbital on morphological and biochemical development of fetal mouse spinal cord neurons in culture. Bergey GK, et al. **Ann Neurol** 1981 Jun;9(6):584-9

Phenobarbital treatments lower DDT body burden in rhesus monkeys. Ferguson PW, et al. **Arch Environ Contam Toxicol** 1981; 10(3):263-70

Effect of phenobarbital pretreatment on benzene biotransformation in the rat. II. 9,000 g supernatant and isolated perfused liver versus living rat. Gut I, et al. **Arch Toxicol** 1981 Mar;47(1):13-24

Testosterone oxidation by rat liver microsomes: effects of phenobarbital pretreatment and the detection of seven metabolites by HPLC. van der Hoeven T. **Biochem Biophys Res Commun** 1981 Jun 16; 100(3):1285-91

Inhibition of microsomal phenobarbital metabolism by valproic acid. Kapetanović IM, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1361-3

Comparison of gamma-glutamyl transferase induction by phenobarbital in the rat, guinea pig and rabbit. Rooms MW, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1563-71

Effects of phenobarbital, 3-methylcholanthrene and beta-naphthoflavone pretreatment on mouse liver microsomal enzymes and on metabolite patterns of benzo[a]pyrene. Wang IY. **Biochem Pharmacol** 1981 Jun 1; 30(11):1337-43

The effect of phenobarbital and 3'-methyl-N,N-dimethyl-4-aminoazobenzene administration on catalytic, binding and immunological properties of ligandin subunits in rat liver. Ohmi N, et al. **Biochim Biophys Acta** 1981 Jul; 675(2):276-80

In vitro cellular adaptation of serotonergic processes after chronic central phenobarbital administration. Lyness WH, et al. **Brain Res** 1981 Jan 5;204(1):248-52

Calcium uptake mechanisms affected by some convulsant and anticonvulsant drugs. Pincus JH, et al. **Brain Res** 1981 Jul 27; 217(1):119-27

Induction by phenobarbital of ornithine decarboxylase activity in rat liver after initiation with diethylnitrosamine. Yanagi S, et al. **Cancer Lett** 1981 Mar;12(1-2):87-91

Apparent differential response of nuclear envelope cytochrome P-450 following phenobarbital induction arising from a preferential loss during gradient purification. Clawson GA, et al. **Cancer Res** 1981 Aug; 41(8):3122-7

Polyhalogenated biphenyls and phenobarbital: evaluation as inducers of drug metabolizing enzymes in the sheepshead, Archosargus probatocephalus. James MO, et al. **Chem Biol Interact** 1981 Aug; 36(2):229-48

Qualitative and quantitative studies of methylphenobarbital metabolism in man. Hooper WD, et al. **Drug Metab Dispos** 1981 Jul-Aug; 9(4):381-5

The liver-protective enzymes against reduced forms of oxygen in phenobarbital-treated rats. Torres M, et al. **Enzyme** 1981; 26(3):129-35

Effect of diphenylhydantoin and its main hydroxylated metabolite on the pharmacokinetics and the urinary and biliary excretion of phenobarbital and its p-hydroxy metabolite. Sarhan F, et al. **Eur J Drug Metab Pharmacokinet** 1981;6(2):99-108

Neuronal deficits after neonatal exposure to phenobarbital. Yanai J, et al. **Exp Neurol** 1981 Jul;73(1):199-208

Effects of dietary lipid and phenobarbitone on the distribution and concentration of cytochrome P-450 in the liver studied by quantitative cytochemistry. Smith MT, et al. **FEBS Lett** 1981 May 5;127(1):33-6

Determination of partition ratios for allylisopropylacetamide during suicidal processing by a phenobarbital-induced cytochrome P-450 isozyme from rat liver. Loosemore MJ, et al. **J Biol Chem** 1981 Aug 25;256(16):8705-12

Simultaneous assay of methylphenobarbital and phenobarbital in plasma using gas chromatography--mass spectrometry with selected ion monitoring. Hooper WD, et al. **J Chromatogr** 1981 May 8; 223(2):426-31

Detection of phenobarbital in bloodstains, semen, seminal stains, saliva, saliva stains, perspiration stains, and hair. Smith FP, et al. **J Forensic Sci** 1981 Jul;26(3):582-6

Interference of pentobarbitone with the contraction of vascular smooth muscle in goat middle cerebral artery. Marín J, et al. **J Pharm Pharmacol** 1981 Jun;33(6):357-61

Phenobarbitone binding sites in rat brain synaptosomal membranes. Willow M, et al. **Neurosci Lett** 1981 Jul 17;24(3):301-6

Sex-dependent differences in phenobarbitone-induced oestradiol-2-hydroxylase activity in rat liver. Theron CN, et al. **S Afr Med J** 1981 Aug 15;60(7):279-282

A new modified method of measurement of diphenylhydantoin and phenobarbital in serum by high pressure liquid chromatography. Lai ML, et al. **Taiwan I Hsueh Hui Tsa Chih** 1980 Nov;79(11):1002-10

Effects of phenobarbital and beta-naphthoflavone on cerium induced biochemical changes in rat serum. Arvela P, et al. **Toxicol Lett** 1981 Jun-Jul;8(4-5):213-6

Comparative induction of xenobiotic metabolism in rodent kidney, testis and liver by commercial mixtures of polybrominated biphenyls and polychlorinated biphenyls, phenobarbital and 3-methylcholanthrene: absolute and temporal effects. Kluwe WM, et al. **Toxicology** 1981; 20(2-3):259-73

[Lack of effect of phenobarbital on bile flow and Na+,K+-ATPase activity of liver plasma membranes in the hamster (author's transl)] Poupon RE, et al. **Gastroenterol Clin Biol** 1981 Jun-Jul; 5(6-7):604-10 (Eng. Abstr.) **(Fre)**

[Comparative study of the rate of release of phenobarbital from dry galenic forms: the Erweka ZT3 apparatus and the Poole balloon] Duru C, et al. **Pharm Acta Helv** 1981;56(4–5):137–41 (Fre)

[Effect of phenobarbital on self-ratings of healthy subjects in comparison to the objective impairment of their performance] Walther H, et al. **Acta Biol Med Ger** 1980;39(8–9):949–60 (Eng. Abstr.) (Ger)

[Gas chromatographic determination of phenytoin, phenobarbital and primidone: flash-methylation after direct addition of trimethyl-phenyl-ammonium hydroxide to the ethyl acetate extract (author's transl)] Brügmann G. **J Clin Chem Clin Biochem** 1981 May; 19(5):305–6 (Eng. Abstr.) (Ger)

[Effects of phenobarbital on the elimination of valproic acid] Borchert HH, et al. **Pharmazie** 1981 Apr;36(4):298–9 (Ger)

[Interactions between alkaloids of benzyl-isoquinoline structure and barbiturates. Interaction between papaverine hydrochloride an sodium phenobarbitol. I. Study of interactions by physical, chemical and biological methods] Rácz I, et al. **Acta Pharm Hung** 1980 Nov; 50(6):248–56 (Eng. Abstr.) (Hun)

[Interactions between alkaloids of benzyl-isoquinoline structure and barbiturates. Interaction between papaverine hydrochloride and sodium phenobarbitol. II. Pharmacotechnological possibilities of preventing incompatibility] Rácz I, et al. **Acta Pharm Hung** 1980 Nov; 50(6):257–62 (Eng. Abstr.) (Hun)

[Rapid determination, using HPLC, of sodium phenobarbital and its degradation products in syrup] Bennati E, et al. **Boll Chim Farm** 1981 Mar;120(3):172–8 (Eng. Abstr.) (Ita)

[Increase in the number of repeating sequences of DNA in transcriptionally active sites of rat genome induced by cortisol and phenobarbital] Dudareva NA, et al. **Biokhimiia** 1981 Jul; 46(7):1258–66 (Eng. Abstr.) (Rus)

[Possible role of nucleases in the mechanism of the induction effect of phenobarbital] Matiushin AI, et al. **Farmakol Toksikol** 1981 Mar–Apr; 44(2):208–10 (Eng. Abstr.) (Rus)

[Age and the effects of barbiturates on rat liver microsome oxidative enzymes] Paramonova GI. **Farmakol Toksikol** 1981 Jan–Feb; 44(1):98–101 (Eng. Abstr.) (Rus)

[Effect of the long-term administration of testosterone on induction of cytochrome P-450 in female rat live tissue using phenobarbital] Chistiakov VV, et al. **Vopr Med Khim** 1981 May–Jun;27(3):340–2 (Eng. Abstr.) (Rus)

PHENOTHIAZINE TRANQUILIZERS

Gas—liquid chromatographic determination of pipotiazine in plasma of psychiatric patients. Cooper SF, et al. **J Chromatogr** 1981 Feb 13; 222(2):291–6

Clinical blood chemistry values and long acting phenothiazines. Schneider SJ, et al. **Pharmacopsychiatria** 1981 May;14(3):107–14

PHENOTHIAZINES

Determination of promethazine and other phenothiazine compounds by liquid chromatography wih electrochemical detection. Wallace JE, et al. **Anal Chem** 1981 Jun;53(7):960–2

A comparison of the in vivo metabolism of phenothiazine and promazine in the neonatal guinea pig. Mitchell SC, et al. **Biol Neonate** 1981; 39(5–6):285–9

Thionins: plant peptides that modify membrane permeability in cultured mammalian cells. Carrasco L, et al. **Eur J Biochem** 1981 May; 116(1):185–9

Photodecomposition of some substituted phenothiazines. Sharples D. **J Pharm Pharmacol** 1981 Apr;33(4):242–3

The correlation between drug binding to the human erythrocyte and its hemolytic activity. Horie T, et al. **J Pharmacobiodyn** 1981 Feb; 4(2):116–22

Inhibition by phenothiazine antipsychotic drugs of calcium-dependent phosphorylation of cerebral cortex proteins regulated by phospholipid or calmodulin. Wrenn RW, et al. **Life Sci** 1981 Aug 17;29(7):725–33

Influence of UV rays on Feulgen-type staining with azure A-SO2 prepared with normal hydrochloric acid and sodium thiosulphate. Dutt MK. **Microsc Acta** 1981 Jul;84(4):339–44

The influence of psychotropic drugs on the phosphodiesterase activity in the rat brain meninges. Janiec W, et al. **Pol J Pharmacol Pharm** 1980 May–Jun;32(3):297–303

[Electrochemical behavior of phenothiazine in 90% dimethylsulfoxyde–10% water. Analytical application (author's transl)] Livertoux MH, et al. **Ann Pharm Fr** 1980;38(6):513–20 (Eng. Abstr.) (Fre)

[Romanowsky dyes and romanowsky-Giemsa effect. 1. Azure B, purity and content of dye samples, association (author's transl)] Zipfel E, et al. **Histochemistry** 1981;72(2):279–90 (Eng. Abstr.) (Ger)

[Formation of precipitate in an injection solution containing a phenothiazine derivative and novamidazophene] Takács M, et al. **Acta Pharm Hung** 1981 Mar;51(2):55–60 (Eng. Abstr.) (Hun)

[Mutagenicity tests on mequitazine (author's transl)] Sono A, et al. **J Toxicol Sci** 1981 May;6(2):123–8 (Eng. Abstr.) (Jpn)

[Effect of nonachlazine on the calcium mechanism of regulating coronary artery tone] Shishkin SB, et al. **Farmakol Toksikol** 1981 Mar–Apr; 44(2):184–7 (Eng. Abstr.) (Rus)

[Protection of myocardial mitochondria from penetration by calcium ions using isoquinoline and phenothiazine derivatives] Urakov AL, et al. **Farmakol Toksikol** 1981 Jan–Feb;44(1):60–2 (Eng. Abstr.) (Rus)

PHENOXYBENZAMINE

Specific antibodies against the irreversible alpha-adrenergic antagonist, phenoxybenzamine. Goodhardt M, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1685–92

Effects of methysergide or phenoxybenzamine on the renal and cardiovascular responses to endotoxin in rats. Keeler R. **Circ Shock** 1981;8(3):361–8

The effect of phenoxybenzamine on the gastrin response to glycine stimulation. Loh B. **Gastroenterol Jpn** 1981;16(3):205–12

Effects of prazosin and phenoxybenzamine on alpha- and beta-receptor-mediated responses in intestinal resistance and capacitance vessels. Patel P, et al. **J Cardiovasc Pharmacol** 1981 Sep–Oct;3(5):1050–9

Influence of propranolol, phenoxybenzamine of phentolamine in the in vivo nocturnal rise of pineal melatonin levels in the Syrian hamster. Lipton JS, et al. **Life Sci** 1981 May 21;28(21):2377–82

[Phenoxybenzamine in prostatic pathology. 300 cases (author's transl)] Lardennois B, et al. **J Urol (Paris)** 1981;87(4):243–8 (Eng. Abstr.) (Fre)

[Alkylation of ganglionic cholinergic receptors with haloalkyl amines] Blazsó G, et al. **Acta Pharm Hung** 1980 May;50(3):137–44 (Eng. Abstr.) (Hun)

[Effect of phenoxybenzamine on the adrenergic neurone blocking action of guanethidine in isolated guinea pig vas deferens (author's transl)] Kontani H. **Yakugaku Zasshi** 1980 Dec;100(12):1247–51 (Eng. Abstr.) (Jpn)

PHENYLALANINE

Dextro-phenylalanine as inhibitor of the noradrenaline release from the isolated rat hypothalamus. Pardal JF, et al. **Acta Neurol Latinoam** 1979; 25(3–4):235–48

Blood-brain transport of tryptophan and phenylalanine: effect of portacaval shunt in dogs. Huet PM, et al. **Am J Physiol** 1981 Aug; 241(2):G163–9

Dynamics of amino acid side chains in membrane proteins by high field solid state deuterium nuclear magnetic resonance spectroscopy. Phenylalanine, tyrosine, and tryptophan. Kinsey RA, et al. **J Biol Chem** 1981 Sep 10;256(17):9028–36

Analysis of some tryptophan and phenylalanine metabolites in urine by a straight-phase high-performance liquid chromatographic technique. Ghebregzabher M, et al. **J Chromatogr** 1981 Feb 13;222(2):191–201

Potential thyroliberin affinity labels. 1. Chloroacetyl-substituted phenylalanylpyrrolidines. Goebel RJ, et al. **J Med Chem** 1981 Apr; 24(4):366–70

Dietary phenylalanine and tyrosine interrelationships in the Sprague-Dawley rat. Elkin RG, et al. **Proc Soc Exp Biol Med** 1981 Jul;167(3):310–7

[Influence of supplementary tyrosine or phenylalanine on bacterial growth and pigmentation of 'Pseudomonas aeruginosa' (author's transl)] Labeyrie S, et al. **Ann Microbiol (Paris)** 1981 Jan–Feb; 132A(1):31–40 (Eng. Abstr.) (Fre)

PHENYLBUTYRATES

Studies of possible bovine urinary excretion and rumen decomposition of fenvalerate insecticide and metabolite. Wszolek PC, et al. **Bull Environ Contam Toxicol** 1981 Feb;26(2):262–6

Enzymatic synthesis of the coenzyme A ester of o-succinylbenzoic acid, an intermediate in menaquinone (vitamin K2) biosynthesis. Heide L, et al. **FEBS Lett** 1981 Jun 15;128(2):201–4

Preliminary human pharmacology studies on the inhibition of platelet aggregation by indobufen (K 3920). Pogliani E, et al. **Haematologica (Pavia)** 1981 Apr;66(2):160–70

Determination of fenvalerate, a synthetic pyrethroid, in grapes, peppers, apples, and cottonseeds by gas-liquid chromatography. Greenberg RS. **J Agric Food Chem** 1981 Jul–Aug;29(4):856–60

Face fly and horn fly reduction on cattle with fenvalerate ear tags. Knapp FW, et al. **J Econ Entomol** 1981 Jun;74(3):295–6

PHENYLPROPANOLAMINE

Sensitive assay for pseudoephedrine and its metabolite, norpseudoephedrine in plasma and urine using gas—liquid chromatography with electron-capture detection. Lo LY, et al. **J Chromatogr** 1981 Feb 13;222(2):297–302

High-pressure liquid chromatographic determination of methscopolamine nitrate, phenylpropanolamine hydrochloride, pyrilamine maleate, and pheniramine maleate in tablets. Heidemann DR. **J Pharm Sci** 1981 Jul; 70(7):820–2

High-pressure liquid chromatographic analysis of phenylpropanolamine in human plasma following derivatization with O-phthalaldehyde.

Mason WD, et al. **J Pharm Sci** 1981 Jun;70(6):707-9

Are your patients speeding? Mack RB. **NC Med J** 1981 Jul;42(7):489

PHENYTOIN

Opposite effects of 5,5-diphenylhydantoin and picrotoxin on GABAergic inhibition in crayfish stretch receptor. Aickin CC, et al. **Adv Biochem Psychopharmacol** 1981;29:301-7

Studies with excitatory amino acid antagonists in rat CNS: 2-amino-5-phosphonovaleric acid, phenytoin, and benzodiazepines. Stone TW. **Adv Biochem Psychopharmacol** 1981;29:223-30

Audit of phenytoin prescribing for outpatients. Curry CE Jr, et al. **Am J Hosp Pharm** 1981 Aug;38(8):1158-60

Phenytoin by volume-control set [letter] Graves DA. **Am J Hosp Pharm** 1981 Aug;38(8):1119, 1121

Generic phenytoin versus dilantin for once-a-day dosing [letter] Tindula RJ. **Am J Hosp Pharm** 1981 Aug;38(8):1114, 1116

Decreased clearance of phenytoin with cimetidine [letter] Algozzine GJ, et al. **Ann Intern Med** 1981 Aug;95(2):244-5

Saliva carbamazepine and phenytoin level monitoring. Rylance GW, et al. **Arch Dis Child** 1981 Aug;56(8):637-40

The effects of phenytoin on in vitro protein synthesis in oral and non-oral tissues of the rat. Kusek JC. **Arch Oral Biol** 1980;25(11-12):745-7

Acetanilide and paracetamol pharmacokinetics before and during phenytoin administration: genetic control of induction? Cunningham JL, et al. **Br J Clin Pharmacol** 1981 Jan;11(6):591-5

Distinction between the effects of barbiturates, benzodiazepines and phenytoin on responses to gamma-aminobutyric acid receptor activation and antagonism by bicuculline and picrotoxin. Simmonds MA. **Br J Pharmacol** 1981 Jul;73(3):739-47

Cimetidine interaction with phenytoin [letter] Neuvonen PJ, et al. **Br Med J [Clin Res]** 1981 Aug 15;283(6289):501

Effects of phenytoin on [3H]diazepam binding in dissociated primary cortical cell culture. Gallager DW, et al. **Brain Res** 1981 Aug 10; 218(1-2):319-30

Calcium uptake mechanisms affected by some convulsant and anticonvulsant drugs. Pincus JH, et al. **Brain Res** 1981 Jul 27; 217(1):119-27

Phenytoin in the treatment of IgA mesengial glomerulonephritis (Berger's disease) [letter] Egido J, et al. **Clin Nephrol** 1981 Mar;15(3):164-5

Isolation of peptides from uremic plasma that inhibit phenytoin binding to normal plasma proteins. Kinniburgh DW, et al. **Clin Pharmacol Ther** 1981 Aug;30(2):276-80

Comment on phenytoin dosage [letter] Knouse BF. **Drug Intell Clin Pharm** 1981 Mar;15(3):215

Elevated serum phenytoin concentrations in a uremic patient when measured by enzyme-multiplied immunoassay. Matzke GR, et al. **Drug Intell Clin Pharm** 1981 May;15(5):386-8

Effect of diphenylhydantoin and its main hydroxylated metabolite on the pharmacokinetics and the urinary and biliary excretion of phenobarbital and its p-hydroxy metabolite. Sarhan F, et al. **Eur J Drug Metab Pharmacokinet** 1981;6(2):99-108

Chronic treatment with phenytoin in rats: effects of peripheral nervous system. Moglia A, et al. **Farmaco [Sci]** 1981 Jun;36(6):419-24

Inhibition of in vitro diphenylhydantoin hydroxylation by different anticonvulsant drug combinations: a kinetic analysis. Patsalos PN, et al. **Gen Pharmacol** 1981;12(1):51-5

A nonmetabolized analogue of phenytoin. Henderson JD, et al. **J Med Chem** 1981 Jul;24(7):843-7

Estimating dosage of phenytoin [letter] Dodson WE, et al. **J Pediatr** 1981 Jul;99(1):169-70

Comparison of anticonvulsant potencies of cyheptamide, carbamazepine, and phenytoin. Jones GL, et al. **J Pharm Sci** 1981 Jun;70(6):618-20

Predicting individual phenytoin dosage. Vozeh S, et al. **J Pharmacokinet Biopharm** 1981 Apr;9(2):131-46

Altered drug binding to serum proteins in pregnant women: therapeutic relevance. Perucca E, et al. **J R Soc Med** 1981 Jun;74(6):422-6

Drug alert: two forms of dilantin. Gever LN. **Nursing (Horsham)** 1981 Sep;11(9):78

Diphenylhydantoin-induced pseudolymphoma syndrome. With severe thrombocytopenia. Cacatian AA, et al. **NY State J Med** 1981 Jun; 81(7):1085-7

Single point estimation of phenytoin dosing requirement. Koup JR, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jan;31(1):3-12

Phenytoin-induced interstitial nephritis. Hoffman EW. **South Med J** 1981 Sep;74(9):1160-1

Phenytoin-dexamethasone interaction: a previously unreported observation. Lawson LA, et al. **Surg Neurol** 1981 Jul;16(1):23-4

A new modified method of measurement of diphenylhydantoin and phenobarbital in serum by high pressure liquid chromatography. Lai ML, et al. **Taiwan I Hsueh Hui Tsa Chih** 1980 Nov;79(11):1002-10

[Gas chromatographic determination of phenytoin, phenobarbital and primidone: flash-methylation after direct addition of trimethyl-phenyl-ammonium hydroxide to the ethyl acetate extract (author's transl)] Brügmann G. **J Clin Chem Clin Biochem** 1981 May; 19(5):305-6 (Eng. Abstr.) (Ger)

[Pharmacological influences on the brain level and transport of GABA. I) Effect of various antipileptic drugs on brain levels of GABA] Varotto M, et al. **Boll Soc Ital Biol Sper** 1981 Apr 30;57(8):904-8 (Eng. Abstr.) (Ita)

[Five autopsied cases of chronic diphenylhydantoin intoxication — with special reference to the distribution of cerebellar degeneration and marked degeneration of nucleus fasciculi dorsalis (author's transl)] Ando S, et al. **Seishin Shinkeigaku Zasshi** 1980;82(7):423-43 (Eng. Abstr.) (Jpn)

[Quantitative measurement of phenytoin and hydroxyphenytoin in human serum by column extraction-high-performance liquid chromatography (author's transl)] Sato A, et al. **Yakugaku Zasshi** 1980 Dec; 100(12):1215-9 (Eng. Abstr.) (Jpn)

PHOBIC DISORDERS

Treatment of spontaneous panic attacks with chlomipramine. Gloger S, et al. **Am J Psychiatry** 1981 Sep;138(9):1215-7

School phobia: a therapeutic trial with clomipramine and short-term outcome. Berney T, et al. **Br J Psychiatry** 1981 Feb;138:110-8

A multicenter controlled trial in phobic-obsessive psychoneurosis. The effect of chlorimipramine and of its combinations with haloperidol and diazepam. Cassano GB, et al. **Prog Neuropsychopharmacol** 1981; 5(2):129-38

Is the isolated animal a possible model for phobia and anxiety? Garattini S, et al. **Prog Neuropsychopharmacol** 1981;5(2):159-65 (56 ref.)

PHYSOSTIGMINE

Physostigmine in amoxapine overdose [letter] Ross SR, et al. **Am J Hosp Pharm** 1981 Aug;38(8):1121-2

Physostigmine and lithium response in the schizophrenias. Edelstein P, et al. **Am J Psychiatry** 1981 Aug;138(8):1078-81

An analysis of the respiratory stimulant effect of physostigmine and neostigmine in the conscious rabbit. Weinstock M, et al. **Clin Exp Pharmacol Physiol** 1981 Mar-Apr;8(2):151-8

[2 patients poisoned with a centrally acting anticholinergic agent] Ruprecht J, et al. **Ned Tijdschr Geneeskd** 1981 Jun 27;125(26):1041-2 (Eng. Abstr.) (Dut)

PILOCARPINE

Regular fetal breathing induced by pilocarpine infusion in the near-term fetal lamb. Brown ER, et al. **J Appl Physiol** 1981 Jun;50(6):1348-52

High-performance liquid chromatographic analysis of pilocarpine hydrochloride, isopilocarpine, pilocarpic acid and isopilocarpic acid in eye-drop preparations. Kennedy JM, et al. **J Chromatogr** 1981 Aug 7;212(3):331-8

[Comparison of bioavailability of pilocarpine] Eyal E, et al. **Harefuah** 1980 Dec 15;99(12):445-7 (Eng. Abstr.) (Heb)

PIPRADROL

The acquisition of responding with conditioned reinforcement: effects of cocaine, (+)-amphetamine and pipradrol. Beninger RJ, et al. **Br J Pharmacol** 1981 Sep;74(1):149-54

PITUITARY HORMONE RELEASING HORMONES

Gonadotrophin release by gonadotrophs incubated with gonadotrophin-releasing hormone is independent of intracellular cAMP accumulation. Benoist L, et al. **Acta Endocrinol (Copenh)** 1981; 97(3):329-37

Immunohistochemical localization of gonadotropin releasing hormone (GnRH) in the bovine hypothalamus and infundibulum. Dees WL, et al. **Anat Rec** 1981 Jul;200(3):281-5

GnRH-receptor interaction. V. Down-regulation of pituitary receptors for GnRH in ovariectomized ewes by infusion of homologous hormone. Nett TM, et al. **Biol Reprod** 1981 Jun;24(5):1145-55

Evolutionary significance of the phylogenetic distribution of the mammalian hypothalamic releasing hormones. Jackson IM. **Fed Proc** 1981 Sep;40(11):2545-52

The metabolic serum clearance of GnRH. Relationship to age, sex and male puberty. Tharandt L, et al. **Horm Metab Res** 1981 May; 13(5):277-82

Hypophysiotropic hormones of the hypothalamus. Negro-Vilar A, et al. **Int Rev Physiol** 1981;24:97-156 (378 ref.)

Repetitive treatment with gonadotrophin releasing factor or a long-acting analogue upon gonadotrophin secretion in the ferret. Gledhill B, et al. **J Endocrinol** 1981 Aug;90(2):275-83

Reversible inhibition of testicular steroidogenesis and spermatogenesis by a potent gonadotropin-releasing hormone agonist in normal men: an approach toward the development of a male contraceptive. Linde R, et al. **N Engl J Med** 1981 Sep 17;305(12):663-7

Estimation of GnRH pulse amplitude during pubertal development. Corley KP, et al. **Pediatr Res** 1981 Feb;15(2):157-62

Characterization of a 41-residue ovine hypothalamic peptide that stimulates secretion of corticotropin and beta-endorphin. Vale W, et al. **Science** 1981 Sep 18;213(4514):1394–7

[Effect of gonadotropin releasing hormone, clomide and L-dopa on the secretion of chorionic gonadotropins, follicle-stimulating hormone and prolactin in the first trimester of uncomplicated pregnancy] Rzempołuch J. **Ginekol Pol** 1981 Jan;52(2):211–4 **(Pol)**

PITUITARY HORMONES

[Clinical implications of present knowledge respecting neuropharmacologic control of antipituitary hormones] Martin-Du Pan R, et al. **Schweiz Med Wochenschr** 1980 Nov 29;110(48):1784–1814 (346 ref.) (Eng. Abstr.) **(Fre)**

[Hypophyseal hormones--neurotransmitters? (editorial)] Korczyn A. **Harefuah** 1980 Dec 15;99(12):441–2 **(Heb)**

[Effects of cerebral, hypothalamic and hypophyseal peptides on the central nervous system] Comaru-Schally AM, et al. **Medicina (B Aires)** 1981; 41(2):244–56 (108 ref.) **(Spa)**

PITUITARY HORMONES, ANTERIOR

Processing, turnover and release of corticotropins, endorphins and melanotropin in the toad pituitary intermediate lobe. Loh YP. **Ciba Found Symp** 1981;(81):55–78

Functions of alpha-melanotropin and other opiomelanocortin peptides in labour, intrauterine growth and brain development. Swaab DF, et al. **Ciba Found Symp** 1981;(81):196–217

Hypophysiotropic hormones of the hypothalamus. Negro-Vilar A, et al. **Int Rev Physiol** 1981;24:97–156 (378 ref.)

[Effects of intrathecal injection of beta-endorphin on endocrine function in man (author's transl)] Yamaya R. **Masui** 1981 May;30(5):445–52 (Eng. Abstr.) **(Jpn)**

PRAZEPAM

[Pharmacokinetics of oral prazepam] Kölle EU. **Fortschr Med** 1981 Jun 11;99(22):874–9 (Eng. Abstr.) **(Ger)**

PROBLEM SOLVING

Brief fasting, stress, and cognition in children. Pollitt E, et al. **Am J Clin Nutr** 1981 Aug;34(8):1526–33

A new approach to the role of noradrenaline in learning: problem-solving in the marmoset after alpha-noradrenergic receptor blockade. Ridley RM, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):849–55

PROGESTERONE

Effect of 20 alpha-dihydroprogesterone, progesterone, and their 5 alpha-reduced metabolites on serum gonadotropin levels and hypothalamic LHRH content. Gilles PA, et al. **Biol Reprod** 1981 Jun; 24(5):1088–97

Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Rivier C, et al. **Biol Reprod** 1981 Jun;24(5):1061–7

Effects of estradiol and progesterone on plasma gonadotropins, prolactin, and LHRH in specific brain areas of ovariectomized rats. Wise PM, et al. **Biol Reprod** 1981 May;24(4):820–30

The effects of stimulation and lesion of raphe nuclei on luteinizing hormone release in estrogen-progesterone-treated ovariectomized rats. Waloch M, et al. **Brain Res** 1981 Aug 3;217(2):305–13

Electrical stimulation of mesencephalic noradrenergic pathway: effects on luteinizing hormone levels in blood of ovariectomized and ovariectomized, steroid-primed rats. Leung PC, et al. **Endocrinology** 1981 Sep;109(3):720–8

Role of ovarian hormones in the long-term control of glucose homeostasis. Interaction with insulin, glucagon and epinephrine. Ahmed-Sorour H, et al. **Horm Res** 1980;13(6):396–403

Binding of steroids by proteins in follicular fluid of the human ovary. Martin B, et al. **J Clin Endocrinol Metab** 1981 Aug;53(2):443–7

Effect of progesterone on lipid metabolism in the intact rat. Shirling D, et al. **J Endocrinol** 1981 Aug;90(2):285–94

Increase in catecholamine-stimulated cyclic AMP and progesterone synthesis in rat granulosa cells during culture. Kliachko S, et al. **Mol Cell Endocrinol** 1981 Jul;23(1):23–32

[Contraceptive activity and mechanism of action of combinations of 6-methyl-substituted D'6-pentaranes and mestranol] Korkhov VV, et al. **Farmakol Toksikol** 1981 Jan–Feb;44(1):95–8 (Eng. Abstr.) **(Rus)**

PROLACTIN

Effect of short-term bromocriptine treatment on amniotic fluid prolactin concentration in the first half of pregnancy. Lehtovirta P, et al. **Acta Endocrinol (Copenh)** 1981 Aug;97(4):559–61

Effect of electroconvulsive treatment on brain monoamine content, pituitary-adrenal function and plasma prolactin. Arató M, et al. **Acta Physiol Acad Sci Hung** 1980;56(2):163–71

Prolactin secretion in anorexia nervosa. Caufriez A, et al. **Acta Psychiatr Belg** 1980 Jul–Aug;80(4):546–50

TSH, HGH, HPr, and cortisol response to TRH in depressed patients. Ramseier F, et al. **Acta Psychiatr Belg** 1980 Jul–Aug;80(4):399–409

Prolactin and psychiatry. Meltzer HY. **Am J Psychiatry** 1981 Sep; 138(9):1203–6

Daytime variation in serum prolactin level in patients receiving oral and depot antipsychotic medication. Goode DJ, et al. **Biol Psychiatry** 1981 Jul;16(7):653–62

Direct effects of gonadotropin releasing hormone and its antagonist upon ovarian functions stimulated by FSH, prolactin, ans LH. Jones PB, et al. **Biol Reprod** 1981 May;24(4):747–59

Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Rivier C, et al. **Biol Reprod** 1981 Jun;24(5):1061–7

Site of action of prolactin in the suppression of gonadotropin secretion during lactation in the rat: effect on pituitary responsiveness to LHRH. Smith MS. **Biol Reprod** 1981 Jun;24(5):967–76

Effects of ageing and gonadal steroid hormones on prolactin concentrations in the anterior pituitary of the chicken. Kono T, et al. **Br Poult Sci** 1980 Nov;21(6):431–6

Lack of a relationship between concentrations of plasma luteinising hormone, thyroxine and prolactin at nine week's of age and subsequent egg production in the domestic hen. Sharp PJ, et al. **Br Poult Sci** 1981 Jan;22(1):53–8

The direct effect of reserpine in vitro on prolactin release from rat anterior pituitary glands. Login IS, et al. **Brain Res** 1981 Jan 5;204(1):79–85

Marked and selective suppression of prolactin secretion after interruption of neural connections of the medial basal hypothalamus of the rat. Mioduszewski R, et al. **Brain Res** 1981 Jul 6;216(1):35–44

Monosodium glutamate: acute and chronic effects on rhythmic growth hormone and prolactin secretion, and somatostatin in the undisturbed male rat. Terry LC, et al. **Brain Res** 1981 Jul 27;217(1):129–42

Prolactin pulsatility in patients with gonadal dysfunction. Moult PJ, et al. **Clin Endocrinol (Oxf)** 1981 Apr;14(4):387–94

Inhibiting effect of atropine on prolactin blood levels after stimulation with TRH. Bizzarro A, et al. **Clin Exp Obstet Gynecol** 1980; 7(2):108–11

Promethazine and diazepam potantiate the haloperidol induced prolactin responses. Arató M. **Commun Psychopharmacol** 1980;4(4):317–22

Delta 9-tetrahydrocannabinol suppression of prolactin secretion in the rat: lack of direct pituitary effect. Hughes CL Jr, et al. **Endocrinology** 1981 Sep;109(3):876–80

Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Huhtaniemi IT, et al. **Endocrinology** 1981 Aug; 109(2):483–90

Dopaminergic and serotonergic involvement in opiate-induced prolactin release in monkeys. Wehrenberg WB, et al. **Endocrinology** 1981 Aug; 109(2):544–7

Effects of lisuride and bromocriptine on inhibition of lactation and on serum prolactin levels: comparative double-blind study. Venturini PL, et al. **Eur J Obstet Gynaecol Reprod Biol** 1981 May;11(6):395–400

Endogenous hyperprolactinaemia enhances amphetamine- and apomorphine-induced stereotypy. Drago F, et al. **Eur J Pharmacol** 1981 Jun 19;72(2–3):249–53

Pharmacological studies with several analogs of mazindol: correlation between effects on dopamine uptake and various in vivo responses. Heikkila RE, et al. **Eur J Pharmacol** 1981 May 8;71(2–3):277–86

The effects of histidyl-proline-diketopiperazine, a metabolite of TRH, on prolactin release by the rat pituitary gland in vitro. Lamberts SW, et al. **Eur J Pharmacol** 1981 May 8;71(2–3):337–41

Contractile effect of prolactin on guinea pig isolated ileum. Pillai NP, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):11–6

Differences in negative and positive feedback of gonadal steroids on release of gonadotropins and prolactin in young and old rats. Meites J, et al. **Exp Brain Res** 1981;Suppl 3:151–7

Regulation of prolactin secretion at the pituitary level. Ruberg M, et al. **Exp Brain Res** 1981;Suppl 3:182–99 (62 ref.)

Pituitary response to luteinizing hormone-releasing hormone during haloperidol-induced hyperprolactinemia. Del Carmen Díaz M, et al. **Fertil Steril** 1981 Jun;35(6):626–8

Prolactin and the small intestine. Effect of hyperprolactinaemia on mucosal structure in the rat. Muller E, et al. **Gut** 1981 Jul; 22(7):558–65

Novel multialveolar epithelial structures from rabbit mammary gland that synthesize milk specific fatty acids in response to prolactin. Carrington CA, et al. **In Vitro** 1981 May;17(5):363–8

Prolactin in maintenance of the corpus luteum of early pseudopregnancy in the golden hamster. Harris KH, et al. **J Endocrinol** 1981 Aug; 90(2):145–50

2-hydroxyoestradiol inhibits prolactin release from the superfused rat pituitary gland. Linton EA, et al. **J Endocrinol** 1981 Sep; 90(3):315–22

Role of serotonin in the regulation of growth hormone and prolactin secretion in the domestic fowl. Rabii J, et al. **J Endocrinol** 1981 Sep; 90(3):355–8

Dissociation in the regulation of luteinizing hormone and follicle-stimulating hormone in a hyperprolactinaemic rat model: interrelationships between gonadotrophin and prolactin control. Tresguerres JA, et al. **J Endocrinol** 1981 Jul;90(1):41-51

The failure of prolactin to enhance the inhibitory effect of oestradiol-17 beta on LH synthesis and release in ewes. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):537-42

Prolactin and LH release in response to LH-RH and TRH in ewes during dioestrus, pregnancy and post partum. Wright PJ, et al. **J Reprod Fertil** 1981 Jul;62(2):447-53

In vivo studies on prolactin function in the female rat: divergent effects of treatment with bromergocryptine and antisera to rat prolactin. Kofler R, et al. **J Reprod Immunol** 1981 Sep;3(4):219-25

Treatment of hyperprolactinaemia with pergolide mesylate: acute effects and preliminary evaluation of long-term treatment. Franks S, et al. **Lancet** 1981 Sep 26;2(8248):659-61

Neuroendocrine effects of D,L-propranolol [letter] Malas KL, et al. **Lancet** 1981 Aug 22;2(8243):424

Functional and anatomical segregation of hypothalamic opiate receptors involved in prolactin and growth hormone secretion in cynomolgus monkeys. Belchetz PE. **Life Sci** 1981 Jun 29;28(26):2961-71

During one year's neuroleptic treatment in rats striatal dopamine receptor blockade decreases but serum prolactin levels remain elevated. Dyer RG, et al. **Life Sci** 1981 Jan 12;28(2):167-74

Pharmacological difference of L-dopa, apomorphine, and bromocriptine against metoclopramide. Fang VS. **Life Sci** 1981 May 11; 28(19):2143-9

Effect of 3-PPP, a putative dopamine autoreceptor agonist, on rat serum prolactin levels. Meltzer HY, et al. **Life Sci** 1981 Jul 6;29(1):99-105

Effect of estradiol benzoate and clomiphene on tyrosine hydroxylase activity and on luteinizing hormone and prolactin levels in ovariectomized rats. Tobias H, et al. **Life Sci** 1981 Aug 17; 29(7):711-6

Hyperprolactinemia in chronic renal failure: impaired responsiveness to stimulation and suppression. Normalization after transplantation. Peces R, et al. **Nephron** 1981;28(1):11-6

Stimulation of prolactin secretion in rhesus monkeys by vasoactive intestinal polypeptide. Frawley LS, et al. **Neuroendocrinology** 1981 Aug; 33(2):79-83

Modulation by dopamine antagonists of DNA synthesis in the pituitary gland of the male rat. Jacobi JM, et al. **Neuroendocrinology** 1981 Aug; 33(2):97-100

Hyperprolactinemia counteracts the testosterone-induced inhibition of the preoptic area dopamine turnover. Kalra PS, et al. **Neuroendocrinology** 1981 Aug;33(2):118-22

Effect of lergotrile mesylate and methysergide on morphine induced increase in prolactin release. Ratner A, et al. **Proc West Pharmacol Soc** 1981;24:335-9

The prolactin response in patients receiving neuroleptic therapy. The effect of fluphenazine decanoate. Dotti A, et al. **Prog Neuropsychopharmacol** 1981;5(1):69-77

The prolactin-stimulating potency of reserpine in man. Asnis GM, et al. **Psychiatry Res** 1981 Aug;5(1):39-45

Effect of intramuscular chlorpromazine on serum prolactin levels in schizophrenic patients and normal controls. Meltzer HY, et al. **Psychiatry Res** 1981 Aug;5(1):95-105

The posterior pituitary: regulation of anterior pituitary prolactin secretion. Peters LL, et al. **Science** 1981 Aug 7;213(4508):659-61

[Hyperprolactinemia and primary amenorrhea] Christensen JB. **Ugeskr Laeger** 1981 Apr 6;143(15):933-4 (Eng. Abstr.) **(Dan)**

[Charges in the gonadotrophins, in the prolactin and in the sexual steroid levels throughout the normal menstrual cycle (author's transl)] Buvat J, et al. **J Gynecol Obstet Biol Reprod (Paris)** 1981;10(2):99-108 (Eng. Abstr.) **(Fre)**

[Bromocriptine in the treatment of normal prolactinemic anovulation] Messalli E, et al. **Riv Ital Ginecol** 1980;59(2-3):111-8 **(Ita)**

[Our experience in the inhibition of lactation (Controlled clinical study with bromocriptine, methergoline and pyridoxine)] Vecchione A, et al. **Riv Ital Ginecol** 1980;59(2-3):311-9 (Eng. Abstr.) **(Ita)**

[Effect of gonadotropin releasing hormone, clomide and L-dopa on the secretion of chorionic gonadotropins, follicle-stimulating hormone and prolactin in the first trimester of uncomplicated pregnancy] Rzempołuch J. **Ginekol Pol** 1981 Jan;52(2):211-4 **(Pol)**

PROMAZINE

A comparison of the in vivo metabolism of phenothiazine and promazine in the neonatal guinea pig. Mitchell SC, et al. **Biol Neonate** 1981; 39(5-6):285-9

PROMETHAZINE

Determination of promethazine and other phenothiazine compounds by liquid chromatography wih electrochemical detection. Wallace JE, et al. **Anal Chem** 1981 Jun;53(7):960-2

Interactions of carbon tetrachloride and promethazine in the rat—II. Elimination of carbon tetrachloride and chloroform in expired air as indications of their metabolism in the intact animal. Reddrop CJ, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1449-55

Interactions of carbon tetrachloride and promethazine in the rat—I. Effects of promethazine on the concentrations of carbon tetrachloride in blood and liver, and on the production of chloroform. Reddrop CJ, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1443-7

Promethazine and diazepam potantiate the haloperidol induced prolactin responses. Arató M. **Commun Psychopharmacol** 1980;4(4):317-22

[Protection of myocardial mitochondria from penetration by calcium ions using isoquinoline and phenothiazine derivatives] Urakov AL, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):60-2 (Eng. Abstr.) **(Rus)**

PROPANEDIOLS

Acute and chronic propylene glycol dinitrate exposure in the monkey. Mattsson JL, et al. **Aviat Space Environ Med** 1981 Jun;52(6):340-5

Hemoperfusion for detoxification of mercury. A model:treatment of severe mercury poisoning by encapsulated chelating spheres, Part I. Margel S, et al. **Biomater Med Devices Artif Organs** 1981;9(2):107-25

Intramuscular injections of 1,2-propanediol can stimulate rumen papillar development of milk-fed kids. Hamada T, et al. **Experientia** 1981 Jun; 37(6):579-80

PROPRANOLOL

Effect of inotropic interventions on rate of change of ventricular diastolic dimensions. Sabbah HN, et al. **Am J Physiol** 1981 Sep; 241(3):H376-80

Questioning a contraindication of propranolol [letter] Gitlin M. **Am J Psychiatry** 1981 Sep;138(9):1261-2

Effect of propranolol on circulatory responses to induction of diazepam-nitrous oxide anesthesia and to endotracheal intubation. McCammon RL, et al. **Anesth Analg (Cleve)** 1981 Aug;60(8):579-83

Propranolol and retroperitoneal fibrosis [letter] Pierce JR Jr, et al. **Ann Intern Med** 1981 Aug;95(2):244

Effect of isoproterenol and propranolol on the mast cell degranulation and on the passive cutaneous anaphylaxis in mice. Małolepszy J, et al. **Arch Immunol Ther Exp (Warsz)** 1980;28(6):873-8

Influence of propranolol and acebutolol on isoprenaline-induced changes in heart rate and peripheral blood flow in man. Mougeot G, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):116-25

Interesting uses of beta blockers (2): propranolol in schizophrenia. Chiu E. **Aust Fam Physician** 1981 May;10(5):376-9, 381-2

Effects of d- and l-propranolol on the responsiveness of human fibroblasts to choleragen and prostaglandin E1. Moss J, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1263-9

Propranolol, alprenolol and oxprenolol metabolism in the dog. Identification of N-methylated metabolites. Walle UK, et al. **Biomed Mass Spectrom** 1981 Feb;8(2):78-84

Bioavailability of propranolol and bendrofluazide formulations. McAinsh J, et al. **Biopharm Drug Dispos** 1981 Apr-Jun;2(2):167-75

Effect of metoclopramide on the bioavailability of long-acting propranolol. Charles BG, et al. **Br J Clin Pharmacol** 1981 May; 11(5):517-8

A comparison of the effects of propranolol and oxprenolol on forearm blood flow and skin temperature. Vandenburg MJ, et al. **Br J Clin Pharmacol** 1981 May;11(5):485-90

Influence of cimetidine on pharmacokinetics of propranolol [letter] Bauman JH. **Br Med J [Clin Res]** 1981 Jul 18;283(6285):232

Influence of cimetidine on pharmacokinetics of propranolol [letter] Kitis G. **Br Med J [Clin Res]** 1981 Jul 25;283(6286):309

Effects of indomethacin, renal denervation, and propranolol on plasma renin activity in conscious dogs with chronic thoracic caval constriction. Echtenkamp SF, et al. **Circ Res** 1981 Aug;49(2):492-500

Beneficial effects of adding propranolol to multidose potassium cardioplegia. Kanter KR, et al. **Circulation** 1981 Aug; 64(2 Pt 2):84-90

No stereoselective first-pass hepatic extraction of propranolol. Jackman GP, et al. **Clin Pharmacol Ther** 1981 Sep;30(3):291-6

Systemic and forearm haemodynamic and metabolic effects of racemic propranolol or D-propranolol in healthy subjects. Hartling OJ, et al. **Clin Sci** 1981 Jun;60(6):675-9

Effect of beta-adrenoceptor blockade on exercise performance and metabolism. Lundborg P, et al. **Clin Sci** 1981 Sep;61(3):299-305

Possible toxic interaction of propranolol and narcotic analgesics [letter] Davis WM, et al. **Drug Intell Clin Pharm** 1981 Apr;15(4):290-300

Retroperitoneal fibrosis after treatment with propranolol [letter] Henri L, et al. **Drug Intell Clin Pharm** 1981 Sep;15(9):696

Propranolol and thyroxine metabolism [letter] Nester TJ. **Drug Intell Clin Pharm** 1981 Feb;15(2):131-2

A comparison of circulatory responsiveness following the sudden withdrawal from atenolol and propranolol. Schwartz J, et al. **Eur Heart J** 1981 Feb;2(1):31-9

Physiological evidence (hypothermia) for central effects of beta-blocker agents. Ben-Uriah Y, et al. **Int J Neurosci** 1981;14(1-2):41-6

Effects of concentration and steric configuration of propranolol on AV conduction and ventricular repolarization in the dog. Brorson L, et al. **J Cardiovasc Pharmacol** 1981 Jul-Aug;3(4):692-703

Interaction in healthy volunteers between prenalterol, a selective beta 1-adrenoceptor agonist, and metoprolol or propranolol. Rönn O, et al. **J Cardiovasc Pharmacol** 1981 May-Jun;3(3):477-84

Myocardial sensitivity to isoproterenol following abrupt propranolol withdrawal in conscious dogs. Webb JG, et al. **J Cardiovasc Pharmacol** 1981 May-Jun;3(3):622-35

Comparison of the inotropic and chronotropic effects of metoprolol and propranolol. Conrad KA. **J Clin Pharmacol** 1981 May-Jun; 21(5-6):213-8

Interaction between aminophylline and beta adrenergic blockers 'propranolol' & 'practolol' on the myocardium and tracheal spirals in experimental animals. el-Gawhary NE, et al. **J Egypt Med Assoc** 1979; 62(1-2):171-83

Avoidance of first pass elimination of propranolol after rectal administration to rats. de Boer AG, et al. **J Pharm Pharmacol** 1981 Jan;33(1):50-1

Interaction of propranolol hydrochloride with montmorillonite. Sánchez Martin MJ, et al. **J Pharm Pharmacol** 1981 Jun;33(6):408-10

High-performance liquid chromatographic determination of propranolol and 4-hydroxypropranolol in plasma. Rosseel MT, et al. **J Pharm Sci** 1981 Jun;70(6):688-9

Nonlinear first-pass metabolism of propranolol in the rat. Suzuki T, et al. **J Pharmacobiodyn** 1981 Feb;4(2):131-41

The inhibitory effect of propranolol pretreatment on its own metabolism in the rat. Schneck DW, et al. **J Pharmacol Exp Ther** 1981 Sep; 218(3):575-81

Propranolol and epinephrine [letter] Stotter ML. **JAMA** 1981 Oct 16; 246(16):1772

Interaction of cimetidine with metoprolol, propranolol, or atenolol [letter] Kirch W, et al. **Lancet** 1981 Sep 5;2(8245):531-2

Propranolol, exercise, and arterial plasma potassium [letter] Lim M, et al. **Lancet** 1981 Sep 12;2(8246):591

Neuroendocrine effects of D,L-propranolol [letter] Malas KL, et al. **Lancet** 1981 Aug 22;2(8243):424

Changes in plasma concentrations of acebutolol, propranolol and indomethacin during physical exercise. Henry JA, et al. **Life Sci** 1981 Apr 27;28(17):1925-9

Influence of propranolol, phenoxybenzamine of phentolamine in the in vivo nocturnal rise of pineal melatonin levels in the Syrian hamster. Lipton JS, et al. **Life Sci** 1981 May 21;28(21):2377-82

Augmentation of thoracic duct lymph flow induced by adrenaline in the rabbits treated previously with propranolol. Toyosawa K, et al. **Nippon Seirigaku Zasshi** 1981;43(2):44-5

In vitro detection of possible in vivo drug interactions. Part 1. The effect of hydrochlorothiazide and frusemide on the in vitro absorption characteristics of propranolol hydrochloride. Anber SA, et al. **Pharmazie** 1981 Jun;36(6):425-7

In vitro detection of possible in vivo drug interactions. Part 2: A study of the effect of hydrochlorothiazide and frusemide on the partition coefficient and solubility characteristics of propranolol hydrochloride. Al-Janabi II, et al. **Pharmazie** 1981;36(7):485-8

Arterial and venous blood sampling in pharmacokinetic studies: propranolol in rabbits and dogs. Lam G, et al. **Res Commun Chem Pathol Pharmacol** 1981 Jul;33(1):33-48

Aromatic hydroxylation of propranolol. Stereochemical aspects of the formation of 4'-hydroxypropranolol in the rat. Powell ML, et al. **Res Commun Chem Pathol Pharmacol** 1980 Dec;30(3):387-400

Cerebroventricular propranolol elevates cerebrospinal fluid norepinephrine and lowers blood pressure. Tackett RL, et al. **Science** 1981 Aug 21;213(4510):911-3

Direct determination of propranolol in serum or plasma by fluoroimmunoassay. Al-Hakiem MH, et al. **Ther Drug Monit** 1981; 3(2):159-65

[Effect of propranolol and pindolol on carotid reflexes induced by lobeline] Silva Carvalho L, et al. **C R Trav Lab Carlsberg** 1981; 175(3):416-9 (Eng. Abstr.) **(Fre)**

[A modified fluorimetric method for the determination of propranolol in human plasma] Migulla H, et al. **Pharmazie** 1981 Jun;36(6):443-4 **(Ger)**

[Effect of portasystemic anastomoses in childhood on propranolol pharmacokinetics] Cario WR, et al. **Schweiz Med Wochenschr** 1981 Jul 18;111(29):1088-93 (Eng. Abstr.) **(Ger)**

[Effect of propranolol, nifedipine and aminophylline on ST and T changes in spontaneous cardiac rhythm in patients with artificial pacemaker] Swiatecka G. **Kardiol Pol** 1981;24(5):343-8 (Eng. Abstr.) **(Pol)**

PROSTAGLANDINS

Effects of vasoactive and inflammatory agents on cyclic AMP levels in W138 fibroblasts, endothelial and vascular smooth muscle cells in culture. Ager A, et al. **Agents Actions** 1980 Dec;10(6):569-72

Bradykinin effects on adrenergic transmission in the canine kidney: relation to prostaglandins. Sušić H, et al. **Am J Physiol** 1981 Sep; 241(3):R146-51

Differential effects of itanoxone--a new hypolipidemic and hypouricemic drug--on platelet and vascular prostaglandin generation in rats. Livio M, et al. **Atherosclerosis** 1981 Jul;39(4):469-77

Evidence against an obligatory role for catecholamine release or prostacyclin synthesis in the effects of relaxin on the rat uterus. Sanborn BM, et al. **Biol Reprod** 1981 Jun;24(5):987-92

Prostacyclin and beta-adrenergic catecholamines inhibit arachidonate release and PGI2 synthesis by vascular endothelium. Adler B, et al. **Blood** 1981 Sep;58(3):514-7

Differential effects of prostaglandins on canine intrapulmonary arteries and veins. Altura BM, et al. **Br J Pharmacol** 1981 Aug;73(4):819-27

Inhibition of anterior pituitary prostaglandin-stimulated adenylyl cyclase activity by somatostatin. Rouleau D, et al. **Can J Biochem** 1981 Apr; 59(4):307-10

Effects of various prostanoids on thyrotropin secretion by superfused anterior pituitary cells. Wright KC, et al. **Endocrinology** 1981 Aug; 109(2):637-43

Effect of prostaglandins D2, E2 and F2alpha on catecholamine release from slices of rat and rabbit brain. Reimann W, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):421-7

Stimulation of cyclic AMP production by vasoactive agents in cultured bovine aortic and pulmonary artery endothelial cells. Makarski JS. **In Vitro** 1981 May;17(5):450-8

A simultaneous radioimmunoassay for aldosterone and its precursors: human plasma levels following the inhibition of converting enzyme, before and after blockade of prostaglandin biosynthesis. Witzgall H, et al. **J Clin Chem Clin Biochem** 1981 Jun;19(6):387-94

Prostacyclin and prostaglandin E2 effects on adrenergic transmission in the kidney of anesthetized dog. Sušić H, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):588-92

Effects of C-terminal octapeptide of cholecystokinin and prostaglandins on adrenergic functions in the guinea-pig gallbladder and sphincter of Oddi. Nakata K, et al. **Jpn J Pharmacol** 1981 Feb;31(1):77-83

Renal kinin-prostaglandin relationship: implications for renal function. Nasjletti A, et al. **Kidney Int** 1981 Jun;19(6):860-8 (73 ref.)

Prostacyclin-induced hypothermia: involvement of central histamine H2-receptors. Kandasamy SB, et al. **Life Sci** 1981 Jun 1; 28(22):2553-60

Interrelationships among prostaglandins and vasoactive substances. Nasjletti A, et al. **Med Clin North Am** 1981 Jul;65(4):881-9 (60 ref.)

The role of prostaglandins in the alpha- and beta-adrenoceptor mediated renin release response to graded renal nerve stimulation. Kopp U, et al. **Pflugers Arch** 1981 Jul;391(1):1-8

Central effects of prostaglandin D2. Brus R, et al. **Pol J Pharmacol Pharm** 1980;32(5):681-4

Relative contracting and relaxing potencies of a series of prostaglandins on isolated canine mesenteric artery strips. Hatano Y, et al. **Prostaglandins** 1981 Apr;21(4):515-29

Low dose aspirin, platelet function and prostaglandin synthesis: influence of epinephrine and alpha adrenergic blockade. Rao GH, et al. **Prostaglandins Med** 1981 May;6(5):485-94

Stimulated platelet aggregation, thromboxane B2 formation and platelet sensitivity to prostacyclin - a critical evaluation. Siess W, et al. **Thromb Haemost** 1981 Jun 30;45(3):204-7

[Prostaglandins and the nervous system (review of the literature)] Muratov VD, et al. **Farmakol Toksikol** 1981 Jan-Feb;44(1):121-8 (117 ref.) **(Rus)**

PSYCHIATRY

The psychiatrist's perspective--two images of the patient. Leibow D. **Ann NY Acad Sci** 1981;368:123-7

A prospective study of 60 consecutive psychiatric consultations in a family medicine clinic. Katon W, et al. **J Fam Pract** 1981 Jul;13(1):47-56

PSYCHOLOGICAL TESTS

[Effectiveness of drug testing with the help of psychometric methods. Possibilities and problems] Oswald WD. **Med Welt** 1981 Aug 21; 32(34):1225-31 **(Ger)**

PSYCHOPHARMACOLOGY

The role of information exchange in psychopharmacology. Vartanian FE. **Prog Neuropsychopharmacol** 1981;5(2):201-3

Psychopharmacotherapy: from the 1950s to the 1980s. Pomara N, et al. **Psychosomatics** 1981 Jun;22(6):526-30

IInd Czechoslovakian Symposium of Psychopharmacology, Smolenice, 28th-30th September 1977. **Agressologie** 1979;20(D):235-318 **(Mul)**

PSYCHOPHYSIOLOGIC DISORDERS

[Depression, somatization, suicide. Part 2: Masked depression, suicide] Hertrich O. **Fortschr Med** 1981 Jul 2;99(25):973-7 **(Ger)**

PSYCHOSES, SUBSTANCE-INDUCED

Anticholinergic psychosis: differential diagnosis and management. Hall RC, et al. **Psychosomatics** 1981 Jul;22(7):581-3, 587

PSYCHOTHERAPY

Effects of althesin in psychotherapy of schizophrenics. Preliminary report. Ladisich W. **Acta Psychiatr Belg** 1980 Jul-Aug;80(4):445-51

Pharmacotherapy as an intervention during the stages of psychotherapy. Beitman BD. **Am J Psychother** 1981 Apr;35(2):206-14

Differential therapeutics: a guide to treatment selection. Frances A, et al. **Hosp Community Psychiatry** 1981 Aug;32(8):537-46

Differential effects of cognitive therapy and pharmacotherapy on depressive symptoms. Rush AJ, et al. **J Affective Disord** 1981 Sep; 3(3):221-9

[Theoretical assessment and personal experience with the combination of psychotropic drugs and psychotherapy] Seidler C. **Z Arztl Fortbild (Jena)** 1981 May 1;75(9):412-5 (Ger)

PSYCHOTHERAPY, GROUP

Group therapy in the management of manic-depressive illness. Volkmar FR, et al. **Am J Psychother** 1981 Apr;35(2):226-34

Enhancing medication compliance in coffee groups. Olarte SW, et al. **Hosp Community Psychiatry** 1981 Jun;32(6):417-9

[Psychiatric practice as it appears in the Balint group] Guyotat J. **Schweiz Arch Neurol Neurochir Psychiatr** 1981;128(2):251-61 (Eng. Abstr.) (Fre)

PSYCHOTIC DISORDERS

Covert values in the treatment of psychosis. Halleck SL. **Am J Psychother** 1981 Apr;35(2):173-86

Daytime variation in serum prolactin level in patients receiving oral and depot antipsychotic medication. Goode DJ, et al. **Biol Psychiatry** 1981 Jul;16(7):653-62

Dopamine hypothesis in acute psychosis [letter] Marsden CD. **Br J Psychiatry** 1981 Mar;138:269-70

Rapid parenteral treatment of acute psychosis. Menuck M, et al. **Compr Psychiatry** 1981 Jul-Aug;22(4):351-61 (69 ref.)

Using drug holidays for chronic outpatients. Sharer DR, et al. **Hosp Community Psychiatry** 1981 Jun;32(6):420-1

Use of psychotropic drugs in psychiatric conditions; psychiatric problems - recent advances in diagnosis and treatment. Tupin JP. **Proc Annu Meet Med Sect Am Counc Life Insur** 1980;5:67-85

Substance P-like immunoreactivity in plasma of psychotic patients and effects of neuroleptics and electroconvulsive therapy. Kaiya H, et al. **Psychiatry Res** 1981 Aug;5(1):11-21

[Clinical experience with the preparation lithium carbonicum retard in psychiatry (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Apr;77(2):110-5 (Eng. Abstr.) (Cze)

[Relationship between pharmacotherapy and psychotherapy of psychoses] Molcan J, et al. **Agressologie** 1979;20(D):283-5 (Eng. Abstr.) (Ger)

[Unsolved problems in the indications for lithium prophylaxis in affective and schizoaffective disorders] Angst J. **Bibl Psychiatr** 1981; (161):32-44 (Eng. Abstr.) (Ger)

[Lithium prophylaxis in schizoaffective psychoses] Lenz G, et al. **Bibl Psychiatr** 1981;(161):45-57 (54 ref.) (Ger)

[High-dosed neuroleptic therapy] Platz T, et al. **Pharmacopsychiatria** 1981 Jul;14(4):141-7 (82 ref.) (Eng. Abstr.) (Ger)

[Comparative characteristics of the preventive properties of short-acting and delayed-action lithium carbonate in endogenous affective psychoses] Panteleeva GP, et al. **Zh Nevropatol Psikhiatr** 1981; 81(3):406-12 (Eng. Abstr.) (Rus)

QUINIDINE

Pharmacokinetic analysis of intravenously and orally administered quinidine in horses. McGuirk SM, et al. **Am J Vet Res** 1981 Jun; 42(6):938-42

Comments on: 'anticholinergic effects of disopyramide and quinidine on guinea pig myocardium--mediation by direct muscarinic receptor blockade' [letter] Benfey BG. **Circ Res** 1981 Sep;49(3):821

Enterogastric cycle and intoxication with hydroquinidine: a case report. Lesne M, et al. **Clin Toxicol** 1981 Jun;18(6):659-62

Clinical aspects of the digoxin-quinidine interaction. Pedersen KE. **Dan Med Bull** 1981 Aug;28(3):128-31

The specificity of the extraction fluorescence assay for serum or plasma quinidine. Greenblatt DJ, et al. **J Clin Pharmacol** 1981 Aug-Sep; 21(8-9):333-6 (17 ref.)

Effects of quinidine, procainamide and disopyramide on automaticity and cyclic AMP content of guinea-pig atria. Mirro MJ. **J Mol Cell Cardiol** 1981 Jul;13(7):641-53

Comparative uptake of quinine and quinidine in rat lung. Minchin RF, et al. **J Pharm Pharmacol** 1981 Jul;33(7):464-6

Assignment of conformation and configuration to potassium permanganate oxidation products of quinidine. Yanuka Y, et al. **J Pharm Sci** 1981 Jun;70(6):675-9

Tissue binding sites involved in quinidine-cardiac glycoside interactions. Kim DH, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):357-62

[Absolute bioavailability of an aqueous solution of quinidine administered orally to the rat and evaluation of the enterohepatic cycle (author's transl)] Koskas JP, et al. **J Pharm Belg** 1981 May-Jun;36(3):193-9 (Eng. Abstr.) (Fre)

[Application of a micromethod for sampling and for the specific quantitative evaluation of quinidine. I. Pharmacokinetic study after intravenous administration in the rat (author's transl)] Koskas JP, et al. **J Pharm Belg** 1981 May-Jun;36(3):187-92 (Eng. Abstr.) (Fre)

[Quinidine increases digoxin levels] Doering W, et al. **Med Klin** 1981 Jul 3;76(14):395-8 (Ger)

[Fluorometric determination of the concentration of quinidine in blood] Gnilitskaia VB, et al. **Lab Delo** 1981;(8):511 (Rus)

RECEPTORS, ADRENERGIC

Dopaminergic and adrenergic effects on plasma LH levels in rats with hypothalamic islands. van Dieten JA, et al. **Acta Endocrinol (Copenh)** 1981;97(3):289-96

Central action of adrenaline. Jagiello-Wójtowicz E. **Acta Physiol Pol** 1981 Mar-Apr;32(2):169-80

A cellular activator of catecholamine-sensitive adenylate cyclase in rat reticulocytes and erythrocytes: changes during reticulocyte development and effects on the beta receptor. Shane E, et al. **Arch Biochem Biophys** 1981 May;208(2):418-25

Differences in the effects of acetylcholine on the vas deferens from normal and castrated rats. A participation of adrenergic mechanisms. Agostini M del C, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):212-20

Effects of dopamine and its antagonist domperidone cannot be explained by an effect on alpha 1-adrenergic receptors. Schuurkes JA, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):324-7

Different sedimentation properties of agonist- and antagonist-labelled platelet alpha 2 adrenergic receptors. Michel T, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):1131-6

Effects on fluorine analogs of norepinephrine on stimulation of cyclic adenosine 3',5'-monophosphate and binding to beta-adrenergic receptors in intact pinealocytes. Auerbach DA, et al. **Biochem Pharmacol** 1981 May 15;30(10):1085-9

No evidence for reverse trans-synaptic regulation of neuronal uptake by beta-adrenoceptors in kitten atria. Cornish EJ, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1439-42

Presynaptic alpha-adrenergic mediation of self-stimulation in locus coeruleus in rats treated neonatally with 6-hydroxydopamine. Umemoto M, et al. **Brain Res** 1981 Aug 24;219(1):107-19

Relative location of alpha- and beta-adrenoceptors to sites of release of sympathetic transmitter in the rabbit facial vein. Winquist RJ, et al. **Circ Res** 1981 Aug;49(2):486-92

Cardiac beta-adrenoreceptors in the thyroxine-treated dog. Ho K, et al. **Clin Exp Pharmacol Physiol** 1981 Mar-Apr;8(2):183-7

Alpha-adrenergic stimulation by clonidine increases plasma concentrations of immunoreactive beta-endorphin in rats. Pettibone DJ, et al. **Endocrinology** 1981 Sep;109(3):798-802

Interaction of desipramine and amitriptyline with adrenergic mechanisms in the human iris in vivo. Szabadi E, et al. **Eur J Clin Pharmacol** 1981; 19(6):403-8

Lack of modulation by presynaptic alpha 2-adrenoceptors of adrenergic transmitters release evoked by activation of 5-hydroxytryptamine and nicotine receptors. Carr SR, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):27-34

Relation between brain catecholamine receptors and dopaminergic stereotypy in rat strains. Helmeste DM, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):465-70

Down-regulation of beta-adrenergic activity in astroglia by chronic treatment with an antidepressant drug. Hertz L, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):267-8

An interaction between prejunctional alpha-adrenoceptors and prejunctional beta-adrenoceptors. Majewski H, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):493-8

Involvement of noradrenergic and dopaminergic neurons in shock-induced jumping in rats. Nishikawa T, et al. **Eur J Pharmacol** 1981 May 22;71(4):429-36

Pre- and postsynaptic alpha-adrenoceptor antagonism by neuroleptics in vivo. Petersen EN. **Eur J Pharmacol** 1981 Feb 19;69(4):399-405

Physiological evidence (hypothermia) for central effects of beta-blocker agents. Ben-Uriah Y, et al. **Int J Neurosci** 1981;14(1-2):41-6

Effects of prazosin and phenoxybenzamine on alpha- and beta-receptor-mediated responses in intestinal resistance and capacitance vessels. Patel P, et al. **J Cardiovasc Pharmacol** 1981 Sep-Oct;3(5):1050-9

Mechanism of the age-related decrease of epinephrine-stimulated lipolysis in isolated rat adipocytes: beta-adrenergic receptor binding, adenylate cyclase activity, and cyclic AMP accumulation. Dax EM, et al. **J Lipid Res** 1981 Aug;22(6):934-43

Age-related changes in the central catecholaminergic function and its interaction with methamphetamine during postnatal life in the rat. Nomura Y, et al. **J Pharm Pharmacol** 1981 Apr;33(4):264-6

Cholinergic and alpha adrenergic augmentation of histamine-induced contraction of canine airway smooth muscle. Leff AR, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):582-7

Site(s) and ionic basis of alpha-autoinhibition and facilitation of [3H]noradrenaline secretion in guinea-pig vas deferens. Alberts P, et al. **J Physiol (Lond)** 1981 Mar;312:297-334

Localization of specialized noradrenaline receptors at neuromuscular junctions on arterioles of the guinea-pig. Hirst GD, et al. **J Physiol (Lond)** 1981;313:343-50

Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Lotti VJ, et al. **Life Sci** 1981 Aug 10;29(6):633-9

Adrenaline activation of phosphofructokinase in rat heart mediated by alpha-receptor mechanism independent of cyclic AMP. Clark MG, et al. **Nature** 1981 Jul 30;292(5822):461-3

Conditions required for the inhibitory feedback loop in noradrenergic transmission. Story DF, et al. **Nature** 1981 Sep 3;293(5827):62-5

Stimulation of prostaglandin E2-synthesis by noradrenaline in primary cell cultures from rabbit splenic pulpa is mediated by atypical alpha-adrenoceptors. Brückner-Schmidt R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):1-7

Two different biophases for adrenaline released by electrical stimulation or tyramine from the sympathetic nerve endings of the dog saphenous vein. Guimarães S, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun;316(3):200-4

The noradrenaline receptor coupled adenylate cyclase system in brain. Lack of modification by changes in the availability of serotonin. Mishra R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun; 316(3):218-24

Norepinephrine uptake in aging adrenergic nerve terminals. Hoffman DW, et al. **Neurobiol Aging** 1980 Summer;1(1):65-8

Evidence for a growth hormone releasing factor mediating alpha-adrenergic influence on growth hormone secretion in the rat. Eden S, et al. **Neuroendocrinology** 1981 Jul;33(1):24-7

Importance of norepinephrine alpha 2-receptor activation for morphine-induced rat growth hormone secretion. Eriksson E, et al. **Neuroendocrinology** 1981 Aug;33(2):91-6

Adaptive changes in catecholamine receptors in the central nervous system. Reisine T. **Neuroscience** 1981;6(8):1471-502

The role of prostaglandins in the alpha- and beta-adrenoceptor mediated renin release response to graded renal nerve stimulation. Kopp U, et al. **Pflugers Arch** 1981 Jul;391(1):1-8

The central noradrenergic transmission and the locus coeruleus: a review of the data, and their implications for neurotransmission and neuromodulation. van Dongen PA. **Prog Neurobiol** 1981; 16(2):117-43 (303 ref.)

[The effects of Citrus aurantium and its active ingredient N-methyltyramine on the cardiovascular receptors (author's transl)] Chen X, et al. **Yao Hsueh Hsueh Pao** 1981 Apr;16(4):253-9 (Eng. Abstr.) **(Chi)**

RECEPTORS, CHOLINERGIC

Interaction of imipramine with the ionic channel of the acetylcholine receptor of motor endplate and electric organ. Eldefrawi ME, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1391-4

Mechanism of inactivation (desensitization) of acetylcholine receptor. Investigations by fast reaction techniques with membrane vesicles. Aoshima H, et al. **Biochemistry** 1981 Jun 9;20(12):3467-74

Muscarinic acetylcholine receptors regulation and protein phosphorylation in primary cultures of rat cerebellum. Burgoyne RD, et al. **Brain Res** 1981 Aug;254(1):55-63

Cholinergic receptor interactions and their effects on long-term memory processing. Flood JF, et al. **Brain Res** 1981 Jun 29;215(1-2):177-85

8-Br-cyclic GMP mimics activation of muscarinic autoreceptor and inhibits acetylcholine release from rat hippocampal slices. Nordström O, et al. **Brain Res** 1981 Jun 1;213(2):467-71

Comments on: 'anticholinergic effects of disopyramide and quinidine on guinea pig myocardium—mediation by direct muscarinic receptor blockade' [letter] Benfey BG. **Circ Res** 1981 Sep;49(3):821

Lack of modulation by presynaptic alpha 2-adrenoceptors of adrenergic transmitters release evoked by activation of 5-hydroxytryptamine and nicotine receptors. Carr SR, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):27-34

The loss of muscarinic acetylcholine receptors in synaptic membranes under phosphorylating conditions is dependent on calmodulin. Burgoyne RD. **FEBS Lett** 1981 May 5;127(1):144-8

Slow cholinergic and peptidergic transmission in sympathetic ganglia. Brown DA, et al. **Fed Proc** 1981 Sep;40(11):2625-30

Acetylcholine receptor kinetics at slow fiber neuromuscular junctions. Dionne VE. **Fed Proc** 1981 Sep;40(11):2614-7

Muscarinic receptors in chromaffin cell cultures mediate enhanced phospholipid labeling but not catecholamine secretion. Fisher SK, et al. **J Neurochem** 1981 Aug;37(2):491-7

Desensitization of the muscarinic acetylcholine receptor of atrium in bullfrogs. Tokimasa T, et al. **Jpn J Physiol** 1981;31(1):83-97

Striatal muscarinic receptors: regulation by dopaminergic agonists. Ehlert FJ, et al. **Life Sci** 1981 May 21;28(21):2441-8

Brain cholinergic dysfunction and memory in aged rats. Lippa AS, et al. **Neurobiol Aging** 1980 Summer;1(1):13-9

Cholinergic actions of false neurotransmitters: acetylpyrrolidinecholine. Buccafusco JJ, et al. **Neurosci Lett** 1981 May 29;23(3):319-24

Muscarinic cholinergic influences on ACTH and beta-endorphin release mechanisms in human subjects. Risch SC, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:95-7

Acetylcholine-induced cation translocation across cell membranes and inactivation of the acetylcholine receptor: chemical kinetic measurements in the millisecond time region. Cash DJ, et al. **Proc Natl Acad Sci USA** 1981 Jun;78(6):3318-22

Ultraviolet light-induced labeling by noncompetitive blockers of the acetylcholine receptor from Torpedo marmorata. Oswald R, et al. **Proc Natl Acad Sci USA** 1981 Jun;78(6):3925-9

Dopaminergic regulation of muscarinic receptor binding in the corpus striatum. Ehlert FJ, et al. **Proc West Pharmacol Soc** 1981;24:93-5

Chronic phencyclidine induced changes in rat central cholinergic receptor regulation. Ward DP, et al. **Proc West Pharmacol Soc** 1981;24:3-4

Failure of muscarinic blockade to antagonize analepsis induced by thyrotropin-releasing hormone and MK-771 in the rat. Santori EM, et al. **Psychopharmacology (Berlin)** 1981;74(1):13-6

[Alkylation of ganglionic cholinergic receptors with haloalkyl amines] Blazsó G, et al. **Acta Pharm Hung** 1980 May;50(3):137-44 (Eng. Abstr.) **(Hun)**

[Regulation of the functioning of molluscan neuron cholinoreceptors by succinate and noradrenaline] Andreev AA, et al. **Dokl Akad Nauk SSSR** 1981;258(6):1466-9 **(Rus)**

RECEPTORS, DOPAMINE

Kainic acid induced lesion of ventral tegmental area: locomotor effect of apomorphine. Morgenstern R. **Acta Biol Med Ger** 1980; 39(8-9):911-5

Dopaminergic and adrenergic effects on plasma LH levels in rats with hypothalamic islands. van Dieten JA, et al. **Acta Endocrinol (Copenh)** 1981;97(3):289-96

Modifications of the dopaminergic receptors sensitivity and learning of normoxic or hypobaric hypoxic rats. Saligaut C, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):80-7

Dopamine receptor alterations with aging in mouse and rat corpus striatum. Marquis JK, et al. **Biochem Pharmacol** 1981 Jul 1; 30(13):1876-8

Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Solomon PR, et al. **Biol Psychiatry** 1981 Jun; 16(6):519-37

Evidence for an inhibitory presynaptic component of neuroleptic drug action. de Belleroche JS, et al. **Br J Pharmacol** 1981 Mar; 72(3):427-33

Puberty of female rats may in part be explained by decreased hypothalamic dopamine receptor sensitivity. Lamberts R, et al. **Brain Res** 1981 [illegible] 29;215(1-2):375-81

Chronic lead treatment induces in rat a specific and differential effect on dopamine receptors in different brain areas. Lucchi L, et al. **Brain Res** 1981 Jun 1;213(2):397-404

[3H]Spiperone binding sites in brain: autoradiographic localization of multiple receptors. Palacios JM, et al. **Brain Res** 1981 Jun 1; 213(2):277-89

Differential functional ontogeny of dopamine presynaptic receptor regulation. Shalaby IA, et al. **Brain Res** 1981 Jun;227(3):434-9

Kainic acid lesions dissociate [3H] spiperone and [3H]cis-flupenthixol binding sites in rat striatum. Cross AJ, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):327-32

Relation between brain catecholamine receptors and dopaminergic stereotypy in rat strains. Helmeste DM, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):465-70

Characteristics of the dopamine receptors in the rabbit isolate splenic artery. Hilditch A, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):287-96

Involvement of dopamine in circling responses to muscimol depends on intranigral site of injection. Kilpatrick IC, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):407-19

Presence of a particular subpopulation of dopamine receptors within the septal nuclei: a behavioural study on cats. Megens AA, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):247-58

Involvement of noradrenergic and dopaminergic neurons in shock-induced jumping in rats. Nishikawa T, et al. **Eur J Pharmacol** 1981 May 22;71(4):429-36

REM sleep deprivation induces subsensitivity of dopamine receptors mediating sedation in rats. Serra G, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):131-5

Synthesis and pharmacological evaluation of sulfonium analogues of dopamine: nonclassical dopamine agonists. Anderson K, et al. **J Med Chem** 1981 Jun;24(6):683-7

Monophenolic 2-(dipropylamino)indans and related compounds: central dopamine-receptor stimulating activity. Hacksell U, et al. **J Med Chem** 1981 Apr;24(4):429-34

Characterization of normal and supersensitive dopamine receptors: effects of ergot drugs and neuropeptides. Fuxe K, et al. **J Neural Transm** 1981; 51(1-2):3-37

The effects of lisuride and some other dopaminergic agonists on receptor binding in human brain. Reynolds GP, et al. **J Neural Transm** 1981; 51(1-2):107-11

Relevance of the rodent area postrema to dopamine-dependent behavioural effects. Costall B, et al. **J Pharm Pharmacol** 1981 Apr; 33(4):257-9

Effect of GABAergic drugs on dopamine catabolism in the nigrostriatal and mesolimbic dopaminergic pathways of the rat. Gundlach AL, et al. **J Pharm Pharmacol** 1981 Jan;33(1):41-3

During one year's neuroleptic treatment in rats striatal dopamine receptor blockade decreases but serum prolactin levels remain elevated. Dyer RG, et al. **Life Sci** 1981 Jan 12;28(2):167-74

Development of dopamine receptor denervation supersensitivity in the neostriatum of the senescent rat. Joseph JA, et al. **Life Sci** 1981 Aug 10;29(6):575-84

Effect of 3-PPP, a putative dopamine autoreceptor agonist, on rat serum prolactin levels. Meltzer HY, et al. **Life Sci** 1981 Jul 6;29(1):99-105

Demonstration of specific vascular dopamine receptors mediating vasodilation on the isolated rabbit mesenteric artery. Brodde OE, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):24-30

Dopamine receptor mediated inhibition by pergolide of electrically-evoked 3H-dopamine release from striatal slices of cat and rat: slight effect of ascorbate. Lehmann J, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):31-5

Effect of combined treatment with dopaminergic and GABA-ergic drugs on the threshold for maximal electroconvulsions in mice. Czuczwar SJ. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):25-35

Dopamine receptor binding in inbred mice: strain differences in mesolimbic and nigrostriatal dopamine binding sites. Boehme RE, et al. **Proc Natl Acad Sci USA** 1981 May;78(5):3255-9

3H-Flupenthixol binding in post-mortem brains of schizophrenics: evidence for a selective increase in dopamine D2 receptors. Cross AJ, et al. **Psychopharmacology (Berlin)** 1981;74(2):122-4

Effect of chronic amphetamine administration on central dopaminergic mechanisms in the vervet. Owen F, et al. **Psychopharmacology (Berlin)** 1981;74(3):213-6

[Interrelationship of the tranquilizers diazepam and lonetil with dopamine mediation in the central nervous system] Ovcharov R, et al. **Eksp Med Morfol** 1981;20(2):88-96 (Eng. Abstr.) **(Bul)**

[Central depletion of transmitters by reserpine and motor behavior in the rat (author's transl)] Funk KF, et al. **Acta Biol Med Ger** 1980; 39(8-9):923-7 (Eng. Abstr.) **(Ger)**

[Role of dopamine receptors in regulating glutamatergic synaptic transmission in the rat neostriatum] Godukhin OV, et al. **Fiziol Zh SSSR** 1981 Mar;67(3):384-9 (Eng. Abstr.) **(Rus)**

RECEPTORS, DRUG

Interaction of depressant, convulsant, and anticonvulsant barbiturates with the [3H]diazepam binding site of the benzodiazepine-GABA-receptor-ionophore complex. Ticku MK. **Biochem Pharmacol** 1981 Jun 15;30(12):1573-9

Stimulation of benzodiazepine binding to rat brain membranes and solubilized receptor complex by avermectin B1a and gamma-aminobutyric acid. Pong SS, et al. **Biochim Biophys Acta** 1981 Aug 6;646(1):143-50

Benzodiazepine and GABA receptors in the rat retina: effect of light and dark adaptation. Biggio G, et al. **Brain Res** 1981 Jul 6; 216(1):210-4

Binding of beta-carboline-3-carboxylic acid ethyl ester to mouse brain benzodiazepine receptors in vivo. Hirsch JD, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):357-60

[3H] Ethyl beta-carboline-3-carboxylate binding to the benzodiazepine receptor is not affected by GABA. Patel J, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):419-20

Action of pyrazolopyridines as modulators of [3H]flunitrazepam binding to the gaba/benzodiazepine receptor complex of the cerebellum. Supavilai P, et al. **Eur J Pharmacol** 1981 Mar 12;70(2):183-93

[3H]Propyl beta-carboline-3-carboxylate as a selective radioligand for the BZ1 benzodiazepine receptor subclass. Braestrup C, et al. **J Neurochem** 1981 Aug;37(2):333-41

Identification and distribution of neuroleptic binding sites in the rat spinal cord. Demenge P, et al. **J Neurochem** 1981 Jul;37(1):53-9

Distribution of specific high-affinity binding sites for [3H]imipramine in human brain. Langer SZ, et al. **J Neurochem** 1981 Aug;37(2):267-71

Benzodiazepine antagonist Ro 15-1788: binding characteristics and interaction with drug-induced changes in dopamine turnover and cerebellar cGMP levels. Möhler H, et al. **J Neurochem** 1981 Sep; 37(3):714-22

GABA-benzodiazepine-barbiturate receptor interactions. Olsen RW. **J Neurochem** 1981 Jul;37(1):1-13 (146 ref.)

Characterization of benzodiazepine and gamma-aminobutyric recognition sites and their endogenous modulators. Massotti M, et al. **J Neurosci** 1981 Apr;1(4):409-18

Reductions in retinal gamma-aminobutyric acid (GABA) content and in [3H]flunitrazepam binding after postnatal monosodium glutamate injections in rats. Regan JW, et al. **J Pharmacol Exp Ther** 1981 Sep; 218(3):791-6

Benzodiazepine receptors are coupled to a subpopulation of gamma-aminobutyric acid (GABA) receptors: evidence from a quantitative autoradiographic study. Unnerstall JR, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):797-804

Antagonism of benzodiazepine receptors by beta carbolines. O'Brien RA, et al. **Life Sci** 1981 Jul 6;29(1):75-82

Pentobarbital enhances [3H]diazepam binding to soluble receptors at the benzodiazepine--GABA-receptor-ionophore complex. Davis WC, et al. **Neurosci Lett** 1981 May 6;23(2):209-13

Receptor autoradiography with tritium-sensitive film: potential for computerized densitometry. Palacios JM, et al. **Neurosci Lett** 1981 Sep 1;25(2):101-5

Regional specificity of benzodiazepine receptor down-regulation during chronic treatment of rats with flurazepam. Rosenberg HC, et al. **Neurosci Lett** 1981 Jun 12;24(1):49-52

Phenobarbitone binding sites in rat brain synaptosomal membranes. Willow M, et al. **Neurosci Lett** 1981 Jul 17;24(3):301-6

Histidine modification with diethyl pyrocarbonate shows heterogeneity of benzodiazepine receptors. Burch TP, et al. **Proc Natl Acad Sci USA** 1981 Jun;78(6):3945-9

[Pharmacological and toxicological aspects of benzodiazepine compounds (author's transl)] Kapp W. **Anaesth Intensivther Notfallmed** 1981 Jun; 16(3):125-7 (Eng. Abstr.) **(Ger)**

RECEPTORS, ENDORPHIN

Interaction of tritiated beta-endorphin with rat brain membranes. Hammonds RG Jr, et al. **Anal Biochem** 1981 Jun;114(1):75-84

Dual action of meperidine on the frog neuromuscular junction: a prejunctional, opiate receptor-mediated depression of transmitter release and a postjunctional, nonopiate receptor effect on the endplate. Durham HD, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):150-65

Development of acute tolerance during exposure of hippocampal explants to an opioid peptide. Gähwiler BH. **Brain Res** 1981 Jul 27; 217(1):196-200

Functional and anatomical segregation of hypothalamic opiate receptors involved in prolactin and growth hormone secretion in cynomolgus monkeys. Belchetz PE. **Life Sci** 1981 Jun 29;28(26):2961-71

Opioid activities of beta-casomorphins. Brantl V, et al. **Life Sci** 1981 Apr 27;28(17):1903-9

Release of immunoreactive-dynorphin from the isolated guinea-pig small intestine is reduced during peristaltic activity. Kromer W, et al. **Neurosci Lett** 1981 Aug 7;25(1):53-6

Localization and opiate receptor binding of enkephalin, CCK and ACTH/beta-endorphin in the rat central nervous system. Stengaard-Pedersen K, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:3-19 (53 ref.)

Relationship between urinary free cortisol and CSF opioid binding activity in depressed patients and normal volunteers. Rubinow DR, et al. **Psychiatry Res** 1981 Aug;5(1):87-93

[Interaction of D-Ala2-[Tyr-3,5-3H]enkephalin(5-D-Leu) with opiate receptors of rat brain] Balashov AM, et al. **Biokhimiia** 1981 Jun; 46(6):1067-72 (Eng. Abstr.) **(Rus)**

[Endogenous opioids in the central nervous system] Hedner T. **Lakartidningen** 1981 Jul 22;78(30-31):2689-93 (Eng. Abstr.) **(Swe)**

RECEPTORS, HORMONE

Potentiation of prostaglandin E2-induced release of LH by the prostaglandin analogue, 7-oxa-13-prostynoic acid. Warberg J. **Acta Endocrinol (Copenh)** 1981;97(3):297-304

Receptor amplifying effect of serotonin and serotonin analogues in a protozoan (Tetrahymena) model system. Csaba G, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):411-6

Long lasting amplification and deformation of thyroid receptors after thyrotropin (TSH) and gonadotropin (GTH) treatment of chickens in the foetal period. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980; 56(3):303-7

Dose dependence of the thyrotropin (TSH) receptor damaging effect of gonadotropin in the newborn rats. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):417-20

Role of GABA-ergic receptors for the synthesis of GABA in different compartments of the rat cerebellum. Carmona E, et al. **Acta Physiol Scand** 1981 May;112(1):109-10

Physiological study of amino acid uptake and receptor desensitization: the GABA system in dorsal root ganglia. Désarménien M, et al. **Adv Biochem Psychopharmacol** 1981;29:309-19

Transport models of the neurotransmitter-receptor interaction. Vieth WR, et al. **Ann NY Acad Sci** 1981;369:99-111

The influence of sodium gamma-hydroxybutyrate on GABA receptors and catecholamine effect potentiation. Kozhechkin SN. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):242-53

Substance P binds to the formylpeptide chemotaxis receptor on the rabbit neutrophil. Marasco WA, et al. **Biochem Biophys Res Commun** 1981 Apr 30;99(4):1065-72

Interaction of depressant, convulsant, and anticonvulsant barbiturates with the [3H]diazepam binding site of the benzodiazepine-GABA-receptor-ionophore complex. Ticku MK. **Biochem Pharmacol** 1981 Jun 15;30(12):1573-9

Stimulation of benzodiazepine binding to rat brain membranes and solubilized receptor complex by avermectin B1a and gamma-aminobutyric acid. Pong SS, et al. **Biochim Biophys Acta** 1981 Aug 6;646(1):143-50

GnRH-receptor interaction. V. Down-regulation of pituitary receptors for GnRH in ovariectomized ewes by infusion of homologous hormone. Nett TM, et al. **Biol Reprod** 1981 Jun;24(5):1145-55

Distinction between the effects of barbiturates, benzodiazepines and phenytoin on responses to gamma-aminobutyric acid receptor activation and antagonism by bicuculline and picrotoxin. Simmonds MA. **Br J Pharmacol** 1981 Jul;73(3):739-47

Benzodiazepine and GABA receptors in the rat retina: effect of light and dark adaptation. Biggio G, et al. **Brain Res** 1981 Jul 6; 216(1):210-4

Ultrastructure of GABA-neurons in cultures of rat neostriatum. Panula P, et al. **Brain Res** 1981 Aug 24;219(1):202-7

Properties of [3H](3-Me-His2)TRH binding to apparent TRH receptors in the sheep central nervous system. Taylor RL, et al. **Brain Res** 1981 Aug 10;218(1-2):207-17

Benzodiazepine binding and interactions with the GABA receptor complex in living cultures of rat cerebral cortex. White WF, et al. **Brain Res** 1981 Jun 29;215(1-2):162-76

Epidermal growth factor induces rapid tyrosine phosphorylation of proteins in A431 human tumor cells. Hunter T, et al. **Cell** 1981 Jun; 24(3):741-52

Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Huhtaniemi IT, et al. **Endocrinology** 1981 Aug; 109(2):483-90

In vivo evidence for GABAergic control of serotonin release in the cat substantia nigra. Soubrié P, et al. **Eur J Pharmacol** 1981 Feb 19; 69(4):483-8

Action of pyrazolopyridines as modulators of [3H]flunitrazepam binding to the gaba/benzodiazepine receptor complex of the cerebellum. Supavilai P, et al. **Eur J Pharmacol** 1981 Mar 12;70(2):183-93

Experimental study of hormone receptor development in a unicellular model system. Csaba G, et al. **Exp Cell Biol** 1981;49(3):173-6

Photo-affinity inactivation of gonadotropin releasing hormone receptors. Hazum E. **FEBS Lett** 1981 Jun 1;128(1):111-3

Neurotransmitter receptors: neuroanatomical localization through autoradiography. Murrin LC. **Int Rev Neurobiol** 1981;22:111-71 (379 ref.)

Epimeric cis-decahydroquinoline-5-carboxylic acids: effects on gamma-aminobutyric acid uptake and receptor binding in vitro. Witiak DT, et al. **J Med Chem** 1981 Jul;24(7):788-94

Characterization of the binding of the GABA agonist [3H]piperidine-4-sulphonic acid to bovine brain synaptic membranes. Krogsgaard-Larsen P, et al. **J Neurochem** 1981 Aug;37(2):401-9

Characterization of gamma-aminobutyric acid binding sites on crude synaptic membranes. Kurioka S, et al. **J Neurochem** 1981 Aug; 37(2):283-8

Effects of sodium and bicarbonate ions on gamma-aminobutyric acid receptor binding in synaptic membranes of rat brain. Kurioka S, et al. **J Neurochem** 1981 Aug;37(2):418-21

GABA-benzodiazepine-barbiturate receptor interactions. Olsen RW. **J Neurochem** 1981 Jul;37(1):1-13 (146 ref.)

Characterization of benzodiazepine and gamma-aminobutyric recognition sites and their endogenous modulators. Massotti M, et al. **J Neurosci** 1981 Apr;1(4):409-18

Different efficacies of d- and l-gamma-amino-beta-hydroxybutyric acids in GABA receptor and transport test systems. Roberts E, et al. **J Neurosci** 1981 Feb;1(2):132-40

Lack of effect of benzodiazepines on bicuculline-insensitive GABA-receptors in the field-stimulated guinea-pig vas deferens preparation. Doble A, et al. **J Pharm Pharmacol** 1981 Apr; 33(4):267-8

Binding of luteinizing hormone-releasing hormone analogues to dispersed rat pituitary cells. Meidan R, et al. **Life Sci** 1981 Apr 27; 28(17):1961-7

Somatostatin modulates effects of angiotensin II in adrenal glomerulosa zone. Aguilera G, et al **Nature** 1981 Jul 16;292(5820):262-3

Modulation of platelet shape and membrane receptor binding by Ca2+-calmodulin complex. Kao KJ, et al. **Nature** 1981 Jul 2; 292(5818):82-4

Human transforming growth factors induce tyrosine phosphorylation of EGF receptors. Reynolds FH Jr, et al. **Nature** 1981 Jul 16; 292(5820):259-62

The effects of muscimol and picrotoxin injections into the cat substantia nigra. Wolfarth S, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):54-60

Endogenous inhibitors of Na+-independent [3H]GABA binding to crude synaptic membranes. Massotti M, et al. **Neurochem Res** 1981 May; 6(5):551-65

Pentobarbital enhances [3H]diazepam binding to soluble receptors at the benzodiazepine--GABA-receptor-ionophore complex. Davis WC, et al. **Neurosci Lett** 1981 May 6;23(2):209-13

GABA receptors distribution in rat substantia nigra. De Montis GM, et al. **Neurosci Lett** 1981 May 29;23(3):257-61

Effect of combined treatment with dopaminergic and GABA-ergic drugs on the threshold for maximal electroconvulsions in mice. Czuczwar SJ. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):25-35

Somatostatin receptors: identification and characterization in rat brain membranes. Srikant CB, et al. **Proc Natl Acad Sci USA** 1981 Jun; 78(6):3930-4

Hindbrain GABA receptors influence parasympathetic outflow to the stomach. Williford DJ, et al. **Science** 1981 Oct 9;214(4517):193-4

RECEPTORS, SEROTONIN

Reactivity of isolated trachea, bronchus and lung strip of cats of carbachol, 5-hydroxytryptamine and histamine: evidence for the existence of methysergide-sensitive receptors. Chand N. **Br J Pharmacol** 1981 Aug; 73(4):853-7

Different hypothalamic receptors mediate 5-hydroxytryptamine- and tryptamine-induced core temperature changes in the rat. Cox B, et al. **Br J Pharmacol** 1981 Mar;72(3):477-82

The maturation of cortical serotonin binding sites. Uphouse LL, et al. **Brain Res** 1981 Jun;227(3):415-7

Supersensitivity of nigral serotonin receptors and rat rotational behaviour. Blackburn TP, et al. **Eur J Pharmacol** 1981 May 8;71(2-3):343-6

Lack of modulation by presynaptic alpha 2-adrenoceptors of adrenergic transmitters release evoked by activation of 5-hydroxytryptamine and nicotine receptors. Carr SR, et al. **Eur J Pharmacol** 1981 Jun 10; 72(1):27-34

Differential effects of electroconvulsive shock and antidepressant drugs on serotonin-2 receptors in rat brain. Kellar KJ, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):515-8

Effects of fluoxetine on a specific serotonergic syndrome in rats. Keshavan HJ, et al. **Indian J Med Res** 1981 Apr;73:653-7

Characterisation of inhibitory 5-hydroxytryptamine receptors that modulate dopamine release in the striatum. Ennis C, et al. **J Neurochem** 1981 Apr;36(4):1515-20

Localisation of tricyclic antidepressant binding sites on serotonin nerve terminals. Sette M, et al. **J Neurochem** 1981 Jul;37(1):40-2

A pre-junctional action of 5-hydroxytryptamine and methysergide on noradrenergic nerves in dog isolated saphenous vein. Watts AD, et al. **J Pharm Pharmacol** 1981 Aug;33(8):515-20

Evidence for 5-HT2 receptors mediating contraction in vascular smooth muscle. Cohen ML, et al. **J Pharmacol Exp Ther** 1981 Aug; 218(2):421-5

5-Hydroxytryptamine-induced hypothermia in rats as an in vivo model for the quantitative study of 5-hydroxytryptamine receptors. Cox B, et al. **J Pharmacol Methods** 1981 Jan;5(1):43-51

Electrophysiological evidence for the existence of separate receptor mechanisms mediating the action of 5-hydroxytryptamine. Berridge MJ. **Mol Cell Endocrinol** 1981 Jul;23(1):91-104

Modulation of affinity of postsynaptic serotonin receptors by antidepressant drugs. Fillion G, et al. **Nature** 1981 Jul 23; 292(5821):349-51

Central action of mepiprazole. Maj J, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):475-84

Effect of chloro-N-desmethyldiazepam on serum and brain tryptophan and serotonin in relation to the activity of central serotonergic neurons. Valzelli L, et al. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):37-42

Uterine serotonin and receptor blockade during estrogen-induced uterine hyperemia. Van Orden DE, et al. **Proc Soc Exp Biol Med** 1981 Sep; 167(4):469-74

Lithium increases serotonin release and decreases serotonin receptors in the hippocampus. Treiser SL, et al. **Science** 1981 Sep 25; 213(4515):1529-31

REFLEX

Arterial baroreceptor reflex function in the conscious rabbit after brainstem lesions coinciding with the A1 group of catecholamine neurons. West MJ, et al. **Circ Res** 1981 Oct;49(4):959-70

Angiotensin and the cardiac baroreflex response to phenylephrine. Lee WB, et al. **Clin Exp Pharmacol Physiol** 1981 Mar-Apr;8(2):109-17

Effects of dopamine on chemoreflexes in breathing. Nishino T, et al. **J Appl Physiol** 1981 Apr;50(4):892-7

The somato-adrenal medullary reflexes in rats. Araki T, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):161-70

Tonic catecholaminergic inhibition of the spinal somato-sympathetic reflexes originating in the ventrolateral medulla oblongata. Dembowsky K, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):277-90

Effects of noradrenergic and serotonergic neurons on blood pressure, heart rate and baroreceptor-heart rate reflex of the conscious rabbit. Korner PI, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):511-23

Interaction between perfusion pressure and sympathetic nerves in renin release by carotid baroreflex in conscious dogs. Gross R, et al. **J Physiol (Lond)** 1981;313:237-50

[Effect of propranolol and pindolol on carotid reflexes induced by lobeline] Silva Carvalho L, et al. **C R Trav Lab Carlsberg** 1981; 175(3):416–9 (Eng. Abstr.) **(Fre)**

[Effect of enkephalins on central processes regulating hemodynamics] Medvedev OS, et al. **Biull Eksp Biol Med** 1981 May;91(5):574–6 (Eng. Abstr.) **(Rus)**

[Changes in lymph flow during reflexes from lymph vessels] Myrzakhanov NM. **Fiziol Zh SSSR** 1981 Mar;67(3):410–3 **(Rus)**

[Effect of drugs potentiating or inhibiting the activity of locus coeruleus neurons on various types of spinal inhibition in the cat] Iakhnitsa IA, et al. **Neirofiziologiia** 1981;13(3):247–58 (Eng. Abstr.) **(Rus)**

REINFORCEMENT (PSYCHOLOGY)

Rewarding effect of noradrenergic stimulation of the amygdala in food deprived rats. Jurkowlaniec E, et al. **Physiol Behav** 1981 Jul; 27(1):27–31

The partial reinforcement extinction effect: influence of chlordiazepoxide in septal lesioned rats. Feldon J, et al. **Psychopharmacology (Berlin)** 1981; 74(3):280–9

REINFORCEMENT SCHEDULE

Drug effects on multiple and alternating mixed-schedule performance. Leander JD. **J Pharmacol Exp Ther** 1981 Sep;218(3):728–33

RESERPINE

Differential effect of REM stimulating and REM inhibiting drugs (reserpine and amitriptylin) on memory. Faber J, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):169–71

The direct effect of reserpine in vitro on prolactin release from rat anterior pituitary glands. Login IS, et al. **Brain Res** 1981 Jan 5;204(1):79–85

Comparison of reserpine-induced supersensitivity of newborn and adult rabbit ventricular muscles to cardiotonic agents. Park MK, et al. **Dev Pharmacol Ther** 1981;2(4):240–9

Effect of cold, restraint, reserpine, and splanchnicotomy on the ornithine decarboxylase activity of rat adrenal medulla and cortex. Ramirez-Gonzalez D, et al. **Exp Neurol** 1981 Sep;73(3):632–41

Reserpine added to neuroleptic-tricyclic in refractory schizophrenics. Bacher N, et al. **J Clin Psychiatry** 1981 Aug;42(8):326

Differential effects of several dopamine uptake inhibitors and releasing agents on locomotor activity in normal and in reserpinized mice. Heikkila RE. **Life Sci** 1981 Apr 27;28(17):1867–73

Kinetic characteristics of newly synthesized 3H-5-HT in the brain of control and reserpinized mice. Evidence for the heterogeneous distribution of 5-HT in serotoninergic neurons. Morot-Gaudry Y, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jul;316(4):311–6

Agonist selectivity of reserpine induced inotropic supersensitivity. Rodgers RL, et al. **Proc West Pharmacol Soc** 1981;24:233–6

The prolactin-stimulating potency of reserpine in man. Asnis GM, et al. **Psychiatry Res** 1981 Aug;5(1):39–45

Antagonism of reserpine rigidity without inducing sedation. Southwick S, et al. **Psychopharmacology (Berlin)** 1981;74(1):29–32

Effects of reserpine treatment on beta-adrenergic/adenylate cyclase modulate secretion and resynthesis by the rat submandibular gland. Cutler LS, et al. **Virchows Arch [Pathol Anat]** 1981;392(2):185–98

[The non-specific pharmacodynamic action of chronic treatment with reserpine-like neuroadrenergic system antagonist (Raunervil) on the stability of sexual function] Simionescu S, et al. **Physiologie** 1981; 18(2):89–97 **(Fre)**

[Central depletion of transmitters by reserpine and motor behavior in the rat (author's transl)] Funk KF, et al. **Acta Biol Med Ger** 1980; 39(8–9):923–7 (Eng. Abstr.) **(Ger)**

[Supersensitivity by reserpine and means of antagonizing it] Westermann KH. **Acta Biol Med Ger** 1980;39(8–9):941–7 (Eng. Abstr.) **(Ger)**

[Influence of the central dopaminergic system on GABAergic activity of the cerebellum. Preliminary results] Di Giorgio RM, et al. **Acta Neurol [Quad] (Napoli)** 1981;42:302–4 (Eng. Abstr.) **(Ita)**

[On the National Institute of Hygienic Sciences standard (the Japanese Pharmacopoeia standard) 'Reserpine Reference Standard (control 761)' (author's transl)] Ohta M. **Eisei Shikenjo Hokoku** 1980;98:132–3 (Eng. Abstr.) **(Jpn)**

[Neuropharmacological drugs effect on functional activity of rat brain] Dzhaliashvili TA, et al. **Ukr Biokhim Zh** 1981 Mar–Apr; 53(2):109–14 (Eng. Abstr.) **(Rus)**

[Interference of magnesium in reserpine and aminophenazone interaction (author's transl)] Zábojníková M, et al. **Bratisl Lek Listy** 1981; 75(6):677–80 (Eng. Abstr.) **(Slo)**

RUBIDIUM

Somatostatin: mechanism of action in pancreatic islet beta-cells. Pace CS, et al. **Diabetes** 1981 Oct;30(10):836–42

Activation of active Na transport in sheep Purkinje fibres by external K or Rb ions. Glitsch HG, et al. **Pflugers Arch** 1981 Jul; 391(1):28–34

[Changes in the alkaline cation transport across the plasma membrane of CHO-K1 cell lines resistant to ethidium bromide] Marakhova II, et al. **Tsitologiia** 1981 Apr;23(4):410–8 (Eng. Abstr.) **(Rus)**

SCHIZOPHRENIA

Effects of althesin in psychotherapy of schizophrenics. Preliminary report. Ladisich W. **Acta Psychiatr Belg** 1980 Jul–Aug;80(4):445–51

Further clinical experiences with optical isomers of the L and D clorothepin. Náhunek K, et al. **Agressologie** 1979;20(D):275–8

Physostigmine and lithium response in the schizophrenias. Edelstein P, et al. **Am J Psychiatry** 1981 Aug;138(8):1078–81

CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Gerner RH, et al. **Am J Psychiatry** 1981 Aug;138(8):1098–101

Very high dose loxapine in refractory schizophrenic patients. Lehmann CR, et al. **Am J Psychiatry** 1981 Sep;138(9):1212–4

The effect of pimozide on CSF norepinephrine in schizophrenia. Sternberg DE, et al. **Am J Psychiatry** 1981 Aug;138(8):1045–50

Span of apprehension deficits during the postpsychotic stages of schizophrenia. A replication and extension. Asarnow RF, et al. **Arch Gen Psychiatry** 1981 Sep;38(9):1006–11

Middle molecular weight substances and tryptophan in cerebrospinal fluid of schizophrenic patients. Sperschneider H, et al. **Artif Organs** 1981 May;5(2):177–8

Interesting uses of beta blockers (2): propranolol in schizophrenia. Chia E. **Aust Fam Physician** 1981 May;10(5):376–9, 381–2

Psychopharmacological and social aspects of schizophrenia: recent developments. Paykel ES. **Aust NZ J Psychiatry** 1980 Dec; 14(4):241–7

Neuroleptics decrease blinking in schizophrenic subjects. Karson C, et al. **Biol Psychiatry** 1981 Jul;16(7):679–82

Total and free serum haloperidol levels in schizophrenic patients and the effect of age thioridazine and fatty acid on haloperidol-serum protein binding in vitro. Rowell FJ, et al. **Br J Clin Pharmacol** 1981 Apr; 11(4):377–82

Changes in the hostility of schizophrenic patients during treatment. Tsiantis J, et al. **Br J Med Psychol** 1981 Sep;54(Pt 3):251–8

Positive and negative schizophrenic symptoms and the role of dopamine [letter] Ashcroft GW, et al. **Br J Psychiatry** 1981 Mar;138:268–9

Phenothiazine withdrawal in schizophrenics in a hostel [letter] Mathur S, et al. **Br J Psychiatry** 1981 Mar;138:271–2

Psychophysiological responses of schizophrenic patients to high and low expressed emotion relatives. Sturgeon D, et al. **Br J Psychiatry** 1981 Jan;138:40–5

Fluphenazine resistant psychosis. Brent R, et al. **Can J Psychiatry** 1981 Mar;26(2):118–9

Acutely ill schizophrenic patients treated with loxapine. A clinical study in a community mental health center. Rasul M. **Clin Ther** 1980; 3(4):242–9

Apomorphine in schizophrenia. Hollister LE, et al. **Commun Psychopharmacol** 1980;4(4):277–81

Differential sensitivity to the effects of psychotropic drugs: psychotics vs normals; Asian vs Western populations. Okuma T. **Folia Psychiatr Neurol Jpn** 1981;35(1):79–87

Protein binding of chlorpromazine in cerebrospinal fluid and serum. Alfredsson G, et al. **Int Pharmacopsychiatry** 1980;15(5):261–9

Gas--liquid chromatographic determination of pipotiazine in plasma of psychiatric patients. Cooper SF, et al. **J Chromatogr** 1981 Feb 13; 222(2):291–6

Reserpine added to neuroleptic-tricyclic in refractory schizophrenics. Bacher N, et al. **J Clin Psychiatry** 1981 Aug;42(8):326

Bilateral skin conductance, finger pulse volume, and EEG orienting response to tones of differing intensities in chronic schizophrenics and controls. Bernstein AS, et al. **J Nerv Ment Dis** 1981 Aug; 169(8):513–28

gamma-Aminobutyric acid concentration in cerebrospinal fluid in schizophrenia. McCarthy BW, et al. **J Neurochem** 1981 Apr; 36(4):1406–8

Pindolol in schizophrenia [letter] O'Connor M. **Med J Aust** 1981 Apr 18;1(8):429

Effects of chronic amphetamine treatment on the glutamate concentration in cerebrospinal fluid and brain: implications for a theory of schizophrenia. Kim JS, et al. **Neurosci Lett** 1981 Jun 12;24(1):93–6

A double-blind comparison of bromperidol and haloperidol in newly admitted schizophrenic patients. Brannen JO, et al. **Pharmacopsychiatria** 1981 Jul;14(4):139–40

Gamma-hydroxybutyrate treatment of schizophrenia: a pilot study. Schulz SC, et al. **Pharmacopsychiatria** 1981 Jul;14(4):129–34

A follow-up study of schizophrenic outpatients treated with depot-neuroleptics. Tegeler J, et al. **Prog Neuropsychopharmacol** 1981; 5(1):79–90

Effects of long-term neuroleptic use on brain density. Lyon K, et al. **Psychiatry Res** 1981 Aug;5(1):33–7

Effect of intramuscular chlorpromazine on serum prolactin levels in schizophrenic patients and normal controls. Meltzer HY, et al. **Psychiatry Res** 1981 Aug;5(1):95–105

Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. van Kammen DP, et al. **Psychiatry Res** 1981 Jun;4(3):313–25

(Des-Tyr)-gamma-endorphin in the treatment of schizophrenia. Manchanda R, et al. **Psychol Med** 1981 May;11(2):401–4

3H-Flupenthixol binding in post-mortem brains of schizophrenics: evidence for a selective increase in dopamine D2 receptors. Cross AJ, et al. **Psychopharmacology (Berlin)** 1981;74(2):122–4

Information and consent in schizophrenic patients in long-term treatment. Linden M, et al. **Schizophr Bull** 1981;7(3):372–8

[On the question of differences between therapeutic responses after particular neuroleptics in comparison to perphenazine in schizophrenics (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981 Feb; 77(1):25–30 (Eng. Abstr.) **(Cze)**

[Flufenazine decanoate in the ambulatory treatment of schizophrenic patients] Populin M, et al. **Minerva Psichiatr** 1981 Apr–Jun; 22(2):85–92 (73 ref.) (Eng. Abstr.) **(Ita)**

[Changes in the levels of adrenergic and serotoninergic indices in patients with depressive states] Misionzhnik EIu, et al. **Zh Nevropatol Psikhiatr** 1981;81(4):543–51 (Eng. Abstr.) **(Rus)**

[Dynamics of the remission of acute schizophrenic episodes during psychopharmacologic treatment] Sverdlov LS. **Zh Nevropatol Psikhiatr** 1981;(5):737–43 (Eng. Abstr.) **(Rus)**

[Treatment of schizophrenic patients with clomacran. A transcultural study (author's transl)] Torres Ruiz A, et al. **Arch Neurobiol (Madr)** 1981 Mar–Apr;44(2):117–24 (Eng. Abstr.) **(Spa)**

SCHIZOPHRENIA, DISORGANIZED

Neuroendocrine function in schizophrenia. Brambilla F. **Acta Psychiatr Belg** 1980 Jul–Aug;80(4):421–35

SELF STIMULATION

The temporal structure of motivation IV: A reexamination of extinction effects in intracranial reward. Katz RJ. **Behav Neural Biol** 1981 Jun; 32(2):191–200

Increase in mesolimbic electrical self-stimulation after chronic haloperidol: reversal by L-DOPA or lithium. Seeger TF, et al. **Brain Res** 1981 Jun 29;215(1–2):404–9

Presynaptic alpha-adrenergic mediation of self-stimulation in locus coeruleus in rats treated neonatally with 6-hydroxydopamine. Umemoto M, et al. **Brain Res** 1981 Aug 24;219(1):107–19

Effects of GABAergic drugs on brain stimulation reward as assessed by a 'threshold' method. Zarevics P, et al. **Brain Res** 1981 Jun 29; 215(1–2):201–9

Post-amphetamine depression of self-stimulation behavior in rats: prophylactic effects of lithium. Predy PA, et al. **Neurosci Lett** 1981 May 29;23(3):343–7

Amphetamine enhancement of reward asymmetry. Glick SD, et al. **Psychopharmacology (Berlin)** 1981;73(4):323–7

Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Leith NJ, et al. **Psychopharmacology (Berlin)** 1981;74(1):23–8

[Effect of euphorigenic drugs on emotionally-positive brain systems] Zvartau EE, et al. **Zh Vyssh Nerv Deiat** 1981;31(2):308–14 (Eng. Abstr.) **(Rus)**

SEROTONIN

Effect of hypophysectomy and adrenalectomy on 5-hydroxytryptamine uptake by rat hypothalamic synaptosomes and blood platelets. Tukiainen E. **Acta Pharmacol Toxicol (Copenh)** 1981 Feb;48(2):139–44

Characterization of 5-hydroxytryptamine uptake in sliced rat lung. Wikberg JE, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Feb; 48(2):151–6

Receptor amplifying effect of serotonin and serotonin analogues in a protozoan (Tetrahymena) model system. Csaba G, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):411–6

Effect of cholecystokinin octapeptide sulphate ester on brain monoamines in the rat. Fekete M, et al. **Acta Physiol Acad Sci Hung** 1981; 57(1):37–46

Effects of high oxygen tension on the metabolism of vasoactive hormones in isolated perfused rat lungs. Toivonen H, et al. **Acta Physiol Scand** 1981 Feb;111(2):185–92

Autoradiographic and immunocytochemical evidence for the existence of GABAergic neurons in the nucleus raphe dorsalis--possible existence of neurons containing 5HT and glutamate decarboxylase. Nanopoulos D, et al. **Adv Biochem Psychopharmacol** 1981;29:519–25

Cyclic AMP modulation of a specific ion channel in an identified nerve cell: possible role for protein phosphorylation. Levitan IB, et al. **Adv Cyclic Nucleotide Res** 1981;14:647–53

Electroencephalographic serotonin synchronization: area postrema and solitary tract nucleus. Yamasaki K, et al. **Am J Physiol** 1981 Sep; 241(3):R158–62

Reverse-phase high-performance liquid chromatographic separation and electrochemical detection of norepinephrine, dopamine, serotonin, and related major metabolites. Kempf E, et al. **Anal Biochem** 1981 Apr; 112(2):223–31

Differential interaction of 5-HT with chicken and rat aorta. Laekeman GM, et al. **Arch Int Pharmacodyn Ther** 1981 Apr;250(2):318–20

Strontium ions induce production of thromboxane B2 and secretion of 5-hydroxytryptamine in washed human platelets. Best LC, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):635–7

Effect of neuroleptics on indoleamine-N-methyltransferase activity and brain metabolism of bufotenin. Gomes UC, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):571–5

Inverse relation of substance P-like immunoreactivity in dorsal raphe nucleus to serotonin levels in pons-medulla following administration of cocaine and 5-hydroxytryptophan. Pradhan S, et al. **Biochem Pharmacol** 1981 May 15;30(10):1071–6

Aromatic L-amino acid decarboxylase activity in central and peripheral tissues and serum of rats with L-DOPA and L-5-hydroxytryptophan as substrates. Rahman MK, et al. **Biochem Pharmacol** 1981 Mar 15; 30(6):645–9

Effects of mianserin, desipramine and maprotiline on blood pressure responses evoked by acetylcholine, histamine and 5-hydroxytryptamine in rats. Cavero I, et al. **Br J Pharmacol** 1981 Sep;74(1):143–8

Reactivity of isolated trachea, bronchus and lung strip of cats of carbachol, 5-hydroxytryptamine and histamine: evidence for the existence of methysergide-sensitive receptors. Chand N. **Br J Pharmacol** 1981 Aug; 73(4):853–7

Anomalous compartmentation of 5-hydroxytryptamine in intact human platelets. Costa JL, et al. **Br J Pharmacol** 1981 Mar;72(3):449–59

Different hypothalamic receptors mediate 5-hydroxytryptamine- and tryptamine-induced core temperature changes in the rat. Cox B, et al. **Br J Pharmacol** 1981 Mar;72(3):477–82

Effects of divalent cations on responses of a sympathetic ganglion to 5-hydroxytryptamine and 1,1-dimethyl-4-phenyl piperazinium. Nash HL, et al. **Br J Pharmacol** 1981 Jul;73(3):759–72

The effects of chronic section of dorsal roots on the responsiveness of motoneurones to 5-hydroxytryptamine and a substance P analogue. Roberts MH, et al. **Br J Pharmacol** 1981 Jul;73(3):589–94

Monoamines in affective illness. Is there a place for 5HT? Eccleston D **Br J Psychiatry** 1981 Mar;138:257–8

The art of measuring serotonin uptake in platelets [letter] Lingjaerde O. **Br J Psychiatry** 1981 1 Feb;138:181

Noradrenergic innervation of serotonergic neurons in the dorsal raphe: demonstration by electron microscopic autoradiography. Baraban JM, et al. **Brain Res** 1981 Jan 5;204(1):1–11

Effect of iontophoretically applied 5-hydroxytryptamine on the excitability of single primary afferent C- and A-fibers in the cat spinal cord. Carstens E, et al. **Brain Res** 1981 Sep 7;220(1):151–8

The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Coote JH, et al. **Brain Res** 1981 Jun 29;215(1–2):135–45

5-Hydroxytryptamine reduces substance P responses on dorsal horn interneurones: a possible interaction of neurotransmitters. Davies JE, et al. **Brain Res** 1981 Aug 3;217(2):399–404

Stimulation of the rat dorsal raphe in vivo releases labeled serotonin from the parietal cortex. Fujiwara H, et al. **Brain Res** 1981 Jul 20; 216(2):351–60

In vitro cellular adaptation of serotonergic processes after chronic central phenobarbital administration. Lyness WH, et al. **Brain Res** 1981 Jan 5;204(1):248–52

The cortical projection of the dorsal raphe nucleus: some electrophysiological and pharmacological properties. Olpe HR. **Brain Res** 1981 Jul 6;216(1):61–71

Relationship between two voltage-dependent serotonin responses of molluscan neurones. Paupardin-Tritsch D, et al. **Brain Res** 1981 Jul 27;217(1):201–6

The uptake and fate of the radiolabeled 5-hydroxytryptamine in isolated cerebral microvessels. Spatz M, et al. **Brain Res** 1981 Sep 7; 220(1):214–9

The maturation of cortical serotonin binding sites. Uphouse LL, et al. **Brain Res** 1981 Jun;227(3):415–7

Disproportionate increases in locomotor activity in response to hormonal and photic stimuli following regional neurochemical depletions of serotonin. Waldbillig RJ, et al. **Brain Res** 1981 Jul 27;217(1):79–91

Forebrain norepinephrine and serotonin concentrations and cardiac conditioning in normal rabbits and rabbits with septal lesions. Hernández LL, et al. **Brain Res Bull** 1981 Jun;6(6):479–86

Effects of serotonin and catecholamines on RNA synthesis in planarians; in vitro and in vivo studies. Franquinet R, et al. **Cell Differ** 1981 Aug; 10(4):201–9

Catecholamines and 5-hydroxytryptamine in photophores of Porichthys notatus. Radioenzymatic detection and radioautographic localization. Anctil M, et al. **Cell Tissue Res** 1981;219(3):557–66

The antidepressant effects of trazodone and inhibition of platelet serotonin reuptake. Mann JJ, et al. **Commun Psychopharmacol** 1980; 4(4):293–301

Biogenic monoamines in early embryos of sea urchins. Manukhin BN, et al. **Dev Neurosci** 1981;4(4):322–8

Serotonin regulation of corticoid secretion in infant rats. Grota LJ. **Dev Psychobiol** 1981 May;14(3):221-8

Intraventricular administration of vasopressin and oxytocin effects the steady-state levels of serotonin, dopamine and norepinephrine in rat brain. Schwarzberg H, et al. **Endocrinol Exp (Bratisl)** 1981; 15(2):75-80

Somatostatin release from rat hypothalamus in vitro: effects of melatonin and serotonin. Richardson SB, et al. **Endocrinology** 1981 Aug; 109(2):602-6

Evidence that a serotonergic mechanism stimulates the secretion of pituitary beta-endorphin-like immunoreactivity in the rat. Sapun DI, et al. **Endocrinology** 1981 Aug;109(2):421-6

Dopaminergic and serotonergic involvement in opiate-induced prolactin release in monkeys. Wehrenberg WB, et al. **Endocrinology** 1981 Aug; 109(2):544-7

In vivo evidence for GABAergic control of serotonin release in the cat substantia nigra. Soubrié P, et al. **Eur J Pharmacol** 1981 Feb 19; 69(4):483-8

The action of 5-hydroxytryptamine and possible 5-hydroxytryptamine antagonists on neurones of the guinea-pig submucous plexus. Neild TO. **Gen Pharmacol** 1981;12(4):281-4

Effects of exposure to trichloroethylene and tetrachloroethylene on the contents of acetylcholine, dopamine, norepinephrine and serotonin in rat brain. Honma T, et al. **Ind Health** 1980;18(4):171-8

Effects of fluoxetine on a specific serotonergic syndrome in rats. Keshavan HJ, et al. **Indian J Med Res** 1981 Apr;73:653-7

Antileprosy and biological antioxidant activity of serotonin. Bergel M. **Int J Lepr** 1981 Jun;49(2):259

Release of serotonin from human platelets in vitro by radiographic contrast media. Ring J, et al. **Invest Radiol** 1981 May-Jun; 16(3):245-8

Depression of serotonin uptake by cultured endothelial cells exposed to high O2 tension. Block ER, et al. **J Appl Physiol** 1981 Jun; 50(6):1212-9

Kinetics of serotonin uptake in the dog lung. Rickaby DA, et al. **J Appl Physiol** 1981 Aug;51(2):405-14

The intracranial injection of drugs in goldfish. II. Preliminary report of behavior of serotonin as a potential hallucinogen when injected intracranially and intraabdominally. Abramson HA, et al. **J Asthma Res** 1980 Jul;17(4):175-6

Effects of noradrenergic and serotonergic neurons on blood pressure, heart rate and baroreceptor-heart rate reflex of the conscious rabbit. Korner PI, et al. **J Auton Nerv Syst** 1981 Apr;3(2-4):511-23

Increased food intake, body weight, and adiposity in rats after regional neurochemical depletion of serotonin. Waldbillig RJ, et al. **J Comp Physiol Psychol** 1981 Jun;95(3):391-405

Role of serotonin in the regulation of growth hormone and prolactin secretion in the domestic fowl. Rabii J, et al. **J Endocrinol** 1981 Sep; 90(3):355-8

Synthesis and serotonin-like activity of 2-amino-5,8-dimethoxy-6-methyl-1,2-dihydronaphthalene. Kothari PJ, et al. **J Med Chem** 1981 Jul;24(7):882-4

Cyclic AMP, 5-HT, and the modulation of transmitter release at the crayfish neuromuscular junction. Enyeart J. **J Neurobiol** 1981 Sep; 12(5):505-13

Diurnal variations in monoamine contents in discrete brain regions of the mongolian gerbil (Meriones unguiculatus). Matsumoto M, et al. **J Neurochem** 1981 Sep;37(3):792-4

Localisation of tricyclic antidepressant binding sites on serotonin nerve terminals. Sette M, et al. **J Neurochem** 1981 Jul;37(1):40-2

Neuronal responses of the globus pallidus to systemic administration of d-amphetamine: investigation of the involvement of dopamine, norepinephrine, and serotonin. Bergstrom DA, et al. **J Neurosci** 1981 Mar;1(3):292-9

The stimulus-induced release of unmetabolized 5-hydroxytryptamine from superfused rat brain synaptosomes. Collard KJ, et al. **J Neurosci Methods** 1981 Aug;4(2):163-79

Immobility test: effects of 5-hydroxytryptaminergic drugs and role of catecholamines in the activity of some antidepressants. Borsini F, et al. **J Pharm Pharmacol** 1981 Jan;33(1):33-7

(—)-m-Chlorophenyl-piperazine, a central 5-hydroxytryptamine agonist, is a metabolite of trazodone. Caccia S, et al. **J Pharm Pharmacol** 1981 Jul;33(7):477-8

A pre-junctional action of 5-hydroxytryptamine and methysergide on noradrenergic nerves in dog isolated saphenous vein. Watts AD, et al. **J Pharm Pharmacol** 1981 Aug;33(8):515-20

Substituted piperazines as central serotonin agonists: comparative specificity of the postsynaptic actions of quipazine and m-trifluoromethylphenylpiperazine. Fuller RW, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):636-41

Interaction of lithium and disulfiram in hexobarbital hypnosis: possible role of the 5-HT system. Minegishi A, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):481-7

Alteration of aminophylline-induced respiratory stimulation by perturbation of biogenic amine systems. Mueller RA, et al. **J Pharmacol Exp Ther** 1981 Sep;218(3):593-9

5-Hydroxytryptamine-induced hypothermia in rats as an in vivo model for the quantitative study of 5-hydroxytryptamine receptors. Cox B, et al. **J Pharmacol Methods** 1981 Jan;5(1):43-51

Dopamine independent rotational response to unilateral intranigral injection of serotonin. Oberlander C, et al. **Life Sci** 1981 Jun 8; 28(23):2595-601

Does high affinity [3H] imipramine binding label serotonin reuptake sites in brain and platelet? Paul SM, et al. **Life Sci** 1981 Jun 15; 28(24):2753-60

Effects of short- and long-term neuroleptic treatment on brain serotonin synthesis and turnover: focus on the serotonin hypothesis of schizophrenia. Rastogi RB, et al. **Life Sci** 1981 Aug 17;29(7):735-41

Electrophysiological evidence for the existence of separate receptor mechanisms mediating the action of 5-hydroxytryptamine. Berridge MJ. **Mol Cell Endocrinol** 1981 Jul;23(1):91-104

Immunoreactive substance P and serotonin present in the same dense-core vesicles. Pelletier G, et al. **Nature** 1981 Sep 3;293(5827):71-2

Further evidence for negative feedback control of serotonin release in the central nervous system. Baumann PA, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):36-43

The noradrenaline receptor coupled adenylate cyclase system in brain. Lack of modification by changes in the availability of serotonin. Mishra R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun; 316(3):218-24

Kinetic characteristics of newly synthesized 3H-5-HT in the brain of control and reserpinized mice. Evidence for the heterogeneous distribution of 5-HT in serotoninergic neurons. Morot-Gaudry Y, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jul;316(4):311-6

Liberation of catecholamines and 5-hydroxytryptamine from human blood-platelets. Peyer M, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):81-6

The filum terminale of the frog spinal cord, a nontransformed glial preparation: II. Uptake of serotonin. Ritchie T, et al. **Neurochem Res** 1981 Apr;6(4):441-52

Postmortem changes of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in mouse brain and their prevention by pargyline and microwave irradiation. Van Wijk M, et al. **Neurochem Res** 1981 Apr; 6(4):425-30

The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour. Carter CJ, et al. **Neuropharmacology** 1981 Mar; 20(3):261-5

Accelerated metabolism of probenecid during long-term treatment of rats with anticonvulsant drugs: effect on central serotonin turnover studies. Sharpless NS. **Neuropharmacology** 1981 Mar;20(3):211-6

Effect of injury to the serotoninergic and noradrenergic brain systems on food and defensive conditioned reflexes in rats. Gromova EA, et al. **Neurosci Behav Physiol** 1981 Jan-Feb;11(1):10-5

Brain levels of noradrenalin, dopamine, and serotonin in rats with different levels of motor activity. Semenova TP, et al. **Neurosci Behav Physiol** 1981 Mar-Apr;11(2):153-5

Serotonergic projections to the spinal cord from the midbrain in the rat: an immunocytochemical and retrograde transport study. Bowker RM, et al. **Neurosci Lett** 1981 Jul 17;24(3):221-6

The immunocytochemical localization of serotonergic neurons in the rat hypothalamus. Frankfurt M, et al. **Neurosci Lett** 1981 Jul 17; 24(3):227-32

Radioautographic study of uptake and storage of indoleamines in the rabbit enterochromaffin cells. Mourre C, et al. **Neurosci Lett** 1981 May 29;23(3):251-6

Visualization of serotonin neurones in the nodose ganglia of the cat. An autoradiographic study. Gaudin-Chazal G, et al. **Neuroscience** 1981; 6(6):1027-37

Release mechanisms of 5-HT from the gastrointestinal tract in rats. Izumikawa F. **Nippon Geka Hokan** 1980 Sep 1;49(5):572-94

Effects of serotonin and L-5-hydroxytryptophan on plasma renin activity in rats. Barney CC, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):895-900

Behavioral assessment of norepinephrine and serotonin function and interaction in the hippocampal formation. Gage FH, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):815-21

Peripheral conversion of L-5-hydroxytryptophan to serotonin induces drinking in rats. Kikta DC, et al. **Pharmacol Biochem Behav** 1981 Jun; 14(6):889-93

Brain serotonin metabolism in hibernation. Popova NK, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):773-7

Temperature preferences and the effect of changes in serotonin in maturing mice. Goodrich C, et al. **Physiol Behav** 1981 Jun; 26(6):1041-7

Effect of chloro-N-desmethyldiazepam on serum and brain tryptophan and serotonin in relation to the activity of central serotonergic neurons. Valzelli L, et al. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):37-42

Uterine serotonin and receptor blockade during estrogen-induced uterine hyperemia. Van Orden DE, et al. **Proc Soc Exp Biol Med** 1981 Sep; 167(4):469-74

The effect of multiple rising doses of Ro 11-2465 (serotonin uptake inhibitor) on serotonin content of human platelets. Lenehan T, et al.

Psychopharmacology (Berlin) 1981;74(1):1-3

Citalopram: a new potent inhibitor of serotonin (5-HT) uptake with central 5-HT-mimetic properties. Pawlowski L, et al. **Psychopharmacology (Berlin)** 1981;74(2):161-5

Circadian variation in the head twitch response produced by 5-methoxy-N1,N1-dimethyltryptamine and p-chloroamphetamine in the mouse. Singleton C, et al. **Psychopharmacology (Berlin)** 1981; 74(2):173-6

Evidence against the involvement of serotonergic mechanisms in wet dog shake behavior induced by carbachol chloride in rats. Turski L, et al. **Psychopharmacology (Berlin)** 1981;73(4):376-80

Release of immunoreactive serotonin into the lumen of the feline gut in response to vagal nerve stimulation. Ahlman H, et al. **Science** 1981 Sep 11;213(4513):1254-5

Lithium increases serotonin release and decreases serotonin receptors in the hippocampus. Treiser SL, et al. **Science** 1981 Sep 25; 213(4515):1529-31

5-hydroxytryptamine and adenine uptake by human blood platelets following the release reaction. Wesemann W, et al. **Thromb Res** 1981 Feb-Mar;21(4-5):367-74

[Serum transaminase activity (GOT and GPT) in rats injected with serotonin] Acunzo S, et al. **Boll Soc Ital Biol Sper** 1981 Jan 15; 57(1):76-9 (Eng. Abstr.) **(Ita)**

[Time course of blood glucose levels in rats after intraperitoneal injection of a dose of serotonin] Brizzi G, et al. **Boll Soc Ital Biol Sper** 1981 Apr 15;57(7):755-8 (Eng. Abstr.) **(Ita)**

[Blood and skin histamine and serotonin levels in rats following second degree burns] Nowik-Jurek M, et al. **Pol Tyg Lek** 1981 May 4; 36(18):631-5 (Eng. Abstr.) **(Pol)**

[Effect of various pharmacologic preparations on the viability of Chinese hamster fibroblasts in vitro] Beuverova EI, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):739-40 (Eng. Abstr.) **(Rus)**

[Role of neuronal and neuropile serotonin in the visual analyzer] Uzbekov MG, et al. **Biull Eksp Biol Med** 1981 Apr;91(4):389-90 (Eng. Abstr.) **(Rus)**

[Use of a 'Microvideomat' television analyzer to evaluate the functional state of a population of rat duodenal enterochromaffin cells] Zhukotskiĭ AV, et al. **Biull Eksp Biol Med** 1981 May;91(5):628-30 (Eng. Abstr.) **(Rus)**

[Desensitization of the isolated rat myometrium to biologically active substances] Bordunovskaia VP, et al. **Fiziol Zh SSSR** 1981 Mar; 67(3):390-7 (Eng. Abstr.) **(Rus)**

[Interstrain differences in the serotonin and 5-hydroxyindoleacetic acid levels in the postnatal ontogeny of C57BL/6J and BALB/cLac strain mice] Lobacheva II, et al. **Ontogenez** 1981;12(3):306-10 (Eng. Abstr.) **(Rus)**

[Participation of the brain serotoninergic system in creating the stress reactivity of the hypophyseal-adrenal axis] Popova NK, et al. **Ontogenez** 1981;12(4):382-9 (Eng. Abstr.) **(Rus)**

[Effect of disturbance of the liver and myocardium innervation on the histamine and serotonin contents in their tissues] Aksenova VM. **Ukr Biokhim Zh** 1980 Sep-Oct;52(5):569-72 (Eng. Abstr.) **(Rus)**

[Effects of certain biologically active compounds and bivalent cations on lactate and malate dehydrogenase activities in cerebral cellular fractions] Bdovichenko LM. **Ukr Biokhim Zh** 1981 May-Jun; 53(3):66-70 (Eng. Abstr.) **(Rus)**

[Effect of the biogenic amine serotonin on the participation of different cell populations in the immune response (IgM and IgG)] Idova GV, et al. **Vestn Akad Med Nauk SSSR** 1981;(5):39-41 (Eng. Abstr.) **(Rus)**

[Role of raphe nuceli in the development of somatosensory cortex neuronal activity in the kitten] Raevskiĭ VV. **Zh Vyssh Nerv Deiat** 1981; 31(2):349-57 (Eng. Abstr.) **(Rus)**

[The effect of beta-adrenoceptor blocking drugs on the release of 5-hydroxytryptamine from isolated mast cells (author's transl)] Drábiková K, et al. **Bratisl Lek Listy** 1981;76(1):52-60 (Eng. Abstr.) **(Slo)**

SEX BEHAVIOR, ANIMAL

Conspecific odor preferences of male albino rats are reversed by intracerebral 6-hydroxydopamine. Cornwell-Jones CA. **Brain Res** 1981 Jun 1;213(2):379-85

Persistence of dihydrotestosterone inhibition of lordosis in estrogen-primed rats fed a tryptophan-deficient diet. Menniti FS, et al. **Brain Res Bull** 1981 Jul;7(1):1-4

Endocrine and behavioral effects of continuous exposure of male rats to a potent luteinizing hormone-releasing hormone (LHRH) agonist: evidence for central nervous system actions of LHRH. Dorsa DM, et al. **Endocrinology** 1981 Sep;109(3):729-35

Comparison of the effects of beta-endorphin and morphine on exploratory and socio-sexual behaviour in the male rat. Meyerson BJ. **Eur J Pharmacol** 1981 Feb 19;69(4):453-63

Estrogen facilitation of lordosis behavior in the female rat. Gorski RA, et al. **Exp Brain Res** 1981;Suppl 3:222-37

The effects of lesions of lateral tegmental noradrenergic neurons on components of sexual behavior and pseudopregnancy in female rats. Hansen S, et al. **Neuroscience** 1981;6(6):1105-17

Facilitation of mounting behavior in male rats by intracranial injections of luteinizing hormone-releasing hormone. Dorsa DM, et al. **Regul Pept** 1980 Oct;1(2):147-55

SLEEP

Suppression of active sleep by chronic treatment with chlorimipramine during early postnatal development: effects upon adult sleep and behavior in the rat. Mirmiran M, et al. **Brain Res** 1981 Jan 5; 204(1):129-46

Studies of diurnal changes in plasma renin activity, and plasma noradrenaline, aldosterone and cortisol concentrations in man. Lightman SL, et al. **Clin Endocrinol (Oxf)** 1981 Mar;14(3):213-23

Effect of a short-acting benzodiazepine on brain electrical activity during sleep. Johnson LC, et al. **Electroencephalogr Clin Neurophysiol** 1981 Jul;52(1):89-97

Effect of monoamine oxidase inhibitors on codeine disposition and pentobarbitone sleep-times in the rat. Findlay JW, et al. **J Pharm Pharmacol** 1981 Jan;33(1):45-7

Interaction of lithium and disulfiram in hexobarbital hypnosis: possible role of the 5-HT system. Minegishi A, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):481-7

Phasic activity induced by p-chlorophenylalanine in the auditory pathway. Ayala-Guerrero F, et al. **Neuropharmacology** 1981 Mar; 20(3):273-5

Dose-related effects of flurazepam on human sleep-walking patterns. Karacan I, et al. **Psychopharmacology (Berlin)** 1981;73(4):332-9

Does para-chlorophenylalanine produce disturbed waking, disturbed sleep or activation by ponto-geniculo-occipital waves in cats? Ursin R. **Waking Sleeping** 1980 Jul-Sep;4(3):211-21

[Physiological and pharmacological study of the regulation of sleep in rats] Borbély AA. **Actual Pharmacol (Paris)** 1981;33:91-104 **(Fre)**

[Effects of the intraventricular injection of methiothepin and methergoline on the sleep of rats] Laguzzi R. **C R Soc Biol (Paris)** 1981; 175(2):160-3 (Eng. Abstr.) **(Fre)**

[Current concepts of the mechanisms of regulation and target function of sleep] Moiseeva NI. **Usp Fiziol Nauk** 1981 Jun-Sep;12(3):86-105 (197 ref.) **(Rus)**

SLEEP DEPRIVATION

REM sleep deprivation induces subsensitivity of dopamine receptors mediating sedation in rats. Serra G, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):131-5

Paradoxical sleep deprivation and performance of an active avoidance task: impairment of c57BR mice and no effect in c57BL/6 mice. Kitahama K, et al. **Physiol Behav** 1981 Jul;27(1):41-50

Sleep deprivation: effects on circadian rhythms of rat brain neurotransmitter receptors. Wirz-Justice A, et al. **Psychiatry Res** 1981 Aug;5(1):67-76

[Inhibitory effect of phenazepam on protein and RNA catabolism in the supraoptic nucleus during REM-sleep deprivation] Demin NN, et al. **Fiziol Zh SSSR** 1981 Mar;67(3):460-3 **(Rus)**

SLEEP, REM

Differential effect of REM stimulating and REM inhibiting drugs (reserpine and amitriptylin) on memory. Faber J, et al. **Act Nerv Super (Praha)** 1981 Jun;23(2):169-71

REM sleep deprivation induces subsensitivity of dopamine receptors mediating sedation in rats. Serra G, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):131-5

Paradoxical sleep deprivation and performance of an active avoidance task: impairment of c57BR mice and no effect in c57BL/6 mice. Kitahama K, et al. **Physiol Behav** 1981 Jul;27(1):41-50

Post-learning paradoxical sleep, reticular activation and noradrenergic activity. Leconte P, et al. **Physiol Behav** 1981 Apr;26(4):587-94

SODIUM

Sodium and water transport in frog skin: effect of indomethacin. Bartha J, et al. **Acta Physiol Acad Sci Hung** 1981;57(1):9-17

Epidermal growth factor stimulates monovalent cation transport in isolated rat hepatocytes. Fehlmann M, et al. **Biochem Biophys Res Commun** 1981 May 15;100(1):254-60

Sodium ion and the effect of acetylcholine on phospholipid and phosphoprotein phosphate turnover in the rabbit iris smooth muscle. Abdel-Latif AA. **Biochem Pharmacol** 1981 Jun 1;30(11):1571-4

Tests of an electrostatic screening hypothesis of the inhibition of neurotransmitter release by cations at the frog neuromuscular junction. Misler S, et al. **Biophys J** 1980 Jul;31(1):9-30

Sodium-dependent relaxation in arterial smooth muscle. Gillespie MN, et al. **Clin Exp Pharmacol Physiol** 1981 May/June;8(3):209-14

Effect of hypertonic and hypotonic infusions on aldosterone in conscious sodium-depleted dogs. Childers JW, et al. **Clin Sci** 1981 Aug; 61(2):191-9

Inner medullary osmolality and sodium concentration are decreased in rats during escape from DOCA-induced salt retention. Düsing R, et al. **Clin Sci** 1981 Apr;60(4):467-9

Sodium dependency of [3H]imipramine binding in rat cerebral cortex. Briley M, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):377-80

The effect of noradrenaline on Na-K transport in rat cerebral cortical slices. Wu PH, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):529-31

Dependence on Na+ of kinetics of the lenticular Na+, K+-activated ATPase. Kern HL, et al. **Exp Eye Res** 1981 Jun;32(6):789-92

Effects of sodium loading, desoxycorticosterone acetate, and corticosterone on urinary kallikrein excretion. Bönner G, et al. **Horm Res** 1981;14(2):87-94

The activity of the lithium--sodium countertransport system in erythrocytes in depression and mania. Rybakowski J, et al. **J Affective Disord** 1981 Mar;3(1):59-64

Inhibitory effects of sodium and other monovalent cations on human platelet adenylate cyclase. Steer ML, et al. **J Biol Chem** 1981 Oct 10;256(19):9990-3

Further studies of hormone-sensitive sodium and potassium transport in red cells from developing chick embryos. Shanbaky NM, et al. **J Cell Physiol** 1981 May;107(2):303-8

Effect of reduced extracellular sodium concentration on the function of adrenal zona glomerulosa: studies in conscious rats. Balla T, et al. **J Endocrinol** 1981 Jun;89(3):411-6

Dependence of water movement on sodium transport in kidney proximal tubule: a microperfusion study substituting lithium for sodium. Corman B, et al. **J Membr Biol** 1981;62(1-2):105-11

Effects of sodium and bicarbonate ions on gamma-aminobutyric acid receptor binding in synaptic membranes of rat brain. Kurioka S, et al. **J Neurochem** 1981 Aug;37(2):418-21

Sidedness of the effects of sodium and potassium ions on the conformational state of the sodium-potassium pump. Karlish SJ, et al. **J Physiol (Lond)** 1981 Mar;312:505-29

Comparison between (RS)-nipecotic acid and GABA transport in cultured astrocytes: coupling with two sodium ions. Larsson OM, et al. **Neurochem Res** 1981 Mar;6(3):257-66

Endogenous inhibitors of Na+-independent [3H]GABA binding to crude synaptic membranes. Massotti M, et al. **Neurochem Res** 1981 May;6(5):551-65

Activation of active Na transport in sheep Purkinje fibres by external K or Rb ions. Glitsch HG, et al. **Pflugers Arch** 1981 Jul;391(1):28-34

Effect of lithium intake on sodium and lithium appetite in sodium deficient cattle. Sly J, et al. **Physiol Behav** 1981 Jul;27(1):147-52

Role of cytosolic calcium and sodium-calcium exchange in regulation of transepithelial sodium and water absorption. Taylor A. **Soc Gen Physiol Ser** 1981;36:233-59 (117 ref.)

[Histochemical localization of Na+, K+-ATPase in rat submandibular gland. The effects of mineralocorticoid and sodium ion (author's transl)] Kida T, et al. **Josai Shika Daigaku Kiyo** 1980;(9):155-8 (Eng. Abstr.) **(Jpn)**

[Changes in the alkaline cation transport across the plasma membrane of CHO-K1 cell lines resistant to ethidium bromide] Marakhova II, et al. **Tsitologiia** 1981 Apr;23(4):410-8 (Eng. Abstr.) **(Rus)**

SOMATOFORM DISORDERS

[Depression in rheumatic diseases or somatic symptoms in depression] Carrière B. **Fortschr Med** 1981 Aug 27;99(31-32):1226-30 (Eng. Abstr.) **(Ger)**

SOMATOTROPIN RELEASE INHIBITING HORMONE

Biosynthesis of somatostatin in pancreatic islets of Wistar rats and its regulation by glucose. Zühlke H, et al. **Acta Biol Med Ger** 1981;40(1):99-103

Stimulation of gastrin and somatostatin secretion from the isolated rat stomach by bombesin. DuVal JW, et al. **Am J Physiol** 1981 Sep;241(3):G242-7

Effects of somatostatin on intestinal calcium transport in the rat. Favus MJ, et al. **Am J Physiol** 1981 Sep;241(3):G215-21

Studies on the inhibition of pancreatic secretion by luminal somatostatin. Konturek SJ, et al. **Am J Physiol** 1981 Aug;241(2):G109-15

Concerning the possible existence of somatostatinergic local neuronal circuits in the rats cerebral cortex. Dorn A, et al. **Anat Anz** 1981;149(2):185-7

On the low energy solution conformation of somatostatin. Arison BH, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):1148-53

Somatostatin is a potent activator of phosphoprotein phosphatases in the digestive tract. Reyl F, et al. **Biochim Biophys Acta** 1981 Jul;675(2):297-300

Somatostatin-28: a conformational analysis. Wünsch E, et al. **Biopolymers** 1981 Aug;20(8):1741-5

The regional distribution of somatostatin, substance P and neurotensin in human brain. Cooper PE, et al. **Brain Res** 1981 Aug 10;218(1-2):219-32

Noradrenaline stimulates somatostatin release from incubated slices of the amygdala and the hypothalamic preoptic area. Epelbaum J, et al. **Brain Res** 1981 Jun 29;215(1-2):393-7

Release of somatostatin from extra-hypothalamic rat brain slices: inhibition by dopamine and morphine. Lee CM, et al. **Brain Res** 1981 Aug 31;219(2):355-61

Chromatographic behaviour and post-mortem stability of somatostatin in the rat and mouse brain. Lee CM, et al. **Brain Res** 1981 Sep 7;220(1):159-66

Monosodium glutamate: acute and chronic effects on rhythmic growth hormone and prolactin secretion, and somatostatin in the undisturbed male rat. Terry LC, et al. **Brain Res** 1981 Jul 27;217(1):129-42

Comparative immunocytochemical localization of enkephalin and somatostatin in the median eminence, hypothalamus and adjacent areas of the guinea-pig brain. Tramu G, et al. **Brain Res** 1981 Jun 29;215(1-2):235-55

Inhibition of anterior pituitary prostaglandin-stimulated adenylyl cyclase activity by somatostatin. Rouleau D, et al. **Can J Biochem** 1981 Apr;59(4):307-10

Somatostatin-immunoreactive fiber projections into the brain stem and the spinal cord of the rat. Krisch B. **Cell Tissue Res** 1981;217(3):531-52

Electron-microscopic immunocytochemical demonstration of separate vasotocinergic, mesotocinergic and somatostatinergic neurons in the hypothalamic magnocellular preoptic nucleus of the frog. Van Vossel-Daeninck J, et al. **Cell Tissue Res** 1981;218(1):7-12

Glucose disposal is not proportional to plasma glucose level in man. Best JD, et al. **Diabetes** 1981 Oct;30(10):847-50

Radioimmunoassay of human plasma somatostatin. Mackes K, et al. **Diabetes** 1981 Sep;30(9):728-34

Somatostatin: mechanism of action in pancreatic islet beta-cells. Pace CS, et al. **Diabetes** 1981 Oct;30(10):836-42

Insulin and glucagon breakthrough of somatostatin suppression: importance of portal vein hormone measurements. Polonsky K, et al. **Diabetes** 1981 Aug;30(8):664-9

Effects of growth hormone excess and deficiency on hypothalamic somatostatin content and release and on tissue somatostatin distribution. Berelowitz M, et al. **Endocrinology** 1981 Sep;109(3):714-9

Potent, highly selective inhibition of growth hormone secretion by position 4 somatostatin analogs. Murphy WA, et al. **Endocrinology** 1981 Aug;109(2):491-5

Somatostatin release from rat hypothalamus in vitro: effects of melatonin and serotonin. Richardson SB, et al. **Endocrinology** 1981 Aug;109(2):602-6

Combined effects of cold and somatostatin on glucose kinetics in dogs. Minaire Y, et al. **Eur J Applied Physiol** 1981;46(3):249-59

The effect of SST, glucagon, calcitonin and PGE1 on exocrine pancreatic secretion in the unrestrained dog in long-term experiments. Funovics J, et al. **Eur Surg Res** 1981;13(3):213-26

Substance P, vasoactive intestinal polypeptide (VIP) and somatostatin levels in ocular tissue of normal and sensorily denervated rabbit eyes. Unger WG, et al. **Exp Eye Res** 1981 Jun;32(6):797-801

Rapid conversion of somatostatin to active metabolite in human plasma. Märki F, et al. **FEBS Lett** 1981 May 5;127(1):22-4

Hypothalamic peptides: central nervous system control of visceral functions. Brown M, et al. **Fed Proc** 1981 Sep;40(11):2565-9 (32 ref.)

Somatostatin inhibition of glucagon-stimulated jejunal secretion in the dog. Barbezat GO, et al. **Gastroenterology** 1981 Sep;81(3):471-4

Somatostatin inhibition of basal and carbachol-stimulated gastrin release in rat antral organ culture. Harty RF, et al. **Gastroenterology** 1981 Oct;81(4):707-12

Somatostatin 28: comparison with somatostatin 14 for plasma kinetics and low-dose effects on the exocrine pancreas in dogs. Vaysse N, et al. **Gastroenterology** 1981 Oct;81(4):700-6

Somatostatin immunoreactive neurons and fibers in the hypothalamus of the newt. Fasolo A, et al. **Gen Comp Endocrinol** 1981 Jun;44(2):256-63

Comparative investigations of human and porcine somatotropin. Schleyer M, et al. **Hoppe Seylers Z Physiol Chem** 1981 Jul;362(7):875-81

Somatostatin action on insulin secretion induced by chicken and porcine vasoactive intestinal peptide in the perfused rat pancreas. Arilla E, et al. **Horm Metab Res** 1981 Jun;13(6):314-7

Development of a sensitive somatostatin radioimmunoassay and its application to plasma of stressed and non-stressed rats. Engelhardt W, et al. **Horm Metab Res** 1981 Jun;13(6):318-23

Isolation and structure of a peptide hormone predicted from a mRNA sequence. A second somatostatin from the catfish pancreas. Andrews PC, et al. **J Biol Chem** 1981 Aug 25;256(16):8267-70

Evidence for somatostatin precursors in human stomach, placenta, and amniotic fluid. Fitz-Patrick D, et al. **J Clin Endocrinol Metab** 1981 Aug;53(2):372-6

Physiological concentrations of growth hormone exert insulin-like and insulin antagonistic effects on both hepatic and extrahepatic tissues in man. MacGorman LR, et al. **J Clin Endocrinol Metab** 1981 Sep;53(3):556-9

Plasma somatostatin-like immunoreactivity during the interdigestive period in the dog. Aizawa I, et al. **J Clin Invest** 1981 Jul; 68(1):206-13

Correlation of endogenous somatostatin, gastric inhibitory polypeptide, glucagon and insulin with gastric function in the conscious calf. Bell FR, et al. **J Endocrinol** 1981 Jun;89(3):451-6

Influence of the sympatho-adrenal system and somatostatin on the secretion of insulin in the rat. Ahrén B, et al. **J Physiol (Lond)** 1981 Mar;312:563-75

High affinity binding sites for a somatostatin-28 analog in rat brain. Reubi JC, et al. **Life Sci** 1981 May 11;28(19):2191-8

Effect of prostaglandin E2 upon release of pancreatic somatostatin-like immunoreactivity. Schusdziarra V, et al. **Life Sci** 1981 May 11; 28(19):2099-102

The effect of ventromedial hypothalamic nuclei destruction on somatostatin and insulin release from the isolated perfused rat pancreas. Seino S, et al. **Life Sci** 1981 May 18;28(20):2231-6

Somatostatin modulates effects of angiotensin II in adrenal glomerulosa zone. Aguilera G, et al. **Nature** 1981 Jul 16;292(5820):262-3

Effect of chemical environment on levels of substance P and somatostatin in cultured sensory neurones. Mudge AW. **Nature** 1981 Aug 20; 292(5825):764-7

A potent cyclic hexapeptide analogue of somatostatin. Veber DF, et al. **Nature** 1981 Jul 2;292(5818):55-8

Effect of capsaicin pretreatment on capsaicin-evoked release of immunoreactive somatostatin and substance P from primary sensory neurons. Gamse R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):38-41

Age-related changes in dopamine, LHRH and somatostatin in the rat hypothalamus. Hoffman GE, et al. **Neurobiol Aging** 1980 Summer; 1(1):27-37

Differential effects of somatostatin on the release of bioactive and immunoactive rat growth hormone in vitro. Russell SM. **Neuroendocrinology** 1981 Aug;33(2):67-72

Effects of CNS active drugs and somatostatin antiserum on growth hormone release in young and old male rats. Sonntag WE, et al. **Neuroendocrinology** 1981 Aug;33(2):73-8

Effects of intraventricular administration of neurotensin and somatostatin on thermoregulation in the rat. Chandra A, et al. **Neuropharmacology** 1981 Jul;20(7):715-8

Pharmacological characterization of scratching behaviour induced by intracranial injection of substance P and somatostatin. Dobry PJ, et al. **Neuropharmacology** 1981 Mar;20(3):267-72

New somatostatin-containing sites in the diencephalon of the neonatal rat. Shiosaka S, et al. **Neurosci Lett** 1981 Aug 7;25(1):69-73

Somatostatin-like immunoreactivity in the facial, glossopharyngeal and vagal lobes of the carp. Tohyama M, et al. **Neurosci Lett** 1981 Jul 17; 24(3):233-6

Neurotensin-like and somatostatin-like immunoreactivity within amacrine cells of the retina. Brecha N, et al. **Neuroscience** 1981;6(7):1329-40

Somatostatin receptors: identification and characterization in rat brain membranes. Srikant CB, et al. **Proc Natl Acad Sci USA** 1981 Jun; 78(6):3930-4

High biological activity of the synthetic replicates of somatostatin-28 and somatostatin-25. Brazeau P, et al. **Regul Pept** 1981 Jan;1(4):255-64

Structure-activity studies with somatostatin: the role of tryptophan in position 8. Hirst BH, et al. **Regul Pept** 1980 Oct;1(2):97-113

The effect of somatostatin and 16,16-dimethyl-prostaglandin E2 on bombesin-stimulated canine gastric acid, plasma gastrin and pancreatic polypeptide secretion. Materia A, et al. **Regul Pept** 1981 Jan; 1(4):297-305

Motilin release by intravenous infusion of nutrients and somatostatin in conscious dogs. Mori K, et al. **Regul Pept** 1981 Jan;1(4):265-70

Effect of bombesin upon plasma somatostatin-like immunoreactivity, insulin and glucagon in normal and chemically sympathectomized dogs. Schusdziarra V, et al. **Regul Pept** 1980 Oct;1(2):89-96

Is somatostatin or a somatostatin-like peptide involved in central nervous system control of gastric secretion? Taché Y, et al. **Regul Pept** 1981 Feb;1(5):307-15

Depolarization- and ionophore-induced release of octacosa somatostatin from stalk median eminence synaptosomes. Kewley CF, et al. **Science** 1981 Aug 21;213(4510):913-5

[Comparison of the in vivo biological activity of an analog of somatostatin, D-Trp8-D-Cys14-somatostatin in 2 different pharmacological models] Cazaubon C, et al. **C R Soc Biol (Paris)** 1981;175(2):200-7 (Eng. Abstr.) (Fre)

[Immunocytochemical evidence of somatostatin fibers in the neurohypophysis of the monkey Macacus irus] Girod C, et al. **C R Trav Lab Carlsberg** 1981;175(3):347-51 (Eng. Abstr.) (Fre)

[Total synthesis of somatostatin-28 (author's transl)] Moroder L, et al. **Hoppe Seylers Z Physiol Chem** 1981 Jun;362(6):697-716 (Eng. Abstr.) (Ger)

[In vitro role of some entero-insular hormones on peripheral insulin receptors] Zandomeneghi R, et al. **Boll Soc Ital Biol Sper** 1981 Apr 15;57(7):723-9 (Eng. Abstr.) (Ita)

SOMATOTROPIN RELEASING HORMONE

Inhibition of hypothalamic GnRH synthesis by inhibin. Moodbidri SB, et al. **Experientia** 1981 May 15;37(5):525-6

Evidence for a growth hormone releasing factor mediating alpha-adrenergic influence on growth hormone secretion in the rat. Eden S, et al. **Neuroendocrinology** 1981 Jul;33(1):24-7

SPACE PERCEPTION

GABA-antagonists and spatial summation in Y-type cat retinal ganglion cells. Kirby AW, et al. **J Physiol (Lond)** 1981 Mar;312:335-44

STARTLE REACTION

Pentylenetetrazol-induced enhancement of reticular formation auditory evoked potentials and acoustic startle responses in the cat. Faingold CL, et al. **Neuropharmacology** 1981 Aug;20(8):787-9

Effects of alpha-MSH and beta-endorphin on startle reflex in rat. Hoehler FK, et al. **Peptides (Fayetteville)** 1981;2 Suppl 1:137-41

Effects of 6-hydroxydopamine lesions of locus coeruleus on startle in rats. Adams LM, et al. **Psychopharmacology (Berlin)** 1981; 73(4):394-8

STEREOTYPED BEHAVIOR

Barrel rotation induced by vasopressin and involvement of dopaminergic and cholinergic functions in rats. Yamada K, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):88-94

Amphetamine behavioral toxicity: rotational behavior after chronic intrastriatal infusion. Dougherty GG Jr, et al. **Biol Psychiatry** 1981 May; 16(5):479-88

Role of dorsal mesencephalic reticular formation and deep layers of superior colliculus as out-put stations for turning behaviour elicited from the substantia nigra pars reticulata. Imperato A, et al. **Brain Res** 1981 Jul 20;216(2):437-43

Behavioural effects of cathinone, an amine obtained from Catha edulis Forsk.: comparisons with amphetamine, norpseudoephedrine, apomorphine and nomifensine. Zelger JL, et al. **Bull Narc** 1980; 32(3):67-81

Apomorphine-induced stereotypy in mature and senescent rats following cessation of chronic haloperidol treatment. Roffman M, et al. **Commun Psychopharmacol** 1980;4(4):283-6

Endogenous hyperprolactinaemia enhances amphetamine- and apomorphine-induced stereotypy. Drago F, et al. **Eur J Pharmacol** 1981 Jun 19;72(2-3):249-53

Relation between brain catecholamine receptors and dopaminergic stereotypy in rat strains. Helmeste DM, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):465-70

Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice. Joshi VV, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):499-502

Differential effects of dopamine agonists in mature and immature rats. McDevitt JT, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):69-75

Sequelae of 6 months continuous administration of cis(Z)-and trans(E)-flupenthixol in the rat. Waddington JL, et al. **Eur J Pharmacol** 1981 Feb 19;69(4):511-3

Effects of microinjection of 2-chloro-11 (2-dimethylaminoethoxy)-dibenzo[b,f]-thiepine (zotepine), thioridazine and haloperidol into the striatum and nucleus accumbens on stereotypic behaviour and motor activity. Lai H, et al. **J Pharm Pharmacol** 1981 Apr;33(4):252-4

Further studies on the potentiating effect of lithium chloride on methamphetamine-induced stereotypy in mice. Miyauchi T, et al. **Jpn J Pharmacol** 1981 Feb;31(1):61-8

The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour. Carter CJ, et al. **Neuropharmacology** 1981 Mar; 20(3):261-5

Effects of chronic haloperidol, thioridazine and zotepine treatment on apomorphine elicited stereotypic behavior and 3H-spiroperidol binding sites in the striatum of the rat. Lai HC, et al. **Proc West Pharmacol Soc** 1981;24:5-6

[Tiapride and verbal or motor stereotypies (author's transl)] Morel-Maroger A. **Sem Hop Paris** 1981 Apr 18-25;57(15-16):825-9 (Eng. Abstr.) (Fre)

STRESS, PSYCHOLOGICAL

Habitual catecholamine excretion and its relation to habitual distress. Forsman L. **Biol Psychol** 1980 Sep;11(2):83-97

Endogenous alpha-melanotropin and central dopamine systems in physical and psychological stress. Monnet F, et al. **Exp Brain Res** 1981; 42(2):203-11

The influence of foot-shock stress upon brain, pituitary and spinal cord pools of immunoreactive dynorphin in rats. Millan MJ, et al. **Neurosci Lett** 1981 Jun 12;24(1):75-9

Effects of nortriptyline treatment on learned helplessness in the rat. Telner

JI, et al. **Pharmacol Biochem Behav** 1981 Jun;14(6):823-6

Corticosterone response in group-housed rats exposed to psychogenic stresses in different social conditions. Armario A, et al. **Physiol Behav** 1981 Jul;27(1):179-81

Humoral indices of stress in rats. Natelson BH, et al. **Physiol Behav** 1981 Jun;26(6):1049-54

Relationships between sex-related psychological characteristics during adolescence and catecholamine excretion during achievement stress. Rauste-von Wright M, et al. **Psychophysiology** 1981 Jul;18(4):362-70

The stress of boredom and monotony: a consideration of the evidence. Thackray RI. **Psychosom Med** 1981 Apr;43(2):165-76

[Influence of the GABAergic system on eating behavior induced by the tail pinching technic in rats] Bereksi B, et al. **C R Trav Lab Carlsberg** 1981;175(3):323-9 (Eng. Abstr.) **(Fre)**

[Emotional stress and biochemical responses of completely recovered manic depressive patients (author's transl)] Nakahara T. **Seishin Shinkeigaku Zasshi** 1981;83(5):263-74 **(Jpn)**

[Plasma catecholamines of August and Wistar strain rats subjected to emotional stress] Kvetnanskiĭ R, et al. **Fiziol Zh SSSR** 1981 Apr; 67(4):516-23 (Eng. Abstr.) **(Rus)**

[Changes in the plasma renin activity of Wistar and August rats during emotional stress] Kvetnanskiĭ R, et al. **Fiziol Zh SSSR** 1981 Jun; 67(6):911-5 **(Rus)**

SUBSTANCE P

Contractile response of longitudinal and circular smooth muscles of guinea pig stomach and ileum to substance P. Nieber K, et al. **Acta Biol Med Ger** 1981;40(2):209-16

Tissue concentration and release of substance P-like immunoreactivity in the dental pulp. Brodin E, et al. **Acta Physiol Scand** 1981 Feb; 111(2):141-9

The role of substance P in simultaneously mediating oral pain and inflammation. Goodale DB. **Anesth Prog** 1981 Mar-Apr;28(2):41-3

Effect of substance P C-terminal heptapeptide on amylase release in rat parotid gland. Togari A, et al. **Arch Oral Biol** 1980;25(8-9):597-600

Substance P binds to the formylpeptide chemotaxis receptor on the rabbit neutrophil. Marasco WA, et al. **Biochem Biophys Res Commun** 1981 Apr 30;99(4):1065-72

Inverse relation of substance P-like immunoreactivity in dorsal raphe nucleus to serotonin levels in pons-medulla following administration of cocaine and 5-hydroxytryptophan. Pradhan S, et al. **Biochem Pharmacol** 1981 May 15;30(10):1071-6

The effects of chronic section of dorsal roots on the responsiveness of motoneurones to 5-hydroxytryptamine and a substance P analogue. Roberts MH, et al. **Br J Pharmacol** 1981 Jul;73(3):589-94

Enkephalins, substance P, bradykinin and angiotensin II: differential sites of action on the hypothalamo-neurohypophysial system. Baertschi AJ, et al. **Brain Res** 1981 Sep 7;220(1):107-19

The regional distribution of somatostatin, substance P and neurotensin in human brain. Cooper PE, et al. **Brain Res** 1981 Aug 10; 218(1-2):219-32

5-Hydroxytryptamine reduces substance P responses on dorsal horn interneurones: a possible interaction of neurotransmitters. Davies JE, et al. **Brain Res** 1981 Aug 3;217(2):399-404

Chemical characterization of substance P-like immunoreactivity in primary afferent neurones. Harmar A, et al. **Brain Res** 1981 Sep 7; 220(1):203-7

Tissue distribution of substance P in the domestic pig during postnatal development. Holzer P, et al. **Brain Res** 1981 Jun;227(3):455-9

Intrathecal substance P elicits a caudally-directed biting and scratching behavior in mice. Hylden JL, et al. **Brain Res** 1981 Jul 27; 217(1):212-5

Substance P-induced depolarization in sympathetic neurons: not simple K-inactivation. Minota S, et al. **Brain Res** 1981 Jul 6;216(1):224-8

A substance P projection to the hippocampus. Vincent SR, et al. **Brain Res** 1981 Jun 29;215(1-2):349-51

Substance P, vasoactive intestinal polypeptide (VIP) and somatostatin levels in ocular tissue of normal and sensorily denervated rabbit eyes. Unger WG, et al. **Exp Eye Res** 1981 Jun;32(6):797-801

Further support for the postsynaptic action of substance P and its blockade with baclofen in neurons of the guinea-pig hypothalamus in vitro. Ogata N, et al. **Experientia** 1981 Jul 15;37(7):759-61

Immunoreactivity for substance P in the Gasserian ganglion, ophthalmic nerve and anterior segment of the rabbit eye. Tervo K, et al. **Histochem J** 1981 May;13(3):435-43

Origin and development of VIP and substance P containing neurons in the embryonic avian gut. Fontaine-Perus J, et al. **Histochemistry** 1981; 71(3):313-23

Substance P-like immunoreactivity in the nervous system of hydra. Grimmelikhuijzen CJ, et al. **Histochemistry** 1981;71(3):325-33

Substance P-like immunoreactive nerve fibers in the trabecular meshwork. Laties AM, et al. **Invest Ophthalmol Vis Sci** 1981 Sep;21(3):484-6

Organization of substance P fibers within the hippocampal formation demonstrated with a biotin-avidin immunoperoxidase technique. Vincent SR, et al. **J Comp Neurol** 1981 Jun 10;199(1):113-23

Peptidergic innervation (substance P) in the human heart. Weihe E, et al. **J Mol Cell Cardiol** 1981 Mar;13(3):331-3

Neuropeptides in striato-nigral pathways. Cuello AC, et al. **J Neural Transm** 1981;51(1-2):83-96

Haloperidol-induced reduction of nigral substance P-like immunoreactivity: a probe for the interactions between dopamine and substance P neuronal systems. Hanson GR, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):568-74

Neurochemical studies in the hypoxic brain: substance P, met-enkephalin, GABA and angiotensin converting enzyme. Arregui A, et al. **Life Sci** 1981 Jun 29;28(26):2925-9

A synthetic peptide as an antagonist of substance P. Engberg G, et al. **Nature** 1981 Sep 17-23;293(5829):222-3

Effect of chemical environment on levels of substance P and somatostatin in cultured sensory neurones. Mudge AW. **Nature** 1981 Aug 20; 292(5825):764-7

Immunoreactive substance P and serotonin present in the same dense-core vesicles. Pelletier G, et al. **Nature** 1981 Sep 3;293(5827):71-2

Release of histamine by substance P. Erjavec F, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug;317(1):67-70

Effect of capsaicin pretreatment on capsaicin-evoked release of immunoreactive somatostatin and substance P from primary sensory neurons. Gamse R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb;316(1):38-41

Time course of capsaicin-induced functional impairments in comparison with changes in neuronal substance P content. Lembeck F, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Jun;316(3):240-3

Pharmacological characterization of scratching behaviour induced by intracranial injection of substance P and somatostatin. Dobry PJ, et al. **Neuropharmacology** 1981 Mar;20(3):267-72

Demonstration of a substance P-like immunoreactivity in retinal cells of the rat. Fukuda M, et al. **Neurosci Lett** 1981 May 29;23(3):239-42

Effects of substance P on neurones and glial cells in cultured rat spinal cord. Hösli L, et al. **Neurosci Lett** 1981 Jul 2;24(2):165-8

Activation by stress of the habenulo-interpeduncular substance P neurons in the rat. Lisoprawski A, et al. **Neurosci Lett** 1981 Aug 7; 25(1):47-51

Substance P immunoreactive sensory nerves supply the rat iris and cornea. Miller A, et al. **Neurosci Lett** 1981 May 29;23(3):243-9

Substance P immunoreactive nerves in the rodent cornea. Tervo K, et al. **Neurosci Lett** 1981 Aug 7;25(1):95-7

Correlation between Met-enkephalin and substance P immunoreactivity in the primate globus pallidus. Haber S, et al. **Neuroscience** 1981; 6(7):1291-7

Regional differences in the response to substance P on the longitudinal muscle and the concentration of substance P in the digestive tract of the guinea-pig. Holzer P, et al. **Neuroscience** 1981;6(7):1433-41

Substance P and leucine-enkephalin changes after chordotomy and morphine treatment. Naftchi NE, et al. **Peptides (Fayetteville)** 1981; 2 Suppl 1:61-70

Substance P-like immunoreactivity in plasma of psychotic patients and effects of neuroleptics and electroconvulsive therapy. Kaiya H, et al. **Psychiatry Res** 1981 Aug;5(1):11-21

Neurotensin and substance P: differential effects on plasma cholesterol levels in conscious ovariectomized rats. Raju K, et al. **Regul Pept** 1981 Aug;2(4):265-74

Distinct classes of substance P receptors revealed by a comparison of the activities of substance P and some of its segments. Teichberg VI, et al. **Regul Pept** 1981 Feb;1(5):327-33

Peptide containing nerves in the nasal mucosa. Uddman R, et al. **Rhinology** 1981 Jun;19(2):75-9

Substance P in principal sympathetic neurons: regulation by impulse activity. Kessler JA, et al. **Science** 1981 Oct 16;214(4518):335-6

[The morphology of substance P in the human brain as determined by an immuno-histo-fluorescence study] Constantinidis J, et al. **Schweiz Arch Neurol Neurochir Psychiatr** 1980;127(2):323-55 (Eng. Abstr.) **(Fre)**

[The effect of substance P on the regeneration of nerve fibres in vitro (author's transl)] Lindner G, et al. **Z Mikrosk Anat Forsch** 1981; 95(3):390-4 (Eng. Abstr.) **(Ger)**

[Phospholipid metabolism in acetylcholine and substance P induced desensitization of guinea pig ileum smooth muscle] Minenko AN, et al. **Ukr Biokhim Zh** 1980 Sep-Oct;52(5):577-81 (Eng. Abstr.) **(Rus)**

SYMPATHOMIMETICS

Vascular responses to REN-293 (2-amino-3[3, 5-dihydroxyphenyl]-1-propanol hydrochloride)—a new sympathomimetic agent. Frost BR, et al. **Aust J Exp Biol Med Sci** 1981 Apr;59(Pt 2):179-82

Effects of adrenergic agonists and antagonists and of the catechol nucleus on the Na+, K+-ATPase and Mg2+-ATPase activities of synaptosomes. Sawas AH, et al. **Biochem Pharmacol** 1981 Jul 1; 30(13):1799-803

Gluconeogenesis in rabbit liver. IV. The effects of glucagon, epinephrine, alpha- and beta-adrenergic agents on gluconeogenesis and pyruvate kinase in hepatocytes given dihydroxyacetone or fructose. Yorek MA, et al. **Biochim Biophys Acta** 1981 Jul 17;675(3-4):309-15

Evidence against significant resting sympathetic coronary vasoconstrictor tone in the conscious dog. Chilian WM, et al. **Circ Res** 1981 Oct; 49(4):866-76

Relative location of alpha- and beta-adrenoceptors to sites of release of sympathetic transmitter in the rabbit facial vein. Winquist RJ, et al. **Circ Res** 1981 Aug;49(2):486-92

Differential effects of dopamine agonists in mature and immature rats. McDevitt JT, et al. **Eur J Pharmacol** 1981 Jun 10;72(1):69-75

Interaction of alpha-adrenergic imidazolines with cardiac histamine H2-receptors. Zavecz JH, et al. **Eur J Pharmacol** 1981 May 8; 71(2-3):297-306

Adrenergic drugs and intraocular pressure. Potter DE, et al. **Gen Pharmacol** 1981;12(1):1-13

Peripheral vascular effects of a new dopamine analog: 5-6-dihydroxy-2-methylaminotetralin (M-8). Maixner W, et al. **J Cardiovasc Pharmacol** 1981 Mar-Apr;3(2):381-9

The effects of alpha and beta adrenergic agonists and cyclic adenosine 3':5'-monophosphate on epidermal metabolism. Harris RR, et al. **J Invest Dermatol** 1981 Oct;77(4):337-40

SYNAPTIC RECEPTORS

Neuroleptic drug effects on neurotransmitter receptors [letter] **Am J Psychiatry** 1981 Jul;138(7):991-2

GABA-benzodiazepine-barbiturate receptor interactions. Olsen RW. **J Neurochem** 1981 Jul;37(1):1-13 (146 ref.)

Age-related alterations in neurotransmitter receptors: an electrophysiological and biochemical analysis. Lippa AS, et al. **Neurobiol Aging** 1981 Spring;2(1):3-8

Histidine modification with diethyl pyrocarbonate shows heterogeneity of benzodiazepine receptors. Burch TP, et al. **Proc Natl Acad Sci USA** 1981 Jun;78(6):3945-9

Sleep deprivation: effects on circadian rhythms of rat brain neurotransmitter receptors. Wirz-Justice A, et al. **Psychiatry Res** 1981 Aug;5(1):67-76

Studies on possible mechanisms of action of electroconvulsive therapy; effects of repeated electrically induced seizures on rat brain receptors for monoamines and other neurotransmitters. Deakin JF, et al. **Psychopharmacology (Berlin)** 1981;73(4):345-9

Hindbrain GABA receptors influence parasympathetic outflow to the stomach. Williford DJ, et al. **Science** 1981 Oct 9;214(4517):193-4

TERRITORIALITY

Territorial behavior of schizophrenics. A phylogenetic approach. Singh MM, et al. **J Nerv Ment Dis** 1981 Aug;169(8):503-12

TESTOSTERONE

Testosterone oxidation by rat liver microsomes: effects of phenobarbital pretreatment and the detection of seven metabolites by HPLC. van der Hoeven T. **Biochem Biophys Res Commun** 1981 Jun 16; 100(3):1285-91

Effects of ageing and gonadal steroid hormones on prolactin concentrations in the anterior pituitary of the chicken. Kono T, et al. **Br Poult Sci** 1980 Nov;21(6):431-6

Differential effects of gonadal steroids on dopamine metabolism in mesolimbic and nigro-striatal pathways of male rat brain. Alderson LM, et al. **Brain Res** 1981 Aug 10;218(1-2):189-206

Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Menniti FS, et al. **Brain Res** 1981 Jul 6; 216(1):89-107

Autoregulation of testosterone secretion in perfused rat testes. Darney KJ Jr, et al. **Endocrinology** 1981 Sep;109(3):993-5

Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Huhtaniemi IT, et al. **Endocrinology** 1981 Aug; 109(2):483-90

Endocrine correlates of sexual development in the male monkey, Macaca fascicularis. Steiner RA, et al. **Endocrinology** 1981 Sep;109(3):914-9

Effect of thyroxine, testosterone, and corticosterone on nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations in adult female mouse submaxillary gland: dissociation of NGF and EGF responses. Walker P, et al. **Endocrinology** 1981 Aug;109(2):582-7

Effect of testosterone on the hypothalamic-pituitary-testicular axis of the old male rat. Larrea GA, et al. **Horm Metab Res** 1981 Jul; 13(7):396-9

Differential effects of testosterone and its metabolites on gonadotrophin secretion in the intact adult male rat. Reymond M, et al. **Horm Res** 1981;14(2):114-29

The effects of testosterone and progestins on the rate of beta-glucuronidase synthesis in mouse kidney as studied with an immunoprecipitation assay. Gupta C, et al. **Int J Androl** 1981 Jun; 4(3):342-54

Hyperprolactinemia counteracts the testosterone-induced inhibition of the preoptic area dopamine turnover. Kalra PS, et al. **Neuroendocrinology** 1981 Aug;33(2):118-22

Sexually dimorphic acquisition of a conditioned taste aversion in rats: effects of gonadectomy, testosterone replacement and water deprivation. Chambers KC, et al. **Physiol Behav** 1981 Jul;27(1):83-8

[Biological and immunological activity similar to digitalis glycosides of synthetic ACTH and some sex hormone 14-hydroxyderivatives (author's transl)] Schreiber V, et al. **Cas Lek Cesk** 1981 May 21; 120(20):616-8 (Eng. Abstr.) **(Cze)**

[Bromocriptine (Parlodel) in the treatment of pseudo-pregnancy in bitches (author's transl)] Janssens LA. **Tijdschr Diergeneeskd** 1981 Aug 1; 106(15):767-70 (Eng. Abstr.) **(Dut)**

[Reaction between steroid hormones, the liver and its plasma membrane] Denisov IuP, et al. **Biull Eksp Biol Med** 1981 Jun;91(6):722-5 (Eng. Abstr.) **(Rus)**

[Effect of the long-term administration of testosterone on induction of cytochrome P-450 in female rat live tissue using phenobarbital] Chistiakov VV, et al. **Vopr Med Khim** 1981 May-Jun;27(3):340-2 (Eng. Abstr.) **(Rus)**

THIORIDAZINE

Total and free serum haloperidol levels in schizophrenic patients and the effect of age thioridazine and fatty acid on haloperidol-serum protein binding in vitro. Rowell FJ, et al. **Br J Clin Pharmacol** 1981 Apr; 11(4):377-82

[Blood level-effect profile of thioridazine] Kühne GE, et al. **Agressologie** 1979;20(D):271-4 (Eng. Abstr.) **(Ger)**

[Influence of thioridazine on cognitive, psychomotor, and reaction performance in patients with dysthymic-depressive syndrome (author's transl)] Meyer FP, et al. **Pharmacopsychiatria** 1981 May;14(3):94-9 **(Ger)**

THIOTHIXENE

Correlation of thiothixene serum levels and age. Yesavage JA, et al. **Psychopharmacology (Berlin)** 1981;74(2):170-2

THYROID HORMONES

Syndrome of 'inappropriate secretion of thyroid-stimulating hormone' by partial target organ resistance to thyroid hormones. Salmerón De Diego J, et al. **Acta Endocrinol (Copenh)** 1981;97(3):361-8

Early auditory and visual function in normal and hyperthyroid rats. Brunjes PC, et al. **Behav Neural Biol** 1981 Apr;31(4):393-412

In vitro stimulation of human red blood cell Ca2+-ATPase by thyroid hormone. Davis PJ, et al. **Biochem Biophys Res Commun** 1981 Apr 30;99(4):1073-80

Thyroid hormone synthesis in thyroglobulin. The mechanism of the coupling reaction. Gavaret JM, et al. **J Biol Chem** 1981 Sep 10; 256(17):9167-73

Thyroid hormone dependency in immature but not mature grafted locus coeruleus neurons. Evidence from intraocular innervation of iris transplants. Granholm AC, et al. **Med Biol** 1981 Feb;59(1):51-7

Tricyclic antidepressants do not alter thyroid hormone levels in patients suffering from a major affective disorder. Linnoila M, et al. **Psychiatry Res** 1981 Jun;4(3):357-60

Effect of anticonvulsant and antidepressant drugs on iodothyronines in serum. Liewendahl K, et al. **Scand J Clin Lab Invest** 1980; 40(8):767-74

Changes in certain diurnal hormonal rhythms in developing male rats exposed to adiurnal environmental cues. Ooka-Souda S. **Mech Ageing Dev** 1981 Mar;15(3):227-33 **(eng)**

THYROTROPIN

Syndrome of 'inappropriate secretion of thyroid-stimulating hormone' by partial target organ resistance to thyroid hormones. Salmerón De Diego J, et al. **Acta Endocrinol (Copenh)** 1981;97(3):361-8

Long lasting amplification and deformation of thyroid receptors after thyrotropin (TSH) and gonadotropin (GTH) treatment of chickens in the foetal period. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980; 56(3):303-7

Dose dependence of the thyrotropin (TSH) receptor damaging effect of gonadotropin in the newborn rats. Nagy SU, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):417-20

TSH, HGH, HPr, and cortisol response to TRH in depressed patients. Ramseier F, et al. **Acta Psychiatr Belg** 1980 Jul-Aug;80(4):399-409

Ultrastructural and cytochemical effects of trypan blue on TSH stimulation of thyroid follicular cells. Payer AF, et al. **Cell Tissue Res** 1981;218(3):547-56

Norepinephrine and thyrotropin effects on the thyroid in vitro: simultaneous stimulation of iodide organification and antagonism of thyroxine release. Maayan ML, et al. **Endocrinology** 1981 Sep; 109(3):930-4

Effects of various prostanoids on thyrotropin secretion by superfused anterior pituitary cells. Wright KC, et al. **Endocrinology** 1981 Aug; 109(2):637-43

Domperidone directly stimulates TSH secretion in vitro. Powell R, et al. **FEBS Lett** 1981 Jun 29;129(1):97-9

Dynamics and regulation of TSH secretion by superfused anterior pituitary cells. Connors JM, et al. **Horm Res** 1981;14(1):1-17

Studies on the role of the pineal gland in the regulation of TSH secretion in postpuberal male rats. Mattila J, et al. **Horm Res** 1981; 14(1):24-35

Thyrotropin-dependence of the distribution of peroxidase in rat thyroid gland. Matsukawa S, et al. **Tohoku J Exp Med** 1981 Apr; 133(4):431-43

THYROXINE

Effect of ovariectomy, thyroidectomy and of thyroxine treatment on the plasma level of corticosterone of the female Japanese quail. Péczely P, et al. **Acta Biol Acad Sci Hung** 1981;32(1):1-6

Plasma corticosterone, thyroxine and triiodothyronine level in the collared dove (Streptopelia decaocto) during the reproductive cycle. Péczely P, et al. **Acta Physiol Acad Sci Hung** 1980;56(4):421-30

GDP binding to rat brown fat mitochondria: effects of thyroxine at different ambient temperatures. Sundin U. **Am J Physiol** 1981 Sep; 241(3):C134-9

Ratio of thyroxine to thyroxine-binding globulin. An assessment of the validity of a single reference range. Cusick CF. **Ann Clin Biochem** 1981 Mar;18(2):93-6

Circulating thyroxine levels in institutionalized children. Perassi NI, et al. **Arch Int Physiol Biochim** 1980 Dec;88(5):491-5

Chloramphenicol inhibits hormone-dependent induction of cytoplasmic mRNA coding for the mitochondrial enzyme, carbamyl phosphate synthetase, in Rana catesbeiana tadpoles. Pouchelet M, et al. **Biochim Biophys Acta** 1981 Jun 26;654(1):67-76

Identification of an intracellular pathway of thyroxine synthesis by dispersed thyroid cells. Rousset B, et al. **Biochim Biophys Acta** 1981 Aug 5;676(1):8-18

Further observations on serum free thyroxine concentrations during pregnancy. Boss AM, et al. **Br Med J [Clin Res]** 1981 Aug 29; 283(6291):584

Lack of a relationship between concentrations of plasma luteinising hormone, thyroxine and prolactin at nine week's of age and subsequent egg production in the domestic hen. Sharp PJ, et al. **Br Poult Sci** 1981 Jan;22(1):53-8

Thyroxin dependency of the developing locus coeruleus. Evidence from intraocular grafting experiments. Seiger A, et al. **Cell Tissue Res** 1981; 220(1):1-15

Evaluation of free thyroxin measurements in patients with non-thyroidal illnesses. Lawlor JF, et al. **Clin Chem** 1981 Aug;27(8):1457-9

Cardiac beta-adrenoreceptors in the thyroxine-treated dog. Ho K, et al. **Clin Exp Pharmacol Physiol** 1981 Mar-Apr;8(2):183-7

The effect of thyroxine on transparency and PAPS synthesis in the avian cornea. Beckenhauer DM, et al. **Dev Biol** 1981 May;84(1):225-9

Propranolol and thyroxine metabolism [letter] Nester TJ. **Drug Intell Clin Pharm** 1981 Feb;15(2):131-2

Norepinephrine and thyrotropin effects on the thyroid in vitro: simultaneous stimulation of iodide organification and antagonism of thyroxine release. Maayan ML, et al. **Endocrinology** 1981 Sep; 109(3):930-4

Effect of thyroxine, testosterone, and corticosterone on nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations in adult female mouse submaxillary gland: dissociation of NGF and EGF responses. Walker P, et al. **Endocrinology** 1981 Aug;109(2):582-7

The influence of thyroid gland and thyroxine on the acetylcholinesterase activity of rat brain and adenohypophysis. Owasoyo JO, et al. **Endokrinologie** 1981 Apr;77(2):242-6

Kinetics of thyroglobulin iodination and thyroid hormone synthesis catalyzed by peroxidases: the role of H2O2. Virion A, et al. **Eur J Biochem** 1981 Jun;117(1):103-9

Effect of thyroid hormone on the regeneration of the hypoglossal nerve in rats. Yu WH, et al. **Exp Neurol** 1981 Jul;73(1):325-9

Specific anti-thyroxine antisera induced by thyroxine sensitized liposomes. Tan CT, et al. **Immunol Commun** 1981;10(1):27-34

Role of thyroxine & gonadotropins on the mobilization of ovarian cholesterol in a teleost Anabas testudineus (Bloch). Sen S, et al. **Indian J Exp Biol** 1981 May;19(5):408-12

The relationship of thyroxine secretion rate to growth of swine. Marple DN, et al. **J Anim Sci** 1981 Mar;52(3):500-4

Ion transport in liver mitochondria from normal and thyroxine-treated rats. Shears SB, et al. **J Bioenerg Biomembr** 1980 Dec; 12(5-6):379-93

Influence of thyroxine on suckling rat intestinal alkaline phosphatase and effects of undernutrition on the same. Subramoniam A, et al. **J Exp Zool** 1980 Dec;214(3):317-22

Retinotectal reorganization in goldfish-III. Effect of thyroxine. Marotte LR, et al. **Neuroscience** 1981;6(8):1591-600

The potentiation of ozone toxicity by thyroxine. Wong DS, et al. **Res Commun Chem Pathol Pharmacol** 1981 Mar;31(3):483-92

[Measurement of free thyroxine in serum with radioimmunoassay (author's transl)] Mitsuma T, et al. **Horumon To Rinsho** 1981 Jan;29(1):127-31 **(Jpn)**

[Studies on free thyroxine measurement with radioimmunoassay kit -evaluation of GammaCoat free T4 kit (author's transl)] Nakagawa T, et al. **Kaku Igaku** 1981 Apr;18(3):385-400 **(Jpn)**

[Studies on the measurement of serum thyroxine with 'Amerlex T4 RIA' kit (author's transl)] Watanabe S, et al. **Kaku Igaku** 1981 Apr; 18(3):333-8 **(Jpn)**

[Structuro-metabolic integration of gastric endocrine cells in the presence of a disruption in hormone balance] Fedchenko SN. **Arkh Anat Gistol Embriol** 1981 Mar;80(3):68-77 (Eng. Abstr.) **(Rus)**

TRANQUILIZING AGENTS

Formation of nitroso compounds and mutagens from tranquilizers by drug/nitrite interaction. Takeda Y, et al. **Cancer Lett** 1981 Mar; 12(1-2):81-6

Cuban women, sex role conflicts and the use of prescription drugs. González DH, et al. **J Psychoactive Drugs** 1981 Jan-Mar; 13(1):47-51

Central action of mepiprazole. Maj J, et al. **Pol J Pharmacol Pharm** 1980 Jul-Aug;32(4):475-84

Drugs used to produce standing chemical restraint in horses. Muir WW. **Vet Clin North Am [Large Anim Pract]** 1981 May;3(1):17-44 (128 ref.)

[Tranquilizers] Ferrand I. **Soins Psychiatr** 1981 Jan;(7):33-6 **(Fre)**

TRANQUILIZING AGENTS, MAJOR

Overall-response parameter analysis applied to butyrophenones. Mager PP. **Act Nerv Super (Praha)** 1981 Jun;23(2):130-5

Neuroleptic drug effects on neurotransmitter receptors [letter] **Am J Psychiatry** 1981 Jul;138(7):991-2

Prescription of neuroleptic drugs by family practice residents [letter] Holt RJ, et al. **Am J Psychiatry** 1981 Aug;138(8):1129

Effect of neuroleptics on indoleamine-N-methyltransferase activity and brain metabolism of bufotenin. Gomes UC, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):571-5

Neuroleptics decrease blinking in schizophrenic subjects. Karson C, et al. **Biol Psychiatry** 1981 Jul;16(7):679-82

Evidence for an inhibitory presynaptic component of neuroleptic drug action. de Belleroche JS, et al. **Br J Pharmacol** 1981 Mar; 72(3):427-33

The constitutional right to refuse antipsychotic medications. Brooks AD. **Bull Am Acad Psychiatry Law** 1980;8(2):179-221

Rapid parenteral treatment of acute psychosis. Menuck M, et al. **Compr Psychiatry** 1981 Jul-Aug;22(4):351-61 (69 ref.)

Pre- and postsynaptic alpha-adrenoceptor antagonism by neuroleptics in vivo. Petersen EN. **Eur J Pharmacol** 1981 Feb 19;69(4):399-405

Differential changes in DOPAC levels in the hippocampal formation, septum and striatum of the rat induced by acute and repeated neuroleptic treatment. Scatton B. **Eur J Pharmacol** 1981 May 22;71(4):499-503

Using drug holidays for chronic outpatients. Sharer DR, et al. **Hosp Community Psychiatry** 1981 Jun;32(6):420-1

Identification and distribution of neuroleptic binding sites in the rat spinal cord. Demenge P, et al. **J Neurochem** 1981 Jul;37(1):53-9

Effects of microinjection of 2-chloro-11 (2-dimethylaminoethoxy)-dibenzo[b,f]-thiepine (zotepine), thioridazine and haloperidol into the striatum and nucleus accumbens on stereotypic behaviour and motor activity. Lai H, et al. **J Pharm Pharmacol** 1981 Apr;33(4):252-4

Comparative effects of classical and atypical antipsychotic drugs in combination with a non-amphetamine stimulant on rat brain dopamine metabolism. McMillen BA. **J Pharm Pharmacol** 1981 Aug; 33(8):544-6

Neuroleptic drugs activate tyrosine hydroxylase of retinal amacrine cells. Cohen J, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):390-4

During one year's neuroleptic treatment in rats striatal dopamine receptor blockade decreases but serum prolactin levels remain elevated. Dyer RG, et al. **Life Sci** 1981 Jan 12;28(2):167-74

Risks of antipsychotic drugs overemphasized [letter] Baldessarini RJ, et al. **N Engl J Med** 1981 Sep 3;305(10):588-9

A double-blind comparison of bromperidol and haloperidol in newly admitted schizophrenic patients. Brannen JO, et al. **Pharmacopsychiatria** 1981 Jul;14(4):139-40

Effects of chronic haloperidol, thioridazine and zotepine treatment on apomorphine elicited stereotypic behavior and 3H-spiroperidol binding sites in the striatum of the rat. Lai HC, et al. **Proc West Pharmacol Soc** 1981;24:5-6

A follow-up study of schizophrenic outpatients treated with depot-neuroleptics. Tegeler J, et al. **Prog Neuropsychopharmacol** 1981; 5(1):79-90

Effects of long-term neuroleptic use on brain density. Lyon K, et al. **Psychiatry Res** 1981 Aug;5(1):33-7

Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. van Kammen DP, et al. **Psychiatry Res** 1981 Jun;4(3):313-25

(Des-Tyr)-gamma-endorphin in the treatment of schizophrenia. Manchanda R, et al. **Psychol Med** 1981 May;11(2):401-4

Antagonism of reserpine rigidity without inducing sedation. Southwick

S, et al. **Psychopharmacology (Berlin)** 1981;74(1):29-32

[On the question of differences between therapeutic responses after particular neuroleptics in comparison to perphenazine in schizophrenics (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981 Feb; 77(1):25-30 (Eng. Abstr.) **(Cze)**

[Mechanism of action and indications for psychopharmaceutic agents; possibilities and limitations in the elderly] Verhoeven WM. **Gerontologie** 1981 Aug;12(3):126-38 (Eng. Abstr.) **(Dut)**

[Diltiazem and anaesthesia] Zerr C, et al. **Ann Cardiol Angeiol (Paris)** 1981 Mar-Apr;30(2):133-7 **(Fre)**

[Influence of the procedure of administration in the activity of some antidepressant or disinhibiting drugs upon behavioural despair (author's transl)] Scotto di Tella AM, et al. **J Pharmacol** 1981 Apr-Jun; 12(2):179-88 (Eng. Abstr.) **(Fre)**

[High-dosed neuroleptic therapy] Platz T, et al. **Pharmacopsychiatria** 1981 Jul;14(4):141-7 (82 ref.) (Eng. Abstr.) **(Ger)**

TRANQUILIZING AGENTS, MINOR

Use of gastric fistula rats for the study of sedative, hypnotic and antianxiety drugs. Nozaki M, et al. **Drug Alcohol Depend** 1981 Jun; 7(3):221-31

Action of pyrazolopyridines as modulators of [3H]flunitrazepam binding to the gaba/benzodiazepine receptor complex of the cerebellum. Supavilai P, et al. **Eur J Pharmacol** 1981 Mar 12;70(2):183-93

Septal driving of hippocampal theta rhythm: a role for gamma-aminobutyrate in the effects of minor tranquillizers? Mellanby J, et al. **Neuroscience** 1981;6(7):1412-21

Effects of buspirone on conflict behavior of laboratory rats and monkeys. Hartmann RJ, et al. **Proc West Pharmacol Soc** 1981;24:179-81

Antianxiety agents and emotional behavior, an information processing analysis. Morris MD, et al. **Prog Neuropsychopharmacol** 1981; 5(3):219-40

Anxiolytics antagonize yohimbine's discriminative stimulus properties. Browne RG. **Psychopharmacology (Berlin)** 1981;74(3):245-9

[Clinical manifestations and treatment of addictions to hypnotics and mild tranquilizers] Shen YC.
Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1980 Apr; 13(4):200-1 **(Chi)**

[Effect of GABA-negative preparations on the anxiolytic and sedative effects of diazepam] Andreev BV, et al. **Biull Eksp Biol Med** 1981 Jun; 91(6):685-7 (Eng. Abstr.) **(Rus)**

[Stimulation of prostaglandin E2 and F2a biosynthesis in the brains of mouse strain F1 (CBA X C57BL) by the tranquilizer phenazepam] Romantsev EF, et al. **Dokl Akad Nauk SSSR** 1981;258(1):239-42 **(Rus)**

[Anxiety; pharmacological bases of treatment] de Andrés Rodriguez-Trelles F. **An R Acad Nac Med (Madr)** 1981; 98(1):69-116 (68 ref.) **(Spa)**

TRANYLCYPROMINE

Rapid response of severe obsessive-compulsive disorder to tranylcypromine. Jenike MA. **Am J Psychiatry** 1981 Sep; 138(9):1249-50

Addiction to tranylcypromine. Griffin N, et al. **Br Med J [Clin Res]** 1981 Aug 1;283(6287):346

Comparison of molindone and tranylcypromine in the treatment of refractory depression. Small JG, et al. **J Clin Pharmacol** 1981 Aug-Sep; 21(8-9):351-8

Amphetamine and tranylcypromine in an animal model of depression: pharmacological specificity of the reversal effect. Katz RJ, et al. **Neurosci Biobehav Rev** 1981 Summer;5(2):259-64

TRIFLUOPERAZINE

Calmodulin antagonists modulate rabbit neutrophil degranulation, aggregation and stimulated oxygen consumption. Alobaidi T, et al. **Biochim Biophys Acta** 1981 Jul 17;675(3-4):316-21

Sensitive gas chromatographic determination of trifluoperazine in human plasma. Gillespie TJ, et al. **J Chromatogr** 1981 Apr 10;223(1):95-102

Modulation of platelet shape and membrane receptor binding by Ca2+-calmodulin complex. Kao KJ, et al. **Nature** 1981 Jul 2; 292(5818):82-4

TRYPTAMINES

Characterization of eight biogenic indoleamines as substrates for type A and type B monoamine oxidase. Suzuki O, et al. **Biochem Pharmacol** 1981 Jun 1;30(11):1353-8

Different hypothalamic receptors mediate 5-hydroxytryptamine- and tryptamine-induced core temperature changes in the rat. Cox B, et al. **Br J Pharmacol** 1981 Mar;72(3):477-82

TRYPTOPHAN

Blood-brain transport of tryptophan and phenylalanine: effect of portacaval shunt in dogs. Huet PM, et al. **Am J Physiol** 1981 Aug; 241(2):G163-9

Tryptophan metabolism in children with attentional deficit disorder. Irwin M, et al. **Am J Psychiatry** 1981 Aug;138(8):1082-5

Nanosecond fluorometry and the luminescence of biological macromolecules. Brand L, et al. **Ann NY Acad Sci** 1981; 366:197-207

A new component in protein fluorescence. Longworth JW. **Ann NY Acad Sci** 1981;366:237-45

Middle molecular weight substances and tryptophan in cerebrospinal fluid of schizophrenic patients. Sperschneider H, et al. **Artif Organs** 1981 May;5(2):177-8

Measurement of distance between fluorescent amino acid residues and metal ion binding sites. Quantitation of energy transfer between tryptophan and terbium(III) or europium(III) in thermolysin. Horrocks WD Jr, et al. **Biochem Biophys Res Commun** 1981 May 15; 100(1):111-7

Tryptophan fluorescence of human hemoglobin. I. Significant change of fluorescence intensity and lifetimes in the T - R transition. Itoh M, et al. **Biochem Biophys Res Commun** 1981 Jun 16;100(3):1259-65

Formation of mutagens from tryptophan by the reaction with nitrite. Ohta T, et al. **Biochem Biophys Res Commun** 1981 May 15;100(1):52-7

Effects of benserazide and carbidopa on the metabolism of L-tryptophan by isolated rat liver cells. Smith SA, et al. **Biochem Pharmacol** 1981 Mar 15;30(6):623-8

Role of tryptophanyl and tyrosyl residues of flavoproteins in binding with flavin coenzymes. X-ray structural studies using model complexes. Inoue M, et al. **Biochemistry** 1981 May;20(10):2936-45

Laser chemically induced dynamic nuclear polarization study of the reaction between photoexcited flavins and tryptophan derivatives at 360 MHz. McCord EF, et al. **Biochemistry** 1981 May;20(10):2880-8

Pausing of RNA polymerase during in vitro transcription of the tryptophan operon leader region. Winkler ME, et al. **Biochemistry** 1981 Jun 23;20(13):3738-44

Nanosecond segmental mobilities of tryptophan residues in proteins observed by lifetime-resolved fluorescence anisotropies. Lakowicz JR, et al. **Biophys J** 1980;32(1):591-601

Distributive profiles of free and protein-incorporated tryptophan and valine in cerebral cortex slices from adult and 2-day-old rats. Korpi ER, et al. **Brain Res** 1981 Jul 6;216(1):219-23

Developmental changes in brain indoles, serum tryptophan and other serum neutral amino acids in the rat. Zeisel SH, et al. **Brain Res** 1981 Jul;227(4):551-64

Persistence of dihydrotestosterone inhibition of lordosis in estrogen-primed rats fed a tryptophan-deficient diet. Menniti FS, et al. **Brain Res Bull** 1981 Jul;7(1):1-4

Mutagenicities of gamma-carboline derivatives related to potent mutagens found in tryptophan pyrolysates. Nagao M, et al. **Carcinogenesis** 1980 May;1(5):451-4

Evidence that a serotonergic mechanism stimulates the secretion of pituitary beta-endorphin-like immunoreactivity in the rat. Sapun DI, et al. **Endocrinology** 1981 Aug;109(2):421-6

The rates of photodestruction of tryptophan residues in human and bovine ocular lens proteins. Borkman RF, et al. **Exp Eye Res** 1981 Jun; 32(6):747-54

Cerebrospinal fluid amine metabolites, tryptophan and clinical parameters in depression. Part 1. Background variables. Banki CM, et al. **J Affective Disord** 1981 Jun;3(2):81-9

Relevance of tryptophan and tyrosine availability in endogenous and 'non-endogenous' depressives treated with imipramine or clomipramine. Møller SE, et al. **J Affective Disord** 1981 Sep;3(3):231-44

Dynamics of amino acid side chains in membrane proteins by high field solid state deuterium nuclear magnetic resonance spectroscopy. Phenylalanine, tyrosine, and tryptophan. Kinsey RA, et al. **J Biol Chem** 1981 Sep 10;256(17):9028-36

Analysis of some tryptophan and phenylalanine metabolites in urine by a straight-phase high-performance liquid chromatographic technique. Ghebregzabher M, et al. **J Chromatogr** 1981 Feb 13;222(2):191-201

Xanthurenic acid excretion in urine after oral intake of 5 grams L-tryptophan by healthy volunteers: standardisation of the reference values. Hoes MJ, et al. **J Clin Chem Clin Biochem** 1981 May; 19(5):259-64

Metabolism of tryptophan by Pseudomonas aureofaciens and its relationship to pyrrolnitrin biosynthesis. Salcher O, et al. **J Gen Microbiol** 1980 Dec;121(Pt. 2):465-71

Nucleotide sequence of Escherichia coli trpE. Anthranilate synthetase component I contains no tryptophan residues. Nichols BP, et al. **J Mol Biol** 1981 Feb 15;146(1):45-54

Indolic substances in plasma, cerebrospinal fluid, and frontal cortex of human subjects infused with saline or tryptophan. Gillman PK, et al. **J Neurochem** 1981 Aug;37(2):410-7

The effect of insulin upon the influx of tryptophan into the brain of the rabbit. Daniel PM, et al. **J Physiol (Lond)** 1981 Mar;312:551-62

Dietary tryptophan and aggressive behavior in rats. **Nutr Rev** 1981 Jul; 39(7):284-5

Influence of unilateral ECT on tryptophan metabolism in endogenous depression. Smith DF, et al. **Pharmacopsychiatria** 1981 Jul;

14(4):135-8

Effect of chloro-N-desmethyldiazepam on serum and brain tryptophan and serotonin in relation to the activity of central serotonergic neurons. Valzelli L, et al. **Pol J Pharmacol Pharm** 1981 Jan-Feb;33(1):37-42

Tandem termination sites in the tryptophan operon of Escherichia coli. Wu AM, et al. **Proc Natl Acad Sci USA** 1981 May;78(5):2913-7

Decreased tryptophan availability in endogenous depression caused by disturbed plasma leucine clearance. Møller SE, et al. **Prog Neuropsychopharmacol** 1981;5(3):277-9

Structure-activity studies with somatostatin: the role of tryptophan in position 8. Hirst BH, et al. **Regul Pept** 1980 Oct;1(2):97-113

[Properties and role of tryptophan residues in the polypeptide chain of elongation factor G from E. coli] Kashparov IA, et al. **Biokhimiia** 1981; 46(8):1488-98 (Eng. Abstr.) **(Rus)**

[Effect of mutations blocking the kynurenine pathway of tryptophan metabolism on neural activity in Drosophila melanogaster] Smirnov VB, et al. **Dokl Akad Nauk SSSR** 1981;258(2):489-91 **(Rus)**

[Relation of lysine and tryptophan content to that of zein, during the germination of corn grain, and its possible link to the vegetative cycle of the plant] Martínez AB, et al. **Arch Latinoam Nutr** 1980 Dec; 30(4):607-33 (Eng. Abstr.) **(Spa)**

TRYPTOPHAN HYDROXYLASE

Maternal influences on tryptophan hydroxylase activity in embryonic rat brain. Lauder JM, et al. **Dev Neurosci** 1981;4(4):291-5

A calmodulin-dependent protein kinase that is involved in the activation of tryptophan 5-monooxygenase is specifically distributed in brain tissues. Yamauchi T, et al. **FEBS Lett** 1981 Jun 29;129(1):117-9

Interaction between the oxygen and tryptophan dependence of synaptosomal tryptophan hydroxylase. Katz IR. **J Neurochem** 1981 Aug; 37(2):447-51

Stability properties of activated tryptophan hydroxylase from rat midbrain. Vitto A, et al. **J Neurochem** 1981 Sep;37(3):601-7

Effects of norepinephrine on pineal tryptophan hydroxylase, using an improved [14C]CO2-trapping microtechnique. Chan A, et al. **J Pharmacol Methods** 1981 Aug;6(1):13-20

Biopterin. VII. Inhibition of synthesis of reduced biopterins and its bearing on the function of cerebral tryptophan-5-hydroxylase in vivo. Gál EM, et al. **Neurochem Res** 1981 Mar;6(3):233-41

TYROSINE

A new component in protein fluorescence. Longworth JW. **Ann NY Acad Sci** 1981;366:237-45

Laser Raman spectroscopy of adrenal iron-sulfur apoprotein: the anomalous tyrosine residue at position 82. Bicknell-Brown E, et al. **Biochem Biophys Res Commun** 1981 Jul 16;101(1):298-305

Role of tryptophanyl and tyrosyl residues of flavoproteins in binding with flavin coenzymes. X-ray structural studies using model complexes. Inoue M, et al. **Biochemistry** 1981 May;20(10):2936-45

Internal dynamics of proteins. Short time and long time motions of aromatic sidechains in PTI. Karplus M, et al. **Biophys J** 1980; 32(1):603-18

Epidermal growth factor induces rapid tyrosine phosphorylation of proteins in A431 human tumor cells. Hunter T, et al. **Cell** 1981 Jun; 24(3):741-52

Syntheses of L-tyrosine-related amino acids by tyrosine phenol-lyase of Citrobacter intermedius. Nagasawa T, et al. **Eur J Biochem** 1981 Jun; 117(1):33-40

Stimulation of synaptosomal tyrosine hydroxylation by phencyclidine in vitro. Vickroy TW, et al. **Eur J Pharmacol** 1981 May 22; 71(4):463-73

Tyrosine aminotransferase as the rate-limiting step for tyrosine catabolism in isolated rat liver cells. Dickson AJ, et al. **FEBS Lett** 1981 May 5; 127(1):28-32

H NMR studies of Tyr-237 of lactate dehydrogenase. Parker DM, et al. **FEBS Lett** 1981 Jun 29;129(1):33-5

Adjuvant activity of 6-amino-6-deoxy-muramyldipeptides and their acylamino derivatives on the induction of delayed hypersensitivity to azobenzenearsonate-N-acetyl-L-tyrosine in guinea pigs. Azuma I, et al. **Infect Immun** 1981 Jun;32(3):1305-8

Relevance of tryptophan and tyrosine availability in endogenous and 'non-endogenous' depressives treated with imipramine or clomipramine. Møller SE, et al. **J Affective Disord** 1981 Sep;3(3):231-44

The structure of hemoglobin Creteil (beta 89 Ser replaced by Asn) is similar to that of abnormal human hemoglobins having sequence changes at Tyr 145 beta. Arnone A, et al. **J Biol Chem** 1981 Aug 25; 256(16):8545-52

Dynamics of amino acid side chains in membrane proteins by high field solid state deuterium nuclear magnetic resonance spectroscopy. Phenylalanine, tyrosine, and tryptophan. Kinsey RA, et al. **J Biol Chem** 1981 Sep 10;256(17):9028-36

Preferential action of a brain detyrosinolating carboxypeptidase on polymerized tubulin. Kumar N, et al. **J Biol Chem** 1981 Jul 25; 256(14):7678-86

Selective dephosphorylation of proteins containing phosphotyrosine by alkaline phosphatases. Swarup G, et al. **J Biol Chem** 1981 Aug 10; 256(15):8197-201

Mechanism of smooth muscle relaxation by tiropramide. Vidal y Plana RR, et al. **J Pharm Pharmacol** 1981 Jan;33(1):19-24

Purified low-molecular-weight protein kinase from murine sarcoma virus particles catalyzes tyrosine phosphorylation endogenously but phosphorylates cellular proteins at serine. Sen A. **J Virol** 1981 Aug; 39(2):612-24

Tyrosine availability and dopamine synthesis in the striatum: studies with gamma-butyrolactone. Sved A, et al. **Life Sci** 1981 Aug 17; 29(7):743-8

Quercetin inhibits tyrosine phosphorylation by the cyclic nucleotide-independent, transforming protein kinase, pp60src. Glossmann H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Aug; 317(1):100-2

Dietary phenylalanine and tyrosine interrelationships in the Sprague-Dawley rat. Elkin RG, et al. **Proc Soc Exp Biol Med** 1981 Jul;167(3):310-7

[Effect of minaprine on the metabolism of tyrosine in the rat] Topall G, et al. **Agressologie** 1981;22(2):55-7 (Eng. Abstr.) **(Fre)**

[Influence of supplementary tyrosine or phenylalanine on bacterial growth and pigmentation of 'Pseudomonas aeruginosa' (author's transl)] Labeyrie S, et al. **Ann Microbiol (Paris)** 1981 Jan-Feb; 132A(1):31-40 (Eng. Abstr.) **(Fre)**

[Localization of tyrosine residues in histone H1 from wheat embryos] Odintsova TI, et al. **Biokhimiia** 1981 Jan;46(1):162-71 (Eng. Abstr.) **(Rus)**

TYROSINE AMINOTRANSFERASE

Glucocorticoid induction of tyrosine aminotransferase in kidney cortex. Elam L, et al. **Biochem Biophys Res Commun** 1981 Jun 16; 100(3):1143-7

Induction of tyrosine aminotransferase by pyridoxine in Drosophila hydei. Belew K, et al. **Chromosoma** 1981;82(1):99-106

Tyrosine aminotransferase as the rate-limiting step for tyrosine catabolism in isolated rat liver cells. Dickson AJ, et al. **FEBS Lett** 1981 May 5; 127(1):28-32

NADH-coupled spectrophotometric assay of tyrosine aminotransferase. Di Cola D, et al. **Ital J Biochem** 1981 Jan-Feb;30(1):30-9

Physical properties, limited proteolysis, and acetylation of tyrosine aminotransferase from rat liver. Hargrove JL, et al. **J Biol Chem** 1981 Aug 10;256(15):8012-7

Ontogenesis of the adrenal glucocorticoids and of the target function of the enzymatic tyrosine transaminase activity in the chick embryo. Marie C. **J Endocrinol** 1981 Aug;90(2):193-200

[Multiple forms of tyrosine aminotransferase in rat liver cells and their role in cell homeostasis] Mertvetsov NP. **Vopr Med Khim** 1981 Mar-Apr;27(2):154-66 (Eng. Abstr.) **(Rus)**

TYROSINE HYDROXYLASE

Evidence for a dual effect of dibutyryl cyclic AMP on the synthesis of tyrosine aminotransferase in rat liver. Granner D, et al. **Adv Cyclic Nucleotide Res** 1981;14:529-37

Regulation by catecholamines of spontaneous growth hormone secretion in the baboon. Stewart JK, et al. **Am J Physiol** 1981 Sep; 241(3):E196-9

Tyrosine 3-monoxygenase is phosphorylated by Ca2+-, calmodulin-dependent protein kinase, followed by activation by activator protein. Yamauchi T, et al. **Biochem Biophys Res Commun** 1981 May 29;100(2):807-13

Catecholamine levels and tyrosine hydroxylase activities in rat brain regions after chronic treatment with, and withdrawal of, methamphetamine. Bardsley ME, et al. **Biochem Pharmacol** 1981 Jun 15;30(12):1543-9

Inactivation of tyrosine 3-monooxygenase by acetone precipitation and its restoration by incubation with a sulfhydryl agent and iron. Okuno S, et al. **Biochim Biophys Acta** 1981 Apr 14;658(2):327-33

Chemical deafferentation of the olfactory bulb: plasticity of the levels of tyrosine hydroxylase, dopamine and norepinephrine. Nadi NS, et al. **Brain Res** 1981 Jun 1;213(2):365-77

Stimulation of the pituitary-adrenocortical axis and induction of tyrosine hydroxylase by nerve growth factor are not dependent on mouse submaxillary gland isorenin. Otten U, et al. **Brain Res** 1981 Jul 27; 217(1):207-11

Fine structure of the nigrostriatal anlage in fetal rat brain by immunocytochemical localization of tyrosine hydroxylase. Specht LA, et al. **Brain Res** 1981 Aug 10;218(1-2):49-65

Influence of adrenal epinephrine on postnatal development of tyrosine hydroxylase activity in the superior cervical ganglion. Markey KA, et al. **Dev Neurosci** 1981;4(4):267-72

Effects of neonatal ACTH4-10 administration on adult adaptive behavior and brain tyrosine hydroxylase activity. Nyakas C, et al. **Dev Neurosci** 1981;4(3):225-32

Light-microscopic immunocytochemical localization of tyrosine hydroxylase in prenatal rat brain. II. Late ontogeny. Specht LA, et al. **J Comp Neurol** 1981 Jun 20;199(2):255–76

Light-microscopic immunocytochemical localization of tyrosine hydroxylase in prenatal rat brain. I. Early ontogeny. Specht LA, et al. **J Comp Neurol** 1981 Jun 20;199(2):233–53

Importance of fixation in immunohistochemistry: use of formaldehyde solutions at variable pH for the localization of tyrosine hydroxylase. Berod A, et al. **J Histochem Cytochem** 1981 Jul;29(7):844–50

Monovalent cations and striatal tyrosine hydroxylase. Kuczenski R. **J Neurochem** 1981 Sep;37(3):681–6

The immunocytochemical localization of tyrosine hydroxylase within rat sympathetic neurons that release acetylcholine in culture. Higgins D, et al. **J Neurosci** 1981 Feb;1(2):126–31

Striatal tyrosine hydroxylase activity: multiple conformational kinetic oscillators and product concentration frequencies. Mandell AJ, et al. **J Neurosci** 1981 Apr;1(4):380–9

Neuroleptic drugs activate tyrosine hydroxylase of retinal amacrine cells. Cohen J, et al. **J Pharmacol Exp Ther** 1981 Aug;218(2):390–4

Dopaminergic agonist and antagonist effects on striatal tyrosine hydroxylase distribution. Smith CP, et al. **Life Sci** 1981 Jan 12; 28(2):193–7

Effect of estradiol benzoate and clomiphene on tyrosine hydroxylase activity and on luteinizing hormone and prolactin levels in ovariectomized rats. Tobias H, et al. **Life Sci** 1981 Aug 17; 29(7):711–6

Tetrahydrobiopterin increases in adrenal medulla and cortex: a factor in the regulation of tyrosine hydroxylase. Abou-Donia MM, et al. **Proc Natl Acad Sci USA** 1981 May;78(5):2703–6

[Increase in the affinity of hypothalamic tyrosine hydroxylase for tyrosine as a result of the action of dopamine on the synaptosome membrane] Mineeva MF, et al. **Dokl Akad Nauk SSSR** 1981;258(2):501–4 **(Rus)**

VANILMANDELIC ACID

Constructing a normal range [letter] Altman DG. **Clin Chem** 1979 Mar; 25(3):492–3

Determination of vanillylmandelic acid in urine by pre-column dansylation using micro high-performance liquid chromatography with fluorescence detection. Yamada K, et al. **J Chromatogr** 1981 Apr 10; 223(1):176–8

VASOPRESSINS

Barrel rotation induced by vasopressin and involvement of dopaminergic and cholinergic functions in rats. Yamada K, et al. **Arch Int Pharmacodyn Ther** 1981 May;251(1):88–94

Immunocytochemistry of luteinizing hormone-releasing hormone, vasopressin, and corticotropin following deafferentation of the basal hypothalamus of the male rat brain. Scott PM, et al. **Cell Tissue Res** 1981;219(2):393–402

Total circulatory capacity in the rat. Effects of epinephrine and vasopressin on compliance and unstressed volume. Trippodo NC. **Circ Res** 1981 Oct;49(4):923–31

Effect of captopril on cardiovascular, sympathetic and vasopressin responses to hemorrhage. Zerbe RL, et al. **Eur J Pharmacol** 1981 Jul 10;72(4):391–5

Regulation of vasopressin-sensitive adenylate cyclase by calmodulin. Ausiello DA, et al. **J Biol Chem** 1981 Oct 10;256(19):9796–8

Fructose 2,6-bisphosphate. Hormonal regulation and mechanism of its formation in liver. Hue L, et al. **J Biol Chem** 1981 Sep 10; 256(17):8900–3

Vasopressin stimulates release of beta-lipotropin and beta-endorphin in conscious rats as measured by radioimmunoassay of unextracted plasma. Anhut H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Feb; 316(1):59–63

Water intake inhibition and vasopressin release following intracerebroventricular administration of tachykinins to rats of the Wistar and Brattleboro strain. Cantalamessa F, et al. **Pharmacol Res Commun** 1981 Jul;13(7):641–55

[Effects of GSH on endocrine function and lysosomal enzyme levels during cardiopulmonary bypass in man (author's transl)] Matsuki A, et al. **Masui** 1981 Feb;30(2):150–7 (Eng. Abstr.) **(Jpn)**

VASOTOCIN

Electron-microscopic immunocytochemical demonstration of separate vasotocinergic, mesotocinergic and somatostatinergic neurons in the hypothalamic magnocellular preoptic nucleus of the frog. Van Vossel-Daeninck J, et al. **Cell Tissue Res** 1981;218(1):7–12

VIOLENCE

The psychiatrically violent patient [letter] **Br Med J [Clin Res]** 1981 Apr 11;282(6271):1232

Violence: the ugly face of amphetamine abuse. Siomopoulos V. **IMJ** 1981 Jun;159(6):375–7

VISUAL PERCEPTION

Changes in brain biogenic amines in cats performing a symmetrically reinforced go-nogo visual discrimination task. Kitsikis A, et al. **Behav Neural Biol** 1981 Jun;32(2):133–47

Stimulating effects of amphetamine on the visual system. Andreeva OG, et al. **Hum Physiol** 1980 May-Jun;6(3):199–205

Use of simple tasks to test for impairment of complex skills by a sedative. Ellinwood EH Jr, et al. **Psychopharmacology (Berlin)** 1981; 73(4):350–4

[Role of neuronal and neuropile serotonin in the visual analyzer] Uzbekov MG, et al. **Biull Eksp Biol Med** 1981 Apr;91(4):389–90 (Eng. Abstr.) **(Rus)**

[Effect of psychic stimulants on the temporal parameters of visual perception] Barkov NK, et al. **Farmakol Toksikol** 1981 Jan-Feb; 44(1):12–4 (Eng. Abstr.) **(Rus)**

WAKEFULNESS

Does para-chlorophenylalanine produce disturbed waking, disturbed sleep or activation by ponto-geniculo-occipital waves in cats? Ursin R. **Waking Sleeping** 1980 Jul-Sep;4(3):211-21

AUTHOR SECTION

A

Aanderud L: A system for pharmacological studies in small animals at high pressure. Undersea Biomed Res 1981 Jun;8(2):69-74

Abdel-Hakim AM, Rioux F, Elhilali M: The contractile effect of bombesin on the rat isolated urinary bladder. Eur J Pharmacol 1981 Mar 12; 70(2):167-73

Abdel-Latif AA: Sodium ion and the effects of acetylcholine on phospholipid and phosphoprotein phosphate turnover in the rabbit iris smooth muscle. Biochem Pharmacol 1981 Jun 1;30(11):1371-4

Abdul-Ghani AS, Coutinho-Netto J, Bradford HF, et al: Effect of beta-bungarotoxin on the release of endogenous amino aids from the sensorimotor cortex. J Neurochem 1981 Jul;37(1):251-4

Abdul-Ghani AS, Norris PJ, Smith CC, et al: Effects of gamma-acetylenic GABA and gamma-vinyl GABA on synaptosomal release and uptake of GABA. Biochem Pharmacol 1981 Jun 1;30(11):1203-9

Abduvakhabov AA, Azliarova M, Brestkin AP, et al: O kholinésteraznom gidrolize spetsificheskikh substratov pri ikh razlichnykh kontsentratsiiakh. Dokl Akad Nauk SSSR 1981;258(5):1233-5 **(Rus)**

Abou-Donia MM, Viveros OH: Tetrahydrobiopterin increases in adrenal medulla and cortex: a factor in the regulation of tyrosine hydroxylase. Proc Natl Acad Sci USA 1981 May;78(5):2703-6

Abraham SF, Beumont PJ, Cobbin DM: Catecholamine metabolism and body weight in anorexia nervosa. Br J Psychiatry 1981 Mar;138:244-7

Abrams WR, Eliraz A, Kimbel P, et al: The effect of the oxidizing agents chloramine-T and cigarette smoke on dog serum proteinase inhibitor(s). Exp Lung Res 1980 Aug;1(3):211-23

Abramson HA, Gettner HH, Rolo A: The intracranial injection of drugs in goldfish. II. Preliminary report of behavior of serotonin as a potential hallucinogen when injected intracranially and intraabdominally. J Asthma Res 1980 Jul;17(4):175-6

Acunzo S, Velotti M, Manganiello C, et al: Le attività transaminasiche sieriche (AST e ALT) in ratti iniettati con serotonina. Boll Soc Ital Biol Sper 1981 Jan 15;57(1):76-9 (Eng. Abstr.) **(Ita)**

Adams LM, Geyer MA: Effects of 6-hydroxydopamine lesions of locus coeruleus on startle in rats. Psychopharmacology (Berlin) 1981; 73(4):394-8

Adams PR, Constanti A, Banks FW: Opposing actions of convulsants and anticonvulsants on GABA responses of crayfish stretch receptors. Adv Biochem Psychopharmacol 1981;29:369-78

Adams PR: Biophysical aspects of transmitter action. Fed Proc 1981 Sep; 40(11):2611-3

Adamskaia EI, Babichev VN: Rol'noradrenalina v sekretsii liuteiniziruiushchego gormona. Biull Eksp Biol Med 1981 Jun; 91(6):730-3 (Eng. Abstr.) **(Rus)**

Ader R, Grota LJ: Immunosuppressive effect of tetrahydrocannabinol plus cyclophosphamide [letter] N Engl J Med 1981 Aug 20;305(8):463

Adler B, Gimbrone MA Jr, Schafer AI, et al: Prostacyclin and beta-adrenergic catecholamines inhibit arachidonate release and PGI2 synthesis by vascular endothelium. Blood 1981 Sep;58(3):514-7

Advenier C, Berdeaux A: Cholinergiques et anticholinergiques. Rev Prat 1981 Aug;31(37):2663-8 (Eng. Abstr.) **(Fre)**

Ager A, Gordon JL: Effects of vasoactive and inflammatory agents on cyclic AMP levels in W138 fibroblasts, endothelial and vascular smooth muscle cells in culture. Agents Actions 1980 Dec;10(6):569-72

Agostini M del C, Borda ES, Gimeno MF, et al: Differences in the effects of acetylcholine on the vas deferens from normal and castrated rats. A participation of adrenergic mechanisms. Arch Int Pharmacodyn Ther 1981 Apr;250(2):212-20

Aguilera G, Harwood JP, Catt KJ: Somatostatin modulates effects of angiotensin II in adrenal glomerulosa zone. Nature 1981 Jul 16; 292(5820):262-3

Ahlman H, DeMagistris L, Zinner M, et al: Release of immunoreactive serotonin into the lumen of the feline gut in response to vagal nerve stimulation. Science 1981 Sep 11;213(4513):1254-5

Ahmed-Sorour H, Bailey CJ: Role of ovarian hormones in the long-term control of glucose homeostasis. Interaction with insulin, glucagon and epinephrine. Horm Res 1980;13(6):396-403

Ahrén B, Järhult J, Lundquist I: Influence of the sympatho-adrenal system and somatostatin on the secretion of insulin in the rat. J Physiol (Lond) 1981 Mar;312:563-75

Aickin CC, Deisz RA, Lux HD: Opposite effects of 5,5-diphenylhydantoin and picrotoxin on GABAergic inhibition in crayfish stretch receptor. Adv Biochem Psychopharmacol 1981;29:301-7

Aizawa I, Itoh Z, Harris V, et al: Plasma somatostatin-like immunoreactivity during the interdigestive period in the dog. J Clin Invest 1981 Jul;68(1):206-13

Akaike N, Brown AM, Nishi K, et al: Actions of verapamil, diltiazem and other divalent cations on the calcium-current of Helix neurones. Br J Pharmacol 1981 Sep;74(1):87-95

Aksel S: On the correlation of luteinizing hormone-releasing hormone, luteinizing hormone, follicle-stimulating hormone, and prolactin levels in plasma of women with normal menstrual cycles. Am J Obstet Gynecol 1981 Oct 15;141(4):362-7

Aksenova VM: Vliianie narusheniia innervatsii pecheni i miokarda na soderzhanie v nikh gistamina i serotonina. Ukr Biokhim Zh 1980 Sep-Oct;52(5):569-72 (Eng. Abstr.) **(Rus)**

Aktories K, Schultz G, Jakobs KH: The hamster adipocyte adenylate cyclase system. II. Regulation of enzyme stimulation and inhibition by monovalent cations. Biochim Biophys Acta 1981 Aug 5;676(1):59-67

Alberts P, Bartfai T, Stjärne L: Site(s) and ionic basis of alpha-autoinhibition and facilitation of [3H]noradrenaline secretion in guinea-pig vas deferens. J Physiol (Lond) 1981 Mar;312:297-334

Alderson LM, Baum MJ: Differential effects of gonadal steroids on dopamine metabolism in mesolimbic and nigro-striatal pathways of male rat brain. Brain Res 1981 Aug 10;218(1-2):189-206

Alexander F, Martin J: Nephrotic syndrome associated with lithium therapy. Clin Nephrol 1981 May;15(5):267-71

Alexander N, Velasquez M, Vlachakis ND: Red blood cells: in vivo site for transport and inactivation of biogenic amines in man and rats. Life Sci 1981 Aug 3;29(5):477-82

Alexander NJ, Fulgham DL, Wicklund R: Adrenergic blocking agents inadequate for nonsurgical male contraception. Fertil Steril 1981 Jul; 36(1):119-21

Alfredsson G, Sedvall G: Protein binding of chlorpromazine in cerebrospinal fluid and serum. Int Pharmacopsychiatry 1980;15(5):261-9

Algozzine GJ, Stewart RB, Springer PK: Decreased clearance of phenytoin with cimetidine [letter] Ann Intern Med 1981 Aug;95(2):244-5

Allen MD, Greenblatt DJ: Comparative protein binding of diazepam and desmethyldiazepam. J Clin Pharmacol 1981 May-Jun;21(5-6):219-23

Allenmark S, Qureshi GA: Studies on dopamine-converting enzymes in human plasma. J Chromatogr 1981 Apr 10;223(1):188-92

Alobaidi T, Naccache PH, Sha'afi RI: Calmodulin antagonists modulate rabbit neutrophil degranulation, aggregation and stimulated oxygen consumption. Biochim Biophys Acta 1981 Jul 17;675(3-4):316-21

Al'perina EL: Uchastie timusa v realizatsii moduliruiushchego vliianiia dofaminergicheskoĭ sistemy na immunogenez. Vestn Akad Med Nauk SSSR 1981;(5):30-3 (Eng. Abstr.) **(Rus)**

Altar A, Goldwag D, Terry RL, et al: Synergistic induction of pineal gland N-acetyltransferase activity by amphetamine and L-DOPA. Proc West Pharmacol Soc 1981;24:101-4

Altman DG: Constructing a normal range [letter] Clin Chem 1979 Mar; 25(3):492-3

Altstein M, Mittman S, Vogel Z: The effect of barbiturates on the degradation of enkephalin by brain enzymes. Life Sci 1981 Jan 12; 28(2):185-91

Altura BM, Chand N: Differential effects of prostaglandins on canine intrapulmonary arteries and veins. Br J Pharmacol 1981 Aug; 73(4):819-27

Amsterdam A, Knecht M, Catt KJ: Hormonal regulation of cytodifferentiation and intercellular communication in cultured granulosa cells. Proc Natl Acad Sci USA 1981 May;78(5):3000-4

Ananth J, Pecknold JC, van den Steen N, et al: Double-blind comparative study of clomipramine and amitriptyline in obsessive neurosis. Prog Neuropsychopharmacol 1981;5(3):257-62

Anber SA, Al-Janabi II, Mustafa RM, et al: In vitro detection of possible in vivo drug interactions. Part 1. The effect of hydrochlorothiazide and frusemide on the in vitro absorption characteristics of propranolol hydrochloride. Pharmazie 1981 Jun;36(6):425-7

Anctil M, Brunel S, Descarries L: Catecholamines and 5-hydroxytryptamine in photophores of Porichthys notatus. Radioenzymatic detection and radioautographic localization. Cell Tissue Res 1981;219(3):557-66

Andermann G, Dietz M: Simultaneous determination of cyclandelate and its metabolite in human plasma by capillary column gas-liquid chromatography. J Chromatogr 1981 May 8;223(2):365-70

Anderson BG, Reker D, Cooper TB: Prolonged adverse effects of haloperidol in normal subjects [letter] N Engl J Med 1981 Sep 10; 305(11):643-4

Anderson GH: Diet, neurotransmitters and brain function. Br Med Bull 1981 Jan;37(1):95-100 (69 ref.)

Anderson K, Kuruvilla A, Uretsky N, et al: Synthesis and pharmacological evaluation of sulfonium analogues of dopamine: nonclassical dopamine agonists. J Med Chem 1981 Jun;24(6):683-7

Ando S, Mizushima S: [Five autopsied cases of chronic diphenylhydantoin intoxication -- with special reference to the distribution of cerebellar degeneration and marked degeneration of nucleus fasciculi dorsalis (author's transl)] Seishin Shinkeigaku Zasshi 1980;82(7):423-43 (Eng. Abstr.) **(Jpn)**

Andreas K, Fischer HD: Toxizität von Organophosphaten unter dem Einfluss von Neuroleptika. Acta Biol Med Ger 1980;39(8-9):987-9 **(Ger)**

Andreev AA, Vul'fius EA, Kondrashova MN, et al: Reguliatsiia funktsionirovaniia kholinoretseptorov neĭronov molliuskov suktsinatom i noradrenalinom. Dokl Akad Nauk SSSR 1981;258(6):1466-9 **(Rus)**

Andreev BV, Ignatov IuD: Vliianie GAMK-negativnykh preparatov na anksioliticheskiĭ i sedativnyĭ éffekty diazepama. Biull Eksp Biol Med 1981 Jun;91(6):685-7 (Eng. Abstr.) **(Rus)**

Andreeva OG, Meerson YA, Shchelkunov EL: Stimulating effects of amphetamine on the visual system. Hum Physiol 1980 May-Jun; 6(3):199-205

Andrews PC, Dixon JE: Isolation and structure of a peptide hormone

AUTHOR SECTION

predicted from a mRNA sequence. A second somatostatin from the catfish pancreas. J Biol Chem 1981 Aug 25;256(16):8267-70

Angel I, Michaelson DM: Determination of delta psi, delta pH and the proton electrochemical gradient in isolated cholinergic synaptic vesicles. Life Sci 1981 Jul 27;29(4):411-6

Angevine LS, Nabeshima T, Ho IK, et al: Effect of chlorphentermine on the pulmonary disposition of norepinephrine in the isolated perfused rabbit lung. Exp Lung Res 1981 May;2(2):71-84

Angst J: Ungelöste Probleme bei der Indikationssetellung zur Lithiumprophylaxe affektiver und schizoaffektiver Erkrankungen. Bibl Psychiatr 1981;(161):32-44 (Eng. Abstr.) **(Ger)**

Anhut H, Knepel W, Nutto D, et al: Vasopressin stimulates release of beta-lipotropin and beta-endorphin in conscious rats as measured by radioimmunoassay of unextracted plasma. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):59-63

Anisman H, Glazier SJ, Sklar LS: Cholinergic influences on escape deficits produced by uncontrollable stress. Psychopharmacology (Berlin) 1981; 74(1):81-7

Anisman H, Ritch M, Sklar LS: Noradrenergic and dopaminergic interactions in escape behavior: analysis of uncontrollable stress effects. Psychopharmacology (Berlin) 1981;74(3):263-8

Anisman H, Sklar LS: Social housing conditions influence escape deficits produced by uncontrollable stress: assessment of the contribution of norepinephrine. Behav Neural Biol 1981 Aug;32(4):406-27

Ankier SI, Martin BK, Rogers MS, et al: Trazodone--a new assay procedure and some pharmacokinetic parameters. Br J Clin Pharmacol 1981 May;11(5):505-9

Annunziato L, Cerrito F, Raiteri M: Characteristics of dopamine release from isolated nerve endings of the tuberoinfundibular neurones. Neuropharmacology 1981 Aug;20(8):727-31

Aoshima H, Cash DJ, Hess GP: Mechanism of inactivation (desensitization) of acetylcholine receptor. Investigations by fast reaction techniques with membrane vesicles. Biochemistry 1981 Jun 9; 20(12):3467-74

Appenzeller O: What makes us run? [editorial] N Engl J Med 1981 Sep 3;305(10):578-80

Aragno R: The effect of catecholamines or sodium lactate on blood lactate distribution in the rat. J Sports Med Phys Fitness 1981 Mar;21(1):7-14

Araie M, Takase M: [Effects of dipivalyl epinephrine and S-596, a new beta-adrenergic blocker, on human aqueous humor dynamics (author's transl)] Nippon Ganka Gakkai Zasshi 1981 May 10;85(5):349-54 (Eng. Abstr.) **(Jpn)**

Araki T, Ito K, Kurosawa M, et al: The somato-adrenal medullary reflexes in rats. J Auton Nerv Syst 1981 Apr;3(2-4):161-70

Arató M, Szontágh L, Telegdy G: Effect of electroconvulsive treatment on brain monoamine content, pituitary-adrenal function and plasma prolactin. Acta Physiol Acad Sci Hung 1980;56(2):163-71

Arató M: Promethazine and diazepam potantiate the haloperidol induced prolactin responses. Commun Psychopharmacol 1980;4(4):317-22

Archer T, Ogren SO, Johansson C: The acute effect of p-chloroamphetamine on the retention of fear conditioning in the rat: evidence for a role of serotonin in memory consolidation. Neurosci Lett 1981 Aug 7;25(1):75-81

Areekul S, Srichairat S, Kirdudom P: Serum and red cell cholinesterase activity in people exposed to organophosphate insecticides. Southeast Asian J Trop Med Public Health 1981 Mar;12(1):94-8

Areekul S: Cholinesterase activity in human blood. J Med Assoc Thai 1981 Aug;64(8):363-6

Arilla E, Prieto JC, López-Martínez JM, et al: Somatostatin action on insulin secretion induced by chicken and porcine vasoactive intestinal peptide in the perfused rat pancreas. Horm Metab Res 1981 Jun; 13(6):314-7

Arison BH, Hirschmann R, Paleveda WJ, et al: On the low energy solution conformation of somatostatin. Biochem Biophys Res Commun 1981 Jun 16;100(3):1148-53

Armario A, Castellanos JM, Balasch J: Chronic and acute stress interrelationship: corticosterone response. Horm Metab Res 1981 Jul; 13(7):413-4

Armario A, Balasch J: Corticosterone response in group-housed rats exposed to psychogenic stresses in different social conditions. Physiol Behav 1981 Jul;27(1):179-81

Arneric SP, Goodale DB, Flynn JR, et al: Rapid and simple analysis of DOPA and 5-HTP using high performance liquid chromatography with electrochemical detection. Brain Res Bull 1981 May;6(5):407-11

Arnone A, Thillet J, Rosa J: The structure of hemoglobin Creteil (beta 89 Ser replaced by Asn) is similar to that of abnormal human hemoglobins having sequence changes at Tyr 145 beta. J Biol Chem 1981 Aug 25;256(16):8545-52

Aronsson S, Enemar A: On the structural and phyletic origin of the aminergic nerves of the hypophysis of frog tadpoles (Rana temporaria) with special reference to pars distalis. J Comp Neurol 1981 Aug 10; 200(3):315-21

Arora SK: Structure of tomaymycin, a DNA binding antitumor antibiotic. J Antibiot (Tokyo) 1981 Apr;34(4):462-4

Arregui A, Barer GR, Emson PC: Neurochemical studies in the hypoxic brain: substance P, met-enkephalin, GABA and angiotensin converting enzyme. Life Sci 1981 Jun 29;28(26):2925-9

Arvela P, Reinilä M, Pelkonen O: Effects of phenobarbital and beta-naphthoflavone on cerium induced biochemical changes in rat serum. Toxicol Lett 1981 Jun-Jul;8(4-5):213-6

Asarnow RF, MacCrimmon DJ: Span of apprehension deficits during the postpsychotic stages of schizophrenia. A replication and extension. Arch Gen Psychiatry 1981 Sep;38(9):1006-11

Ashcroft GW, Blackwood GW, Besson JA, et al: Positive and negative schizophrenic symptoms and the role of dopamine [letter] Br J Psychiatry 1981 Mar;138:268-9

Ashe JH, Libet B: Modulation of slow postsynaptic potentials by dopamine, in rabbit sympathetic ganglion. Brain Res 1981 Jul 27; 217(1):93-106

Aslan S, Nelson L, Carruthers M, et al: Stress and age effects on catecholamines in normal subjects. J Psychosom Res 1981;25(1):33-41

Asnis GM, Sachar EJ, Halbreich U, et al: The prolactin-stimulating potency of reserpine in man. Psychiatry Res 1981 Aug;5(1):39-45

Assaf SY, Crunelli V, Kelly JS: Depolarizing postsynaptic actions of GABA in the rat dentate gyrus. Adv Biochem Psychopharmacol 1981; 29:239-48

Au KS: (Ca2+ + Mg2+)-ATPase of chlorpromazine containing rabbit erythrocyte membrane. Gen Pharmacol 1981;12(4):285-90

Auerbach DA, Klein DC, Kirk KL, et al: Effects on fluorine analogs of norepinephrine on stimulation of cyclic adenosine 3',5'-monophosphate and binding to beta-adrenergic receptors in intact pinealocytes. Biochem Pharmacol 1981 May 15;30(10):1085-9

Ausiello DA, Hall D: Regulation of vasopressin-sensitive adenylate cyclase by calmodulin. J Biol Chem 1981 Oct 10;256(19):9796-8

Avakumov VM, Kovler MA: K mekhanizmu potentsirovaniia pantogamom nekotorykh éffektov geksobarbitala i barbital-natriia i ingibirovaniia fenaminovoĭ giperaktivnosti. Farmakol Toksikol 1981 Jan-Feb; 44(1):30-4 (Eng. Abstr.) **(Rus)**

Ayala-Guerrero F, Perera-Ortiz Y, Vargas L: Phasic activity induced by p-chlorophenylalanine in the auditory pathway. Neuropharmacology 1981 Mar;20(3):273-5

Azhialis VP, Stropus RS, Tamashauskas KA: Primenenie aliuminiia-formal'degida dlia vyiavleniia katekholaminov v kriostatnykh srezakh. Arkh Anat Gistol Embriol 1981 Mar;80(3):102-6 **(Rus)**

Azuma I, Okumura H, Saiki I, et al: Adjuvant activity of 6-amino-6-deoxy-muramyldipeptides and their acylamino derivatives on the induction of delayed hypersensitivity to azobenzenearsonate-N-acetyl-L-tyrosine in guinea pigs. Infect Immun 1981 Jun;32(3):1305-8

Azuma J, Sawamura A, Harada H, et al: Cyclic adenosine monophosphate modulation of contractility via slow Ca2+ channels in chick heart. J Mol Cell Cardiol 1981 Jun;13(6):577-87

B

Baba M, Tatsuta M, Okuda S, et al: [Effects of tetragastrin on catecholamines in gastric juice and gastric tissues in rats (author's transl)] Nippon Shokakibyo Gakkai Zasshi 1981 Jun;78(6):1191-7 (Eng. Abstr.) **(Jpn)**

Babichev VN, Ignatkov VIa, Gorelyi AV: Rol' noradrenalinchuvstvitel'nykh neĭronov preopticheskoĭ oblasti v reguliatsii osvobozhdeniia liuteiniziruiushchego gormona. Fiziol Zh SSSR 1981 Jun;67(6):809-15 (Eng. Abstr.) **(Rus)**

Babu UM, Maurer PH: The expression of anti-poly(LGlu60, LPhe40) idiotypic determinants dictated by the gene products in the major histocompatibility complex. J Exp Med 1981 Sep 1;154(3):649-58

Baca I, Mittmann U, Feurle GE, et al: Effect of neurotensin on regional intestinal blood flow in the dog. Res Exp Med (Berl) 1981;179(1):53-8

Bachelard HS: Biochemistry of central active amino acids. Adv Biochem Psychopharmacol 1981;29:475-97 (97 ref.)

Bacher N, Lewis H: Reserpine added to neuroleptic-tricyclic in refractory schizophrenics. J Clin Psychiatry 1981 Aug;42(8):326

Bacon A, Sattler C, Martin JE: Melatonin effect on the hamster pituitary response to LHRH. Biol Reprod 1981 Jun;24(5):993-9

Bacopoulos NG: High-affinity stereospecific binding of 3H-dopamine in rat brain: interaction with endogenous dopamine. Biochem Pharmacol 1981 Jul 15;30(14):2037-40

Badawy AA, Evans M: Inhibition of rat liver tryptophan pyrrolase activity and elevation of brain tryptophan concentration by administration of antidepressants. Biochem Pharmacol 1981 Jun 1;30(11):1211-6

Baertschi AJ, Zingg HH, Dreifuss JJ: Enkephalins, substance P, bradykinin and angiotensin II: differential sites of action on the hypothalamo-neurohypophysial system. Brain Res 1981 Sep 7; 220(1):107-19

Bagust J, Green KA, Kerkut GA: Strychnine sensitive inhibition in the dorsal horn of mammalian spinal cord. Brain Res 1981 Aug 3; 217(2):425-9

Baillie GR, Smith L, Goel KM: Flupenthixol poisoning in a child. Drug Intell Clin Pharm 1981 May;15(5):388

Bain DJ, Sales CM: Referring children to an ENT department and prescribing psychotropic drugs to their mothers.

AUTHOR SECTION

Br Med J [Clin Res] 1981 Aug 29;283(6291):585-7

Baker JK, Wohlford JG, Bradbury BJ, et al: Mammalian metabolism of phencyclidine. J Med Chem 1981 Jun;24(6):666-9

Bakris GL, Taylor MA, Mulopulos GP, et al: Lithium prophylaxis and the kidney. J Affective Disord 1981 Mar;3(1):37-42

Bala SP, Cohen B, Morris AG, et al: Saccades of hyperactive and normal boys during ocular pursuit. Dev Med Child Neurol 1981 Jun; 23(3):323-36

Balashov AM, Brusov OS, Balakireva NN, et al: Issledovanie vzaimodeistviia D-Ala2-[Tyr-3,5-3H]énkefalina(5-D-Leu) s opiatnymi retseptorami golovnogo mozga krys. Biokhimiia 1981 Jun;46(6):1067-72 (Eng. Abstr.) **(Rus)**

Baldaccini F: Per una standardizzazione della prova da carico con glucosio per via orale. Recenti Prog Med 1981 Apr;70(4):433-6 (18 ref.) **(Ita)**

Baldessarini RJ, Lipinski JF: Risks of antipsychotic drugs overemphasized [letter] N Engl J Med 1981 Sep 3;305(10):588-9

Balla T, Nagy K, Tarján E, et al: Effect of reduced extracellular sodium concentration on the function of adrenal zona glomerulosa: studies in conscious rats. J Endocrinol 1981 Jun;89(3):411-6

Ballard S, Tobin T: Atypical conditions for quantitative recovery of acepromazine and chlorpromazine from plasma. J Toxicol Environ Health 1981 May;7(5):745-51

Banerji TK, Quay WB: Compensatory increase in adrenal weight and dopamine-beta-hydroxylase activity after unilateral adrenalectomy: experimental evidence for a pineal-dependent contribution. Proc Soc Exp Biol Med 1981 Sep;167(4):514-8

Bank RL, Bridenbaugh RH: Reliability of tricyclic antidepressant levels -- further questions [letter] J Clin Psychiatry 1981 Sep;42(9):364

Banki CM, Vojnik M, Molnar G: Cerebrospinal fluid amine metabolites, tryptophan and clinical parameters in depression. Part 1. Background variables. J Affective Disord 1981 Jun;3(2):81-9

Bannon MJ, Bunney EB, Roth RH: Mesocortical dopamine neurons: rapid transmitter turnover compared to other brain catecholamine systems. Brain Res 1981 Aug 10;218(1-2):376-82

Banns H, Ekström J: Acetylcarnitine as a contamination in the radiochemical assay of acetylcholine synthesis in salivary glands and urinary bladders. Acta Physiol Scand 1981 Feb;111(2):165-9

Baraban JM, Aghajanian GK: Noradrenergic innervation of serotonergic neurons in the dorsal raphe: demonstration by electron microscopic autoradiography. Brain Res 1981 Jan 5;204(1):1-11

Baraka A, Wakid N, Mansour R, et al: Effect of neostigmine and pyridostigmine on the plasma cholinesterase activity. Br J Anaesth 1981 Aug;53(8):849-51

Baraka A: Neostigmine and atypical plasma cholinesterase activity [letter] Br J Anaesth 1981 Aug;53(8):907-8

Barbezat GO, Reasbeck PG: Somatostatin inhibition of glucagon-stimulated jejunal secretion in the dog. Gastroenterology 1981 Sep;81(3):471-4

Barbieri C, Caldara R, Ferrari C, et al: Inhibition of the renin-angiotensin-aldosterone system by L-dopa with and without inhibition of extracerebral dopa decarboxylase in man. Clin Sci 1981 Aug;61(2):187-90

Bardsley ME, Bachelard HS: Catecholamine levels and tyrosine hydroxylase activities in rat brain regions after chronic treatment with, and withdrawal of, methamphetamine. Biochem Pharmacol 1981 Jun 15;30(12):1543-9

Bargiel Z, Nowicka H, Wójcikowska J: Swim-stress induced changes of rat adrenal catecholamine level depending on metabolic state and different ambient temperature. Folia Histochem Cytochem (Krakow) 1981;19(1):31-7

Barker HA: Amino acid degradation by anaerobic bacteria. Annu Rev Biochem 1981:50:23-40 (77 ref.)

Barkov NK, Machula AI: Izmenenie vremennykh parametrov zritel'nogo vospriiatiia v usloviiakh deistviia psikhostimuliatorov. Farmakol Toksikol 1981 Jan-Feb;44(1):12-4 (Eng. Abstr.) **(Rus)**

Barney CC, Threatte RM, Kikta DC, et al: Effects of serotonin and L-5-hydroxytryptophan on plasma renin activity in rats. Pharmacol Biochem Behav 1981 Jun;14(6):895-900

Barone FC, Wayner MJ, Tsai WH, et al: Effects of ventral tegmental area stimulation and microiontophoretic application of dopamine and norepinephrine on hypothalamic neurons. Brain Res Bull 1981 Aug; 7(2):181-93

Barritt GJ, Parker JC, Wadsworth JC: A kinetic analysis of the effects of adrenaline on calcium distribution in isolated rat liver parenchymal cells. J Physiol (Lond) 1981 Mar;312:29-55

Bartha J, Hably C: Sodium and water transport in frog skin: effect of indomethacin. Acta Physiol Acad Sci Hung 1981;57(1):9-17

Barton DF: More on lorazepam withdrawal [letter] Drug Intell Clin Pharm 1981 Feb;15(2):134

Bauer K, Beier S, Horsthemke B, et al: Estrogen effects on LH-RH degrading brain and pituitary enzymes. Exp Brain Res 1981;Suppl 3:93-107

Baughman RW, Gilbert CD: Aspartate and glutamate as possible neurotransmitters in the visual cortex. J Neurosci 1981 Apr;1(4):427-39

Bauman JH: Influence of cimetidine on pharmacokinetics of propranolol [letter] Br Med J [Clin Res] 1981 Jul 18;283(6285):232

Baumann PA, Waldmeier PC: Further evidence for negative feedback control of serotonin release in the central nervous system. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):36-43

Baumgartner AM, Jones PF, Black CT: Detection of phencyclidine in hair. J Forensic Sci 1981 Jul;26(3):576-81

Baumhackl U, Herles J, Katschnig H, et al: Lithiumprophylaxe in der nervenärztlichen Praxis. Bibl Psychiatr 1981;(161):221-3 **(Ger)**

Bayon A, Shoemaker WJ, Lugo L, et al: In vivo release of enkephalin from the globus pallidus. Neurosci Lett 1981 Jun 12;24(1):65-70

Bazian AS, Glebov RN: Metodika odnovremennoi registratsii zakhvata i sekretsii 14C-noradrenalina sinaptosomami golovnogo mozga krys. Biull Eksp Biol Med 1981 Mar;91(3):377-9 (Eng. Abstr.) **(Rus)**

Bdovichenko LM: Vliianie nekotorykh biologicheski aktivnykh soedinenii i dvukhvalentnykh kationov na laktat- i malatdegidrogenaznuiu aktivonost' v kletochnykh fraktsiiakh golovnogo mozga. Ukr Biokhim Zh 1981 May-Jun;53(3):66-70 (Eng. Abstr.) **(Rus)**

Beaty O 3d, Collis MG, Shepherd JT: Action of lithium on the adrenergic nerve ending. J Pharmacol Exp Ther 1981 Aug;218(2):309-17

Beauvillain JC, Tramu G, Dubois MP: Ultrastructural immunocytochemical evidence of the presence of a peptide related to ACTH in granules of LHRH nerve terminals in the median eminence of the guinea pig. Cell Tissue Res 1981;218(1):1-6

Beckenhauer DM, Conrad GW: The effect of thyroxine on transparency and PAPS synthesis in the avian cornea. Dev Biol 1981 May;84(1):225-9

Becker D, Schwibbe M, Wuttke W: Effects of gonadal steroids on EEG and performance in the human. Exp Brain Res 1981;Suppl 3:309-17

Behari J, Rai DV: Effect of some physiologically important drugs on the skin impedance. Med Biol Eng Comput 1981 Mar;19(2):244-6

Behbehani MM, Pomeroy SL, Mack CE: Interaction between central gray and nucleus raphe magnus: role of norepinephrine. Brain Res Bull 1981 May;6(5):361-4

Beitman BD: Pharmacotherapy as an intervention during the stages of psychotherapy. Am J Psychother 1981 Apr;35(2):206-14

Bélanger L: Le rôle social des médicaments. Infirm Can 1981 Sep; 23(8):25-7 **(Fre)**

Belchetz PE: Functional and anatomical segregation of hypothalamic opiate receptors involved in prolactin and growth hormone secretion in cynomolgus monkeys. Life Sci 1981 Jun 29;28(26):2961-71

Belew K, Brady T: Induction of tyrosine aminotransferase by pyridoxine in Drosophila hydei. Chromosoma 1981;82(1):99-106

Bell FP, Hubert EV: Membrane-active agents. Effect of various anesthetics and chlorpromazine on arterial lipid metabolism. Atherosclerosis 1981 Jul;39(4):517-25

Bell FR, Webber DE, Wass JA, et al: Correlation of endogenous somatostatin, gastric inhibitory polypeptide, glucagon and insulin with gastric function in the conscious calf. J Endocrinol 1981 Jun;89(3):451-6

Belleville M, Grand M, Briet P: Plasma levels, elimination and metabolic fate of 4a-amino-8-chloro-2-methyl-1,2,3,4,4a,10a-hexahydro-10H-benzopyr acid lactam, a new antidepressive agent, in rats and dogs. Drug Metab Dispos 1981 May-Jun;9(3):233-9

Bellin SI, Ritter S: Insulin-induced elevation of hypothalamic norepinephrine turnover persists after glucorestoration unless feeding occurs. Brain Res 1981 Aug 3;217(2):327-37

Ben-Uriah Y, Yehuda S, Carasso RL: Physiological evidence (hypothermia) for central effects of beta-blocker agents. Int J Neurosci 1981;14(1-2):41-6

Benfey BG: Comments on: 'anticholinergic effects of disopyramide and quinidine on guinea pig myocardium--mediation by direct muscarinic receptor blockade' [letter] Circ Res 1981 Sep;49(3):821

Beninger RJ, Hanson DR, Phillips AG: The acquisition of responding with conditioned reinforcement: effects of cocaine, (+)-amphetamine and pipradrol. Br J Pharmacol 1981 Sep;74(1):149-54

Benjamin AM, Quastel JH: Acetylcholine synthesis in synaptosomes: mode of transfer of mitochondrial acetyl coenzyme A. Science 1981 Sep 25;213(4515):1495-7

Bennati E, Piergiovanni L: Determinazione rapida, mediante HPLC, del fenobarbitale sodico e di un suo prodotto di degradazione in uno sciroppo. Boll Chim Farm 1981 Mar;120(3):172-8 (Eng. Abstr.) **(Ita)**

Bennett BA, Sundberg DK: Catecholamine biosynthesis in specific brain areas of the rat as determined by liquid chromatography and amperometric detection. Life Sci 1981 Jun 22;28(25):2811-7

Benoist L, Le Dafniet M, Rotsztejn WH, et al: Gonadotrophin release by gonadotrophs incubated with gonadotrophin-releasing hormone is independent of intracellular cAMP accumulation. Acta Endocrinol (Copenh) 1981;97(3):329-37

Benson JA, Sullivan RE, Watson WH 3d, et al: The neuropeptide proctolin acts directly on Limulus cardiac muscle to increase the amplitude of contraction. Brain Res 1981 Jun 1;213(2):449-54

Benuck M, Berg MJ, Marks N: A distinct peptidyl dipeptidase that degrades enkephalin: exceptionally high activity in rabbit kidney. Life Sci 1981 Jun 8;28(23):2643-50

Bény JL, Baertschi AJ: Corticotropin-releasing factors (CRF) secreted by the rat median eminence in vitro in the presence or absence of ascorbic acid: quantitative role of vasopressin and catecholamines.

AUTHOR SECTION

Endocrinology 1981 Sep;109(3):813-7

Bereksi B, Gulliand JC, Noirot P, et al: Influence du système GABAergique sur le copmportement alimentaire induit par la technique de pincement de la queue (tail-pinching ou T.P.) chez le rat. C R Trav Lab Carlsberg 1981;175(3):323-9 (Eng. Abstr.) (Fre)

Berelowitz M, Firestone SL, Frohman LA: Effects of growth hormone excess and deficiency on hypothalamic somatostatin content and release and on tissue somatostatin distribution. Endocrinology 1981 Sep; 109(3):714-9

Bergel M: Antileprosy and biological antioxidant activity of serotonin. Int J Lepr 1981 Jun;49(2):259

Bergey GK, Swaiman KF, Schrier BK, et al: Adverse effects of phenobarbital on morphological and biochemical development of fetal mouse spinal cord neurons in culture. Ann Neurol 1981 Jun;9(6):584-9

Bergner EA, Dougherty RC: Detection of urinary primary amines through negative chemical ionization mass spectrometry of fluorescamine derivatives. Biomed Mass Spectrom 1981 May;8(5):208-10

Bergstrom DA, Walters JR: Neuronal responses of the globus pallidus to systemic administration of d-amphetamine: investigation of the involvement of dopamine, norepinephrine, and serotonin. J Neurosci 1981 Mar;1(3):292-9

Berkenbosch F, Vermes I, Tilders FJ: Epinephrine as a potent releaser of immunoreactive beta-endorphin in rats. Eur J Pharmacol 1981 Jun 10;72(1):97-100

Berney T, Kolvin I, Bhate SR, et al: School phobia: a therapeutic trial with clomipramine and short-term outcome. Br J Psychiatry 1981 Feb; 138:110-8

Bernstein AS, Taylor KW, Starkey P, et al: Bilateral skin conductance, finger pulse volume, and EEG orienting response to tones of differing intensities in chronic schizophrenics and controls. J Nerv Ment Dis 1981 Aug;169(8):513-28

Berod A, Hartman BK, Pujol JF: Importance of fixation in immunohistochemistry: use of formaldehyde solutions at variable pH for the localization of tyrosine hydroxylase. J Histochem Cytochem 1981 Jul;29(7):844-50

Berridge K, Grill HJ, Norgren R: Relation of consummatory responses and preabsorptive insulin release to palatability and learned taste aversions. J Comp Physiol Psychol 1981 Jun;95(3):363-82

Berridge MJ: Electrophysiological evidence for the existence of separate receptor mechanisms mediating the action of 5-hydroxytryptamine. Mol Cell Endocrinol 1981 Jul;23(1):91-104

Bertolini AM, Santagostino A: Deficit di aminoacidi precursori di mediatori chimici e di creatina nell'anziano. Minerva Med 1981 Sep 8;72(32):2157-60 (Ita)

Best JD, Taborsky GJ Jr, Halter JB, et al: Glucose disposal is not proportional to plasma glucose level in man. Diabetes 1981 Oct; 30(10):847-50

Best LC, Bone EA, Graham R, et al: Strontium ions induce production of thromboxane B2 and secretion of 5-hydroxytryptamine in washed human platelets. Biochem Pharmacol 1981 Mar 15;30(6):635-7

Beumont PJ, Abraham SF: Continuous infusion of luteinizing hormone releasing hormone (LHRH) in patients with anorexia nervosa. Psychol Med 1981 Aug;11(3):477-84

Beumont PJ, Glaun D, George GC, et al: Thyrotropic hormone and psychiatric symptoms. Biol Psychiatry 1981 Jul;16(7):671-7

Beuverova EI, Bragina EV, Gusarova EV, et al: Vliianie nekotorykh farmakologicheskikh preparatov na vyzhivaemost' fibroblastov kitaiskogo khomiachka in vitro. Biull Eksp Biol Med 1981 Jun; 91(6):739-40 (Eng. Abstr.) (Rus)

Bhargava HN: The effects of thyrotropin releasing hormone on pentobarbital tolerance. Eur J Pharmacol 1981 Jun 10;72(1):63-8

Bhargava VK, Bhargava P, Sharma DN, et al: Modification by strychnine and D-tubocurarine of cardiac vagal inhibition in dogs. Neurosci Lett 1981 May 6;23(2):175-9

Biancani P, CiCalzi LK, McCallum RW: Mechanism of histamine-induced excitation of the cat pylorus. J Clin Invest 1981 Sep;68(3):582-8

Bickford PC, Palmer MR, Rice KC, et al: Electrophysiological effects of phencyclidine on rat hippocampal pyramidal neurons. Neuropharmacology 1981 Aug;20(8):733-42

Bicknell-Brown E, Lim BT, Kimura T: Laser Raman spectroscopy of adrenal iron-sulfur apoprotein: the anomalous tyrosine residue at position 82. Biochem Biophys Res Commun 1981 Jul 16;101(1):298-305

Bidder TG: Electroconvulsive therapy in the medically ill patient. Psychiatr Clin North Am 1981 Aug;4(2):391-405 (60 ref.)

Biegański T, Kusche J, Feussner KD, et al: The importance of human intestinal diamine oxidase in the oxidation of histamine and/or putrescine. Arch Immunol Ther Exp (Warsz) 1980;28(6):901-6

Bielkiewicz B, Nowak JZ, Zandarowska E: Influence of oxotremorine on histamine level and histamine synthesis in the rat brain. Arch Immunol Ther Exp (Warsz) 1980;28(6):921-5

Bierner RJ, McHugh WB, Rahe RH: Biochemical variability in a tem sports situation. J Human Stress 1981 Sep;7(3):12-7

Bigalke H, Heller I, Bizzini B, et al: Tetanus toxin and botulinum A toxin inhibit release and uptake of various transmitters, as studied with particulate preparations from rat brain and spinal cord. Naunyn Schmiedebergs Arch Pharmacol 1981 Jun;316(3):244-51

Biggio G, Guarneri P, Corda MG: Benzodiazepine and GABA receptors in the rat retina: effect of light and dark adaptation. Brain Res 1981 Jul 6;216(1):210-4

Bilikiewicz A, Januskiewicz-Grabiasowa A, Deptulski T, et al: Changes in the electrocardiogram during treatment with tricyclic antidepressant drugs in endogenous depression. Agressologie 1979;20(D):287-9

Billaudel B, Sutter BC: Modulation of the direct effect of corticosterone upon glucose-induced insulin secretion of rat isolated islets of Langerhans. Diabete Metab 1981 Jun;7(2):91-6

Bizzarro A, Iannucci F, Tolino A, et al: Inhibiting effect of atropine on prolactin blood levels after stimulation with TRH. Clin Exp Obstet Gynecol 1980;7(2):108-11

Blackburn TP, Cox B, Heapy CG, et al: Supersensitivity of nigral serotonin receptors and rat rotational behaviour. Eur J Pharmacol 1981 May 8; 71(2-3):343-6

Blackwell B: Adverse effects of antidepressant drugs. Part 1: monoamine oxidase inhibitors and tricyclics. Drugs 1981 Mar;21(3):201-19 (0 ref.)

Blackwell B, Peterson GR, Kuzma RJ, et al: The effect of five tricyclic antidepressants on salivary flow and mood in healthy volunteers. Commun Psychopharmacol 1980;4(4):255-61

Blair H, Kahn AJ, Sadow J, et al: Disassociation of lysosomal enzyme secretion and macrophage-mediated bone resorption. Biochem Biophys Res Commun 1981 Jun 16;100(3):959-64

Blazsó G, Minker E: A ganglionáris kolinerg receptorok alkilálása haloalkilaminokkal. Acta Pharm Hung 1980 May;50(3):137-44 (Eng. Abstr.) (Hun)

Blessing WW, Furness JB, Costa M, et al: Projection of ventrolateral medullary (A1) catecholamine neurons toward nucleus tractus solitarii. Cell Tissue Res 1981;220(1):27-40

Blessing WW, Goodchild AK, Dampney RA, et al: Cell groups in the lower brain stem of the rabbit projecting to the spinal cord, with special reference to catecholamine-containing neurons. Brain Res 1981 Sep 21; 221(1):35-55

Block ER, Stalcup SA: Depression of serotonin uptake by cultured endothelial cells exposed to high O2 tension. J Appl Physiol 1981 Jun; 50(6):1212-9

Blume H: Biotransformation von Amphetamin-Derivaten durch Rattenleber-Mitochondrien. 2. Mitt.: Oxidative Desaminierung von Amphetamin und Reduktion von Phenylaceton. Arzneimittelforsch 1981;31(6):994-7 (Eng. Abstr.) (Ger)

Blume H: Biotransformation von Amphetamin-Derivaten durch Rattenleber-Mitochondrien. 1. Mitt.: Oxidative Entalkylierung von N,N-Dialkyl- und N-Alkylamphetaminen. Arzneimittelforsch 1981; 31(5):805-9 (Eng. Abstr.) (Ger)

Bluth R, Langnickel R, Raubach KH, et al: A simplified enzymatic assay for the determination of acetylcholine and choline in discrete structures of rat brain. Acta Biol Med Ger 1980;39(8-9):881-7

Boarder MR, Erdelyi E, Barchas JD: Synthetic N-dimethyl beta-endorphin, a stabilized opioid peptide. Biochem Pharmacol 1981 Jun 1;30(11):1289-93

Boas RS, Messenger MJ, Mittag TW, et al: The effects of topically applied epinephrine and timolol on intraocular pressure and aqueous humor cyclic-AMP in the rabbit. Exp Eye Res 1981 Jun;32(6):681-90

Bochkina GI, Sukhova GS, Udel'nov MG, et al: Vliianie iontoforeticheskoĭ applikatsii atsetilkholina na ritm razriadov i formu potentsiala deĭstviia kletok peĭsmekera. Biull Eksp Biol Med 1981 Mar;91(3):259-60 (Eng. Abstr.) (Rus)

Bock UE, Waser PG: Gas chromatographic determination of some biogenic amines as their pentafluorobenzoyl derivatives in the picogram range and its applicability to biological materials. J Chromatogr 1981 Sep 4;213(3):413-28

Bockaert J: General characteristics, localization, and adaptative responsiveness of neurotransmitter-sensitive adenylate cyclases in the central nervous system. Adv Cyclic Nucleotide Res 1981;14:611-28

Boehme RE, Ciaranello RD: Dopamine receptor binding in inbred mice: strain differences in mesolimbic and nigrostriatal dopamine binding sites. Proc Natl Acad Sci USA 1981 May;78(5):3255-9

Bohaček N, Mihovilovic M: Usporedba djelovanja standardnog odnosno retard oblika litijeva karbonata u manično-depresivnih psihoza. Lijec Vjesn 1980 Oct;102(10):575-9 (Eng. Abstr.) (Scr)

Boido A, Cappello B, Sparatore F: Andamento dell'alchilazione della 6-benzil-5H-dibenzo(d,f)-(1,3)diazepina. Boll Soc Ital Biol Sper 1981 Apr 15;57(7):759-65 (Eng. Abstr.) (Ita)

Bolland J, Geubelle F: Les intoxications iatrogéniques en pédiatrie. Rev Med Liege 1981 May;36(1):455-8 (Fre)

Bolstad G, Helle KB, Serck-Hanssen G: Heterogeneity in the adrenomedullary storage of catecholamines, ATP, calcium and releasable dopamine beta-hydroxylase activity. J Auton Nerv Syst 1980 Dec;2(4):337-54

Bondarenko BB, Kameneva EM: Sluchaĭ lekarstvennoĭ bolezni, vyzvannoĭ aminalonom. Klin Med (Mosk) 1981 Mar;59(3):109-10 (Rus)

Bongrani S, Schiantarelli P, Papotti M, et al: Evidence of overadditive interaction between fenoterol and ipratropium bromide in the counteraction of cholinomimetic-induced tracheobronchial contractions. Arzneimittelforsch 1981;31(6):970-3

Bönner G, Autenrieth R, Marin-Grez M, et al: Effects of sodium loading.

desoxycorticosterone acetate, and corticosterone on urinary kallikrein excretion. Horm Res 1981;14(2):87–94

Booth RF, Clark JB: Energy metabolism in rat brain: inhibition of pyruvate decarboxylation by 3-hydroxybutyrate in neonatal mitochondria. J Neurochem 1981 Jul;37(1):179–85

Borbély AA: Etude physiologique et pharmacologique de la régulation du sommeil chez le rat. Actual Pharmacol (Paris) 1981;33:91–104 (Fre)

Borchert HH, Gedan A, Döhnert H: Beeinflussung der Elimination von Valproinsäure durch Phenobarbital. Pharmazie 1981 Apr;36(4):298–9 (Ger)

Bordunovskaia VP, Tsirkin VI, Sashenkov SL: Desensitizatsiia izolirovannogo miometriia krys k biologicheski aktivnym veshchestvam. Fiziol Zh SSSR 1981 Mar;67(3):390–7 (Eng. Abstr.) (Rus)

Borea PA: Structure – activity relationships in 1,4-benzodiazepines. Boll Soc Ital Biol Sper 1981 Mar 30;57(6):628–32

Borkman RF, Tassin JD, Lerman S: The rates of photodestruction of tryptophan residues in human and bovine ocular lens proteins. Exp Eye Res 1981 Jun;32(6):747–54

Borkowska J, Tyburczyk W: Działanie monokrotofosu na układ neuroprzenośników ośrodkowego układu nerwowego. Rocz Panstw Zakl Hig 1980;31(6):605–10 (Eng. Abstr.) (Pol)

Borsini F, Bendotti C, Velkov V, et al: Immobility test: effects of 5-hydroxytryptaminergic drugs and role of catecholamines in the activity of some antidepressants. J Pharm Pharmacol 1981 Jan;33(1):33–7

Bortz WM 2d, Angwin P, Mefford IN, et al: Catecholamines, dopamine, and endorphin levels during extreme exercise [letter] N Engl J Med 1981 Aug 20;305(8):466–7

Boss AM, Kingstone D: Further observations on serum free thyroxine concentrations during pregnancy. Br Med J [Clin Res] 1981 Aug 29; 283(6291):584

Boulard G, Cazenave J, Varene N, et al: Dosage du diazépam dans le liquide céphalo-rachidien ventriculaire et dans le sang veineux périphérique chez l'homme. Ann Anesthesiol Fr 1981;22(2):185–90 (Eng. Abstr.) (Fre)

Bourgouin J, Gagnon MA, Elie R, et al: Butriptyline: human pharmacokinetics and comparative bioavailability of conventional and sustained release formulations. Biopharm Drug Dispos 1981 Apr–Jun; 2(2):123–30

Bourguignon JP, Franchimont P: Libération intermittente de gonadolibérine (GnRH) par l'hypothalamus du rat in vitro. C R Trav Lab Carlsberg 1981;175(3):389–96 (Eng. Abstr.) (Fre)

Bowers LD, Johnson PR: On-line cleavage of urinary estriol conjugates with immobilized beta-glucuronidase before liquid-chromatographic analysis. Clin Chem 1981 Sep;27(9):1554–7

Bowker RM, Westlund KN, Coulter JD: Serotonergic projections to the spinal cord from the midbrain in the rat: an immunocytochemical and retrograde transport study. Neurosci Lett 1981 Jul 17;24(3):221–6

Braccini T, Darcourt G, Corti H, et al: Signification clinique du rapport érythro-plasmatique du lithium. Acta Psychiatr Belg 1980 Jul–Aug; 80(4):413–9 (Eng. Abstr.) (Fre)

Braestrup C, Nielsen M: [3H]Propyl beta-carboline-3-carboxylate as a selective radioligand for the BZ1 benzodiazepine receptor subclass. J Neurochem 1981 Aug;37(2):333–41

Brambilla F: Neuroendocrine function in schizophrenia. Acta Psychiatr Belg 1980 Jul–Aug;80(4):421–35

Brand L, Ross JB, Laws WR: Nanosecond fluorometry and the luminescence of biological macromolecules. Ann NY Acad Sci 1981; 366:197–207

Brandenberger G, Follenius M, Wittersheim G, et al: Plasma catecholamines and pituitary adrenal hormones related to mental task demand under quiet and noise conditions. Biol Psychol 1980 Jun; 10(4):239–52

Brannen JO, McEvoy JP, Wilson WH, et al: A double-blind comparison of bromperidol and haloperidol in newly admitted schizophrenic patients. Pharmacopsychiatria 1981 Jul;14(4):139–40

Brantl V, Teschemacher H, Bläsig J, et al: Opioid activities of beta-casomorphins. Life Sci 1981 Apr 27;28(17):1903–9

Brazeau P, Ling N, Esch F, et al: High biological activity of the synthetic replicates of somatostatin-28 and somatostatin-25. Regul Pept 1981 Jan; 1(4):255–64

Brecha N, Karten HJ, Schenker C: Neurotensin-like and somatostatin-like immunoreactivity within amacrine cells of the retina. Neuroscience 1981;6(7):1329–40

Brent R, Kalman T: Fluphenazine resistant psychosis. Can J Psychiatry 1981 Mar;26(2):118–9

Brewster D, Waltham K: TRH degradation rates vary widely between different animal species. Biochem Pharmacol 1981 Mar 15;30(6):619–22

Briley M, Langer SZ: Sodium dependency of [3H]imipramine binding in rat cerebral cortex. Eur J Pharmacol 1981 Jul 10;72(4):377–80

Brizzi G, Foglia M, Acunzo S, et al: Andamento temporale della glicemia nei ratti dopo iniezione intraperitoneale di una dose di serotonina. Boll Soc Ital Biol Sper 1981 Apr 15;57(7):755–8 (Eng. Abstr.) (Ita)

Brodde OE, Meyer FJ, Schemuth W, et al: Demonstration of specific vascular dopamine receptors mediating vasodilation on the isolated rabbit mesenteric artery. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):24–30

Brodde OE, Freistühler J, Meyer FJ: Stereospecific antagonism by d-butaclamol of dopamine-induced relaxation of the isolated rabbit mesenteric artery. J Cardiovasc Pharmacol 1981 Jul–Aug;3(4):828–37

Brodin E, Gazelius B, Olgart L, et al: Tissue concentration and release of substance P-like immunoreactivity in the dental pulp. Acta Physiol Scand 1981 Feb;111(2):141–9

Brogden RN, Heel RC, Speight TM, et al: Trazodone: a review of its pharmacological properties and therapeutic use in depression and anxiety. Drugs 1981 Jun;21(6):401–29 (156 ref.)

Bromberg MB, Penney JB Jr, Stephenson BS, et al: Evidence for glutamate as the neurotransmitter of corticothalamic and corticorubral pathways. Brain Res 1981 Jun 29;215(1–2):369–74

Brønstad GO, Christoffersen T: Inhibitory effect of prostaglandins on the stimulation by glucagon and adrenaline of formation of cyclic AMP in rat hepatocytes. Eur J Biochem 1981 Jul;117(2):369–74

Brooks AD: The constitutional right to refuse antipsychotic medications. Bull Am Acad Psychiatry Law 1980;8(2):179–221

Brookshank BW, Atkinson DJ, Balázs R: Biochemical development of the human brain. II. Some parameters of the GABA-ergic system. Dev Neurosci 1981;4(3):188–200

Brorson L, Reele S, Dupont W, et al: Effects of concentration and steric configuration of propranolol on AV conduction and ventricular repolarization in the dog. J Cardiovasc Pharmacol 1981 Jul–Aug; 3(4):692–703

Brown DA, Higgins AJ, Marsh S, et al: Actions of GABA on mammalian neurones, axons, and nerve terminals. Adv Biochem Psychopharmacol 1981;29:321–6 (33 ref.)

Brown DA, Constanti A, Adams PR: Slow cholinergic and peptidergic transmission in sympathetic ganglia. Fed Proc 1981 Sep;40(11):2625–30

Brown EA, Pawlikowski TR: Lithium intoxication treated by peritoneal dialysis. Br J Clin Pract 1981 Feb;35(2):90–1

Brown ER, Lawson EE, Jansen A, et al: Regular fetal breathing induced by pilocarpine infusion in the near-term fetal lamb. J Appl Physiol 1981 Jun;50(6):1348–52

Brown M, Taché Y: Hypothalamic peptides: central nervous system control of visceral functions. Fed Proc 1981 Sep;40(11):2565–9 (32 ref.)

Browne RG: Anxiolytics antagonize yohimbine's discriminative stimulus properties. Psychopharmacology (Berlin) 1981;74(3):245–9

Brückner-Schmidt R, Jackisch R, Hertting G: Stimulation of prostaglandin E2-synthesis by noradrenaline in primary cell cultures from rabbit splenic pulpa is mediated by atypical alpha-adrenoceptors. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):1–7

Brügmann G: Gaschromatographische Bestimmung von Phenytoin, Phenobarbital und Primidon: Methylierung im Einspritzblock nach direktem Zusatz von Trimethyl-phenyl-ammonium-hydroxid zum Ethylacetat-Extrakt. J Clin Chem Clin Biochem 1981 May;19(5):305–6 (Eng. Abstr.) (Ger)

Brunjes PC, Alberts JR: Early auditory and visual function in normal and hyperthyroid rats. Behav Neural Biol 1981 Apr;31(4):393–412

Brus R, Herman ZS, Szklinik R: Central effects of prostaglandin D2. Pol J Pharmacol Pharm 1980;32(5):681–4

Brzeziński J: Schemat eksperymentalnej oceny skuteczności leków psychotropowych. Psychiatr Pol 1981 Jan–Feb;15(1):37–47 (Eng. Abstr.) (Pol)

Buccafusco JJ, Aronstam RS: Cholinergic actions of false neurotransmitters: acetylpyrrolidinecholine. Neurosci Lett 1981 May 29;23(3):319–24

Buckroyd JE: Mesantoin (methoin) [letter] Med J Aust 1981 Apr 18; 1(8):431

Budd RD: Benzodiazepine structure versus reactivity with EMIT oxazepam antibody. Clin Toxicol 1981 May;18(5):643–55

Burch JE, Hullin RP: Amitriptyline pharmacokinetics. A crossover study with single doses of amitriptyline and nortriptyline. Psychopharmacology (Berlin) 1981;74(1):35–42

Burch JE, Hullin RP: Amitriptyline pharmacokinetics. Single doses of Lentizol compared with ordinary amitriptyline tablets. Psychopharmacology (Berlin) 1981;74(1):43–50

Burch TP, Ticku MK: Histidine modification with diethyl pyrocarbonate shows heterogeneity of benzodiazepine receptors. Proc Natl Acad Sci USA 1981 Jun;78(6):3945–9

Burgoyne RD: The loss of muscarinic acetylcholine receptors in synaptic membranes under phosphorylating conditions is dependent on calmodulin. FEBS Lett 1981 May 5;127(1):144–8

Burgoyne RD, Pearce B: Muscarinic acetylcholine receptors regulation and protein phosphorylation in primary cultures of rat cerebellum. Brain Res 1981 Aug;254(1):55–63

Bustamante JC, Mann GE, Yudilevich DL: Specificity of neutral amino acid uptake at the basolateral side of the epithelium in the cat salivary gland in situ. J Physiol (Lond) 1981;313:65–79

Butler DE, Poschel BP, Marriott JG: Cognition-activating properties of 3-(Aryloxy)pyridines. J Med Chem 1981 Mar;24(3):346–50

Butler EG, Robinson T, Schultes RE: Petunia violacea: hallucinogen or not? J Ethnopharmacol 1981 Jul;4(1):111–4

Buvat J, Buvat-Herbaut M: Variations des gonadotrophines, de la prolactine et des stéroïdes sexuels au cours du cycle menstruel normal.

AUTHOR SECTION

J Gynecol Obstet Biol Reprod (Paris) 1981;10(2):99-108 (Eng. Abstr.) (Fre)

C

Cacatian AA, Rando J: Diphenylhydantoin-induced pseudolymphoma syndrome. With severe thrombocytopenia. NY State J Med 1981 Jun; 81(7):1085-7

Caccia S, Ballabio M, Fanelli R, et al: Determination of plasma and brain concentrations of trazodone and its metabolite, 1-m-chlorophenylpiperazine, by gas-liquid chromatography. J Chromatogr 1981 Jun 5;210(2):311-8

Caccia S, Ballabio M, Samanin R, et al: (--)-m-Chlorophenyl-piperazine, a central 5-hydroxytryptamine agonist, is a metabolite of trazodone. J Pharm Pharmacol 1981 Jul;33(7):477-8

(Cade JF), John Frederick Joseph Cade. Med J Aust 1981 May 2;1(9):489

(Cade JF), Johnson FN: John F.J. Cade, 1912 to 1980: a reminiscence. Pharmacopsychiatria 1981 Jul;14(4):148-9

Campbell IC: Blood platelets and psychiatry. Br J Psychiatry 1981 Jan; 138:78-80

Cannella G, Picotti GB, Scolari F, et al: Comportamento delle catecolamine plasmatiche in rapporto alle modificazioni pressorie indotte con l'emodialisi o con l'ulrafiltrazione. Minerva Nefrol 1979 Jul-Sep; 26(3):365-72 **(Ita)**

Cano JP, Sumirtapura YC: Pharmacocinétique comparée du diazépam et du flunitrazépam. Ann Anesthesiol Fr 1981;22(2):175-9 (Eng. Abstr.) **(Fre)**

Cantalamessa F, de Caro G, Perfumi M: Water intake inhibition and vasopressin release following intracerebroventricular administration of tachykinins to rats of the Wistar and Brattleboro strain. Pharmacol Res Commun 1981 Jul;13(7):641-55

Cardenas H, Zapata P: Dopamine-induced ventilatory depression in the rat, mediated by carotid nerve afferents. Neurosci Lett 1981 Jun 12; 24(1):29-33

Cardinali DP: Melatonin. A mammalian pineal hormone. Endocr Rev 1981 Summer;2(3):327-46 (266 ref.)

Cario RW, Glende M, Grossmann P, et al: Ernährungsgewohnheiten von Kindern mit portosystemischen Anastomosen—Auswirkungen auf den Serumammoniak und Aminosäurenspiegel. Kinderaerztl Prax 1981 May; 49(5):245-51 (Eng. Abstr.) **(Ger)**

Cario WR, Glende M, Lampe D, et al: Auswirkungen porto-systemischer Anastomosen im Kindesalter auf die Propranolol-Pharmakokinetik. Schweiz Med Wochenschr 1981 Jul 18;111(29):1088-93 (Eng. Abstr.) **(Ger)**

Carlin RK, Grab DJ, Siekevitz P: Function of a calmodulin in postsynaptic densities. III. Calmodulin-binding proteins of the postsynaptic density. J Cell Biol 1981 Jun;89(3):449-55

Carlton PL, Siegel JL, Murphree HB, et al: Effects of diazepam on operant behavior in man. Psychopharmacology (Berlin) 1981;73(4):314-7

Carmona E, Gomes C, Trolin G: Role of GABA-ergic receptors for the synthesis of GABA in different compartments of the rat cerebellum. Acta Physiol Scand 1981 May;112(1):109-10

Carolei A, Frontoni M: Triciclici, IMAO ed elettroshockterapia nel trattamento delle sindromi depressive. Clin Ter 1981 Jul 15;98(1):75-86 (29 ref.) **(Ita)**

Carr DB, Bullen BA, Skrinar GS, et al: Physical conditioning facilitates the exercise-induced secretion of beta-endorphin and beta-lipotropin in women. N Engl J Med 1981 Sep 3;305(10):560-3

Carr SR, Fozard JR: Lack of modulation by presynaptic alpha 2-adrenoceptors of adrenergic transmitters release evoked by activation of 5-hydroxytryptamine and nicotine receptors. Eur J Pharmacol 1981 Jun 10;72(1):27-34

Carrasco L, Vázquez D, Hernández-Lucas C, et al: Thionins: plant peptides that modify membrane permeability in cultured mammalian cells. Eur J Biochem 1981 May;116(1):185-9

Carrière B: Depression bei rheumatischen Erkrankungen oder körperliche Beschwerden bei Depression. Fortschr Med 1981 Aug 27; 99(31-32):1226-30 (Eng. Abstr.) **(Ger)**

Carrington CA, Hosick HL, Forsyth IA, et al: Novel multialveolar epithelial structures from rabbit mammary gland that synthesize milk specific fatty acids in response to prolactin. In Vitro 1981 May; 17(5):363-8

Carsia RV, Segre GV, Clark I, et al: Corticosteroidogenesis in vitro: effects of parathyroid hormone, ACTH, and calcium. Proc Soc Exp Biol Med 1981 Jul;167(3):402-6

Carstens E, Klumpp D, Randic M, et al: Effect of iontophoretically applied 5-hydroxytryptamine on the excitability of single primary afferent C- and A-fibers in the cat spinal cord. Brain Res 1981 Sep 7;220(1):151-8

Carter CJ, Pycock CJ: The role of 5-hydroxytryptamine in dopamine-dependent stereotyped behaviour. Neuropharmacology 1981 Mar;20(3):261-5

Cash CD, Rumigny JF, Mandel P, et al: Enzymology of the alternative reductive pathway of GABA catabolism leading to the biosynthesis of gamma-hydroxybutyrate. Adv Biochem Psychopharmacol 1981; 29:527-35 (31 ref.)

Cash DJ, Aoshima H, Hess GP: Acetylcholine-induced cation translocation across cell membranes and inactivation of the acetylcholine receptor: chemical kinetic measurements in the millisecond time region. Proc Natl Acad Sci USA 1981 Jun;78(6):3318-22

Cassano GB, Castrogiovanni P, Mauri M, et al: A multicenter controlled trial in phobic-obsessive psychoneurosis. The effect of chlorimipramine and of its combinations with haloperidol and diazepam. Prog Neuropsychopharmacol 1981;5(2):129-38

Casu M, Gale K: Intracerebral injection of gamma vinyl GABA: method for measuring rates of GABA synthesis in specific brain regions in vivo. Life Sci 1981 Aug 17;29(7):681-8

Caufriez A, Wolter R, Robyn C, et al: Prolactin secretion in anorexia nervosa. Acta Psychiatr Belg 1980 Jul-Aug;80(4):546-50

Cavero I, Lefèvre-Borg F, Roach AG: Effects of mianserin, desipramine and maprotiline on blood pressure responses evoked by acetylcholine, histamine and 5-hydroxytryptamine in rats. Br J Pharmacol 1981 Sep; 74(1):143-8

Cawthon RM, Pintar JE, Haseltine FP, et al: Differences in the structure of A and B forms of human monoamine oxidase. J Neurochem 1981 Aug;37(2):363-72

Cazaubon C, Diaz J, Gagnol JP: Comparaison de l'activité biologique in vivo d'un analogue de la somatostatine, le D Trp8 D Cys14 somatostatine dans deux modèles pharmacologiques différents. C R Soc Biol (Paris) 1981;175(2):200-7 (Eng. Abstr.) **(Fre)**

Chakrabarti P, Venkatesan K, Singh UC, et al: Systematic variation in bond lengths of peptides. Biochim Biophys Acta 1981 Aug 28; 670(1):134-7

Chambers KC, Sengstake CB, Yoder RL, et al: Sexually dimorphic acquisition of a conditioned taste aversion in rats: effects of gonadectomy, testosterone replacement and water deprivation. Physiol Behav 1981 Jul;27(1):83-8

Chamley WA, Adams NR, Hooley RD, et al: Hypothalamic-pituitary function in normal ewes and ewes which grazed oestrogenic subterranean clover for several years. Aust J Biol Sci 1981;34(2):239-44

Chan A, Ebadi M: Effects of norepinephrine on pineal tryptophan hydroxylase, using an improved [14C]CO2-trapping microtechnique. J Pharmacol Methods 1981 Aug;6(1):13-20

Chand N: Reactivity of isolated trachea, bronchus and lung strip of cats of carbachol, 5-hydroxytryptamine and histamine: evidence for the existence of methysergide-sensitive receptors. Br J Pharmacol 1981 Aug;73(4):853-7

Chandra A, Chou HC, Chang C, et al: Effects of intraventricular administration of neurotensin and somatostatin on thermoregulation in the rat. Neuropharmacology 1981 Jul;20(7):715-8

Chappel SC: The presence of two species of follicle-stimulating hormone within hamster anterior pituitary glands as disclosed by concanavalin A chromatography. Endocrinology 1981 Sep;109(3):935-42

Charette C, McGilveray IJ, Midha KK: Gas-liquid chromatographic procedure with alkali flame ionization detection for the determination of maprotiline in plasma. J Chromatogr 1981 Jun 12;224(1):128-32

Charles BG, Renshaw PJ, Kay JJ, et al: Effect of metoclopramide on the bioavailability of long-acting propranolol. Br J Clin Pharmacol 1981 May;11(5):517-8

Charles L, Schain R, Zelniker T: Optimal dosages of methylphenidate for improving the learning and behavior of hyperactive children. JDBP 1981 Sep;2(3):78-81

Checkley SA, Slade AP, Shur E, et al: A pilot study of the mechanism of action of desipramine. Br J Psychiatry 1981 Mar;138:248-51

Chen X, Liu LY, Deng HW, et al: [The effects of Citrus aurantium and its active ingredient N-methyltyramine on the cardiovascular receptors (author's transl)] Yao Hsueh Hsueh Pao 1981 Apr;16(4):253-9 (Eng. Abstr.) **(Chi)**

Childers JW, Schneider EG: Effect of hypertonic and hypotonic infusions on aldosterone in conscious sodium-depleted dogs. Clin Sci 1981 Aug; 61(2):191-9

Chilian WM, Boatwright RB, Shoji T, et al: Evidence against significant resting sympathetic coronary vasoconstrictor tone in the conscious dog. Circ Res 1981 Oct;49(4):866-76

Chistiakov VV, Prikhod'ko AZ: Vliianie prodolzhitel'nosti vvedeniia testosterona na induktsiiu tsitokhroma P-450 v pecheni samok krys fenobarbitalom. Vopr Med Khim 1981 May-Jun;27(3):340-2 (Eng. Abstr.) **(Rus)**

Chiu E: Interesting uses of beta blockers (2): propranolol in schizophrenia. Aust Fam Physician 1981 May;10(5):376-9, 381-2

Choi SJ, Derman RM, Lee KS: Bipolar affective disorder, lithium carbonate and Ca++ ATPase. J Affective Disord 1981 Jun;3(2):77-9

Chotoev ZhA, Nasaeva MT: Vliianie natriia oksibutirata na okislitel'noe fosforilirovanie mitokhondriI i aktivnost' fermentov pentoznogo tsikla miokarda pri vysokogornoI gipoksii. Farmakol Toksikol 1981 Mar-Apr; 44(2):159-62 (Eng. Abstr.) **(Rus)**

Christensen JB: Hyperprolaktinaemi og primaer amenoré. Ugeskr Laeger 1981 Apr 6;143(15):933-4 (Eng. Abstr.) **(Dan)**

Christensen S: DDAVP (1-desamino-8-D-arginine-vasopressin) treatment of lithium-induced polyuria in the rat. Scand J Clin Lab Invest 1980 Apr;40(2):151-7

Chronwall BM, Wolff JR: Development of GABA-accumulating neurons and glial cells in the rat visual cortex. Adv Biochem Psychopharmacol 1981;29:453–8

Chungsamarnyart N, Fujioka T, Kitoh J: Correlative light–, fluorescence– and electron–microscopic studies of catecholamine–storing cells in the adrenal medulla of the domestic fowl. Cell Tissue Res 1981;217(3):471–7

Churchill PC, McDonald FD, Churchill MC: Effect of diltiazem, a calcium antagonist, on renin secretion from rat kidney slices. Life Sci 1981 Jul 27;29(4):383–9

Ciganek E, Uyeda RT, Cohen M, et al: Imine analogues of tricyclic antidepressants. J Med Chem 1981 Mar;24(3):336–41

Clark CC: Mass spectral quantitation of cocaine HCl in powders. J Assoc Off Anal Chem 1981 Jul;64(4):884–8

Clark MG, Patten GS: Adrenaline activation of phosphofructokinase in rat heart mediated by alpha–receptor mechanism independent of cyclic AMP. Nature 1981 Jul 30;292(5822):461–3

Clark SM, Lipton JM: Effects of diazepam on body temperature of the aged squirrel monkey. Brain Res Bull 1981 Jul;7(1):5–9

Clawson GA, Moody DE, Woo CH, et al: Apparent differential response of nuclear envelope cytochrome P–450 following phenobarbital induction arising from a preferential loss during gradient purification. Cancer Res 1981 Aug;41(8):3122–7

Clayton PJ, Lewis CE: The significance of secondary depression. J Affective Disord 1981 Mar;3(1):25–35

Clifton PG: Veratridine as an amnestic agent in the domestic chick. Behav Neural Biol 1981 Jul;32(3):295–307

Cohen J, Iuvone PM, Neff NH: Neuroleptic drugs activate tyrosine hydroxylase of retinal amacrine cells. J Pharmacol Exp Ther 1981 Aug;218(2):390–4

Cohen M, Dailey G, Meshad M, et al: In normal young men acute dopaminergic blockade does not impair free water excretion following a standard water load. Commun Psychopharmacol 1980;4(4):323–6

Cohen ML, Fuller RW, Wiley KS: Evidence for 5–HT2 receptors mediating contraction in vascular smooth muscle. J Pharmacol Exp Ther 1981 Aug;218(2):421–5

Cohn JB: Multicenter double–blind efficacy and safety study comparing alprazolam, diazepam and placebo in clinically anxious patients. J Clin Psychiatry 1981 Sep;42(9):347–51

Collard KJ, Cassidy DM, Pye MA, et al: The stimulus–induced release of unmetabolized 5–hydroxytryptamine from superfused rat brain synaptosomes. J Neurosci Methods 1981 Aug;4(2):163–79

Collins GG, Anson J, Probett GA: Patterns of endogenous amino acid release from slices of rat and guinea–pig olfactory cortex. Brain Res 1981 Jan 5;204(1):103–20

Comaru–Schally AM, Schally AV: Effectos de péptidos cerebrales, hipotalámicos e hipofisarios sobre el sistema nervioso central. Medicina (B Aires) 1981;41(2):244–56 (108 ref.) (Spa)

Commissaris RL, Mokler DJ, Lyness WH, et al: The behavioral effects of hallucinogens in rats following 5,7–dihydroxytryptamine administration into the medial forebrain bundle. Pharmacol Biochem Behav 1981 Jun;14(6):915–8

Cone EJ, Buchwald W, Yousefnejad D: Simultaneous determination of phencyclidine and monohydroxylated metabolites in urine of man by gas chromatography–mass fragmentography with methane chemical ionization. J Chromatogr 1981 May 8;223(2):331–9

Conn PM, Chafouleas JG, Rogers D, et al: Gonadotropin releasing hormone stimulates calmodulin redistribution in rat pituitary. Nature 1981 Jul 16;292(5820):264–5

Connors JM, Wright KC, Judd AM, et al: Dynamics and regulation of TSH secretion by superfused anterior pituitary cells. Horm Res 1981;14(1):1–17

Conrad KA: Comparison of the inotropic and chronotropic effects of metoprolol and propranolol. J Clin Pharmacol 1981 May–Jun;21(5–6):213–8

Consolo S, Ladinsky H, Pugnetti P, et al: Increase in rat striatal acetylcholine content by bromocriptine: evidence for an indirect dopaminergic action. Life Sci 1981 Aug 3;29(5):457–65

Consroe P, Fish BS: Behavioral pharmacology of tetrahydrocannabinol convulsions in rabbits. Commun Psychopharmacol 1980;4(4):287–91

Constantinidis J, Taban C, Guntern R, et al: Etude morphologique de la substance P dans le cerveau humain par immuno–histo–fluorescence. Schweiz Arch Neurol Neurochir Psychiatr 1980;127(2):323–55 (Eng. Abstr.) (Fre)

Conway JF: Flupenthixol versus combined fluphenazine–nortriptyline in depressive illness. Practitioner 1981 Mar;225(1353):400–4

Cooper PE, Fernstrom MH, Rorstad OP, et al: The regional distribution of somatostatin, substance P and neurotensin in human brain. Brain Res 1981 Aug 10;218(1–2):219–32

Cooper SF, Lapierre YD: Gas—liquid chromatographic determination of pipotiazine in plasma of psychiatric patients. J Chromatogr 1981 Feb 13;222(2):291–6

Cooper TB, Bark N, Simpson GM: Prediction of steady state plasma and saliva levels of desmethylimipramine using a single dose, single time point procedure. Psychopharmacology (Berlin) 1981;74(2):115–21

Coote JH, Macleod VH, Fleetwood–Walker S, et al: The response of individual sympathetic preganglionic neurones to microelectrophoretically applied endogenous monoamines. Brain Res 1981 Jun 29;215(1–2):135–45

Corley KP, Valk TW, Kelch RP, et al: Estimation of GnRH pulse amplitude during pubertal development. Pediatr Res 1981 Feb;15(2):157–62

Corman B, Roinel N, de Rouffignac C: Dependence of water movement on sodium transport in kidney proximal tubule: a microperfusion study substituting lithium for sodium. J Membr Biol 1981;62(1–2):105–11

Cornish EJ, Krstew EV: No evidence for reverse trans–synaptic regulation of neuronal uptake by beta–adrenoceptors in kitten atria. Biochem Pharmacol 1981 Jun 15;30(12):1439–42

Cornwell–Jones CA: Conspecific odor preferences of male albino rats are reversed by intracerebral 6–hydroxydopamine. Brain Res 1981 Jun 1;213(2):379–85

Corona GL, Zerbi F, Pinelli P, et al: Amitriptyline and nortriptyline plasma levels monitoring. Perspective in clinical practice. Commun Psychopharmacol 1980;4(4):309–16

Correa FM, Innis RB, Hester LD, et al: Diffuse enkephalin innervation from caudate to globus pallidus. Neurosci Lett 1981 Aug 7;25(1):63–8

Correy JF, Newman NM: Debendox and limb reduction deformities. Med J Aust 1981 Apr 18;1(8):417–8

Costa JL, Kirk KL, Murphy DL, et al: Anomalous compartmentation of 5–hydroxytryptamine in intact human platelets. Br J Pharmacol 1981 Mar;72(3):449–59

Costall B, Fortune DH, Naylor RJ: Relevance of the rodent area postrema to dopamine–dependent behavioural effects. J Pharm Pharmacol 1981 Apr;33(4):257–9

Coulter HD, Elde RP, Unverzagt SL: Co–localization of neurophysin– and enkephalin–like immunoreactivity in cat pituitary. Peptides (Fayetteville) 1981;2 Suppl 1:51–5

Cox B, Lee TF, Martin D: Different hypothalamic receptors mediate 5–hydroxytryptamine– and tryptamine–induced core temperature changes in the rat. Br J Pharmacol 1981 Mar;72(3):477–82

Cox B, Lee TF: 5–Hydroxytryptamine–induced hypothermia in rats as an in vivo model for the quantitative study of 5–hydroxytryptamine receptors. J Pharmacol Methods 1981 Jan;5(1):43–51

Crabbe JC Jr, Allen RG, Gaudette ND, et al: Strain differences in pituitary beta–endorphin and ACTH content in inbred mice. Brain Res 1981 Aug 24;219(1):219–23

Craelius W, Fricke RA: Release of 3H–gamma–aminobutyric acid (GABA) by inhibitory neurons of the crayfish. J Neurobiol 1981 May;12(3):249–58

Craig TJ, Lin SP: Mortality among psychiatric inpatients. Age–adjusted comparison of populations before and after psychotropic drug era. Arch Gen Psychiatry 1981 Aug;38(8):935–8

Creates MS, Grayson J: The effect of adrenaline and noradrenaline on coronary vascular reserve in the dog. J Physiol (Lond) 1980 Dec;309:557–68

Creighton H: Law for the nurse manager: forced medication of mental patients. Nurs Manage 1981 Sep;12(9):72–3

Crim LW, Evans DM, Coy DH, et al: Control of gonadotrophic hormone release in trout: influence of synthetic LH–RH and LH–RH analogues in vivo and in vitro. Life Sci 1981 Jan 12;28(2):129–35

Cross AJ, Waddington JL: Kainic acid lesions dissociate [3H] spiperone and [3H]cis–flupenthixol binding sites in rat striatum. Eur J Pharmacol 1981 May 8;71(2–3):327–32

Cross AJ, Crow TJ, Owen F: 3H–Flupenthixol binding in post–mortem brains of schizophrenics: evidence for a selective increase in dopamine D2 receptors. Psychopharmacology (Berlin) 1981;74(2):122–4

Crowley WR, Terry LC: Effects of an epinephrine synthesis inhibitor, SKF64139, on the secretion of luteinizing hormone in ovariectomized female rats. Brain Res 1981 Jan 5;204(1):231–5

Csaba G, Németh G, Vargha P: Experimental study of hormone receptor development in a unicellular model system. Exp Cell Biol 1981;49(3):173–6

Csaba G, Bierbauer J: Effect of cortisol, deoxycorticosterone and 19–nortestosterone on the gametogenesis of the snail Helix pomatia. Acta Biol Acad Sci Hung 1981;32(1):15–8

Csaba G, Németh G, Juvancz I, et al: Receptor amplifying effect of serotonin and serotonin analogues in a protozoan (Tetrahymena) model system. Acta Physiol Acad Sci Hung 1980;56(4):411–6

Cuello AC, Del Fiacco M, Paxinos G, et al: Neuropeptides in striato–nigral pathways. J Neural Transm 1981;51(1–2):83–96

Cullheim S, Kellerth JO: Two kinds of recurrent inhibition of cat spinal alpha–motoneurones as differentiated pharmacologically. J Physiol (Lond) 1981 Mar;312:209–24

Cunningham J, Neal MJ: On the mechanism by which veratridine causes a calcium–independent release of gamma–aminobutyric acid from brain slices. Br J Pharmacol 1981 Jul;73(3):655–67

Cunningham JL, Evans DA: Acetanilide and paracetamol pharmacokinetics before and during phenytoin administration: genetic control of induction? Br J Clin Pharmacol 1981 Jan;11(6):591–5

Cuomo V, Cagiano R, Coen E, et al: Enduring behavioural and biochemical effects in the adult rat after prolonged postnatal administration of haloperidol. Psychopharmacology (Berlin) 1981;74(2):166–9

Cuomo V, Cortese I, Racagni G: Effects of morphine and chlordiazepoxide on avoidance behaviour in two inbred strains of mice.

Neuropharmacology 1981 Mar;20(3):301–4

Curry CE Jr, Antal EG, Keys PW, et al: Audit of phenytoin prescribing for outpatients. Am J Hosp Pharm 1981 Aug;38(8).1158–60

Cusick CF: Ratio of thyroxine to thyroxine-binding globulin. An assessment of the validity of a single reference range.
Ann Clin Biochem 1981 Mar;18(2):93–6

Cutler LS, Boccuzzi J, Yaeger L, et al: Effects of reserpine treatment on beta-adrenergic/adenylate cyclase modulate secretion and resynthesis by the rat submandibular gland.
Virchows Arch [Pathol Anat] 1981;392(2):185–98

Cutler NR, Zavadil AP 3d, Eisdorfer C, et al: Concentrations of desipramine in elderly women. Am J Psychiatry 1981 Sep;138(9):1235–7

Cutz E, Chan W, Track NS: Bombesin, calcitonin and leu-enkephalin immunoreactivity in endocrine cells of human lung. Experientia 1981 Jul 15;37(7):765–7

Czuczwar SJ: Effect of combined treatment with dopaminergic and GABA-ergic drugs on the threshold for maximal electroconvulsions in mice. Pol J Pharmacol Pharm 1981 Jan–Feb;33(1):25–35

D

Damian E, Ianăs O, Bădescu I, et al: Inhibition of pituitary-testicular axis response to gonadotropin releasing hormone by pineal treatment. Endocrinologie 1981 Apr–Jun;19(2):93–6

Dani JA, Levitt DG: Binding constants of Li+, K+, and Tl+ in the gramicidin channel determined from water permeability measurements. Biophys J 1981 Aug;35(2):485–99

Daniel PM, Love ER, Moorhouse SR, et al: The effect of insulin upon the influx of tryptophan into the brain of the rabbit.
J Physiol (Lond) 1981 Mar;312:551–62

Darney KJ Jr, Ewing L: Autoregulation of testosterone secretion in perfused rat testes. Endocrinology 1981 Sep;109(3):993–5

Das R, Kanungo MS: In vitro methylation of chromosomal proteins of the brain of rats of various ages & its modulation by epinephrine. Indian J Biochem Biophys 1980 Dec;17(6):429–31

Dascal N, Landau EM, Lass Y: Divalent cations and transmitter release at low concentration of tetrodotoxin. Biophys J 1981 Sep;35(3):573–86

Datta PC, King MG: alpha-MSH, MIF-I and melatonin: effects on novelty-induced defecation, plasma 11-OHCS and central catecholamines in rats. Peptides (Fayetteville) 1981;2 Suppl 1:143–54

Davidoff RA: Amino acids and presynaptic inhibition.
Adv Biochem Psychopharmacol 1981;29:249–55 (50 ref.)

Davies JE, Roberts MH: 5-Hydroxytryptamine reduces substance P responses on dorsal horn interneurones: a possible interaction of neurotransmitters. Brain Res 1981 Aug 3;217(2):399–404

Davies MA: Postsynaptic pharmacology of psychoactive substances in Aplysia californica. Brain Res Bull 1981 Jun;6(6):495–502

Davis BA, Boulton AA: Excretion of m-hydroxymandelic acid in human urine. J Chromatogr 1981 Feb 13;222(2):271–5

Davis KL, Samuel A, Mathé AA, et al: Intracerebral des-tyrosine-gamma-endorphin inhibits methylphenidate induced locomotor activity. Life Sci 1981 May 21;28(21):2421–4

Davis KL, Rosenberg GS: Induction of behavioral supersensitivity to apomorphine by DFP treatment. Life Sci 1981 Apr 27;28(17):1953–9

Davis PJ, Blas SD: In vitro stimulation of human red blood cell Ca2+-ATPase by thyroid hormone.
Biochem Biophys Res Commun 1981 Apr 30;99(4):1073–80

Davis WC, Ticku MK: Pentobarbital enhances [3H]diazepam binding to soluble receptors at the benzodiazepine--GABA-receptor-ionophore complex. Neurosci Lett 1981 May 6;23(2):209–13

Davis WM, Hatoum NS: Possible toxic interaction of propranolol and narcotic analgesics [letter] Drug Intell Clin Pharm 1981 Apr; 15(4):290–300

Dawling S, Lynn K, Rosser R, et al: The pharmacokinetics of nortriptyline in patients with chronic renal failure. Br J Clin Pharmacol 1981 Jul; 12(1):39–45

Dax EM, Partilla JS, Gregerman RI: Mechanism of the age-related decrease of epinephrine-stimulated lipolysis in isolated rat adipocytes: beta-adrenergic receptor binding, adenylate cyclase activity, and cyclic AMP accumulation. J Lipid Res 1981 Aug;22(6):934–43

Dé Montigny C, Grunberg F, Mayer A, et al: Lithium induces rapid relief of depression in tricyclic antidepressant drug non-responders.
Br J Psychiatry 1981 Mar;138:252–6

Deakin JF, Owen F, Cross AJ, et al: Studies on possible mechanisms of action of electroconvulsive therapy; effects of repeated electrically induced seizures on rat brain receptors for monoamines and other neurotransmitters. Psychopharmacology (Berlin) 1981;73(4):345–9

de Andrés Rodríguez-Trelles F: Ansiedad: bases farmacologicas de su tratamiento. An R Acad Nac Med (Madr) 1981;98(1):69–116 (68 ref.) (Spa)

de Belleroche JS, Bradford HF: Evidence for an inhibitory presynaptic component of neuroleptic drug action. Br J Pharmacol 1981 Mar; 72(3):427–33

de Boer AG, Gubbens-Stibbe JM, Breimer DD: Avoidance of first pass elimination of propranolol after rectal administration to rats.
J Pharm Pharmacol 1981 Jan;33(1):50–1

Debray Q, Galopin JC: Neurophysiologie de l'anxiété. Soins Psychiatr 1981 Mar;(8):3–5 (Fre)

Decino P: Transmitter release properties along regenerated nerve processes at the frog neuromuscular junction. J Neurosci 1981 Mar; 1(3):308–17

Dees WL, McArthur NH: Immunohistochemical localization of gonadotropin releasing hormone (GnRH) in the bovine hypothalamus and infundibulum. Anat Rec 1981 Jul;200(3):281–5

DeFeudis FV, Ossola L, Sarliève LL, et al: GABA and muscimol binding processes in CNS tissue culture preparations.
Adv Biochem Psychopharmacol 1981;29:405–10

de Gier JJ, 't Hart BJ, Nelemans FA, et al: Psychomotor performance and real driving performance of outpatients receiving diazepam.
Psychopharmacology (Berlin) 1981;73(4):340–4

de Lanerolle NC, Elde RP, Sparber SB, et al: Distribution of methionine-enkephalin immunoreactivity in the chick brain: an immunohistochemical study. J Comp Neurol 1981 Jul 10;199(4):513–33

Delarue C, Perroteau I, Leboulenger F, et al: In vitro effect of prostaglandins on corticosterone and aldosterone production by frog interrenal gland. Biochem Biophys Res Commun 1981 May 29; 100(2):769–77

Del Carmen Díaz M, Morita E, Goljman S, et al: Pituitary response to luteinizing hormone-releasing hormone during haloperidol-induced hyperprolactinemia. Fertil Steril 1981 Jun;35(6):626–8

DeMarinis RM, Bryan WM, Hillegass LM, et al: Inhibitors of phenylethanolamine N-methyltransferase and epinephrine biosynthesis. 3. Bis[tetrahydroisoquinoline]s. J Med Chem 1981 Jun;24(6):756–9

Dembowsky K, Lackner K, Czachurski J, et al: Tonic catecholaminergic inhibition of the spinal somato-sympathetic reflexes originating in the ventrolateral medulla oblongata. J Auton Nerv Syst 1981 Apr; 3(2–4):277–90

Demenge P, Mouchet P, Guerin B, et al: Identification and distribution of neuroleptic binding sites in the rat spinal cord. J Neurochem 1981 Jul;37(1):53–9

Demin NN, Krivenko NE, Rubinskaia NL: Tormoziashchee vliianie fenazepama na katabolizm belkov i RNK v supraopticheskom iadre pri lishenii paradoksal'noi fazy sna. Fiziol Zh SSSR 1981 Mar;67(3):460–3 (Rus)

De Montis GM, Olianas MC, Mulas G, et al: GABA receptors distribution in rat substantia nigra. Neurosci Lett 1981 May 29;23(3):257–61

Demoulin A, Donnez J, Volders-Keuliens L, et al: Activité de type gonadocrinine dans le liquide péritonéal pendant le cycle menstruel chez la femme normale. C R Trav Lab Carlsberg 1981;175(3):377–84 (Eng. Abstr.) (Fre)

Denisov IuP, Shutko GV, Sergeev PV: Vzaimodeistvie steroidnykh gormonov s gepatotsitami i ikh plazmaticheskimi membranami.
Biull Eksp Biol Med 1981 Jun;91(6):722–5 (Eng. Abstr.) (Rus)

DePaulo JR Jr, Correa EI, Sapir DG: Renal toxicity of lithium and its implications. Johns Hopkins Med J 1981 Jul;149(1):15–21

Désarménien M, Santangelo F, Linck G, et al: Physiological study of amino acid uptake and receptor desensitization: the GABA system in dorsal root ganglia. Adv Biochem Psychopharmacol 1981;29:309–19

Deschaux P, Ardail D, Jouve de Guibert C: Enzymatic changes in rat thymus after intraperitoneal injections of adrenocorticotrophic hormone and corticosterone. Thymus 1981 Apr;2(6):299–304

Desiles M, Rips R: Use of potentiation of thyrotrophin releasing hormone (TRH)-induced hyperthermia as a test for screening antidepressants which activate alpha-adrenoceptor systems. Br J Pharmacol 1981 Sep; 74(1):81–6

Désir D, van Cauter E, Golstein J, et al: Circadian and ultradian variations of ACTH and cortisol secretion. Horm Res 1980;13(4–5):302–16

Desire B, Saint-Andre S: Effet accélérateur de sels d'ammoniums quaternaires hétérocycliques sur l'hydrolyse d'esters neutres par l'acétylcholinestérase et la butyrylcholinestérase.
Biochim Biophys Acta 1981 Jun 15;659(2):267–82 (Eng. Abstr.) (Fre)

DeVane CL, Jusko WJ: Plasma concentration monitoring of hydroxylated metabolites of imipramine and desipramine. Drug Intell Clin Pharm 1981 Apr;15(4):263–6

Dias RD, Perry ML, Carrasco MA, et al: Effect of electroconvulsive shock on beta-endorphin immunoreactivity of rat brain, pituitary gland, and plasma. Behav Neural Biol 1981 Jun;32(2):265–8

Dickenson AH, Rivot JP, Chaouch A, et al: Diffuse noxious inhibitory controls (DNIC) in the rat with or without pCPA pretreatment.
Brain Res 1981 Jul 20;216(2):313–21

Dickson AJ, Marston FA, Pogson CI: Tyrosine aminotransferase as the rate-limiting step for tyrosine catabolism in isolated rat liver cells.
FEBS Lett 1981 May 5;127(1):28–32

Di Cola D, Federici G: NADH-coupled spectrophotometric assay of tyrosine aminotransferase. Ital J Biochem 1981 Jan–Feb;30(1):30–9

Diebler MF, Morot-Gaudry Y: Acetylcholine incorporation by cholinergic synaptic vesicles from Torpedo marmorata. J Neurochem 1981 Aug; 37(2):467–75

Di Giorgio RM, Nicoletti F, Amico-Roxas M, et al: Influenza del sistema dopaminergico centrale sull'attività gabaergica del cervelletto. Primi risultati. Acta Neurol [Quad] (Napoli) 1981;42:302–4 (Eng. Abstr.) (Ita)

AUTHOR SECTION

Dionne VE: Acetylcholine receptor kinetics at slow fiber neuromuscular junctions. Fed Proc 1981 Sep;40(11):2614-7

Dishovski K, Panova I, Uzunov P: Vliiani na fosfororganichnoto sûedinenie neguvon vûrkhu sûdûrzhanieto na dopamin v glaven mozûk na plûkh. Eksp Med Morfol 1981;20(2):62-6 (Eng. Abstr.) (Bul)

Dittami JP: Seasonal changes in the behavior and plasma titers of various hormones in barheaded geese, Anser indicus. Z Tierpsychol 1981; 55(4):289-324

Dittmann RW, Hein H, Wallis H: Zur Psychopharmaka-Anwendung im Säuglings-, Kleinkindes- und Vorschulalter. Ergebnisse einer Elternbefragung von Schulanfängern. Monatsschr Kinderheilkd 1981 Jun;129(6):349-53 (Eng. Abstr.) (Ger)

Divoll M, Greenblatt DJ, Lacasse Y, et al: Benzodiazepine overdosage: plasma concentrations and clinical outcome. Psychopharmacology (Berlin) 1981;73(4):381-3

Djamgoz MB, Stell WK, Chin CA, et al: An opiate system in the goldfish retina. Nature 1981 Aug 13;292(5824):620-3

Djørup A, Jahnsen H, Laursen AM: The dendritic response to GABA in CA1 of the hippocampal slice. Brain Res 1981 Aug 24;219(1):196-201

Dobbs JH: Drug histories obtained by pharmacists from psychiatric inpatients. Hosp Community Psychiatry 1981 Sep;32(9):639-40

Doble A, Turnbull MJ: Lack of effect of benzodiazepines on bicuculline-insensitive GABA-receptors in the field-stimulated guinea-pig vas deferens preparation. J Pharm Pharmacol 1981 Apr; 33(4):267-8

Dobry PJ, Piercey MF, Schroeder LA: Pharmacological characterization of scratching behaviour induced by intracranial injection of substance P and somatostatin. Neuropharmacology 1981 Mar;20(3):267-72

Dobson JG Jr: Catecholamine-induced phosphorylation of cardiac muscle proteins. Biochim Biophys Acta 1981 Jun 11;675(1):123-31

Döcke F, Rohde W, Badell J, et al: Influence of neonatal ovariectomy on the developmental patterns of serum gonadotropins, hypothalamic LH-RH concentration and organ weights in female rats. Endokrinologie 1981 Mar;77(3):273-85

Dodson WE, Collins G: Estimating dosage of phenytoin [letter] J Pediatr 1981 Jul;99(1):169-70

Doering W, König E: Chinidin erhöht den Digoxin-Spiegel. Med Klin 1981 Jul 3;76(14):395-8 (Ger)

Doerr-Schott J, Dubois MP, Lichte C: Immunohistochemical localisation of substances reactive to antisera against alpha- and beta-endorphin and met-enkephalin in the brain of Rana temporaria L. Cell Tissue Res 1981;217(1):79-92

Doggrell SA: Effect of antimuscarinic agents on the contractile responses to cholinomimetics in the rat anococcygeus muscle. Br J Pharmacol 1981 Aug;73(4):829-35

Doležal V, Tuček S: Utilization of citrate, acetylcarnitine, acetate, pyruvate and glucose for the synthesis of acetylcholine in rat brain slices. J Neurochem 1981 Apr;36(4):1323-30

Dooley DJ, Namkung MJ, Hungar AA, et al: Catecholaminergic involvement in the biphasic effect of ADATN on temperature in mice. Eur J Pharmacol 1981 May 8;71(2-3):269-76

Dorn A, Bernstein HG: Concerning the possible existence of somatostatinergic local neuronal circuits in the rats cerebral cortex. Anat Anz 1981;149(2):185-7

Dornbush RL, Shapiro B, Freedman AM: Effects of an ACTH short chain neuropeptide in man. Am J Psychiatry 1981 Jul;138(7):962-4

Dorsa DM, Smith ER: Facilitation of mounting behavior in male rats by intracranial injections of luteinizing hormone-releasing hormone. Regul Pept 1980 Oct;1(2):147-55

Dorsa DM, Majumdar LA, Chapman MB: Regional distribution of gamma- and beta-endorphin-like peptides in the pituitary and brain of the rat. Peptides (Fayetteville) 1981;2 Suppl 1:71-7

Dorsa DM, Smith ER, Davidson JM: Endocrine and behavioral effects of continuous exposure of male rats to a potent luteinizing hormone-releasing hormone (LHRH) agonist: evidence for central nervous system actions of LHRH. Endocrinology 1981 Sep; 109(3):729-35

Doshi PS, Edwards DJ: Effects of L-dopa on dopamine and norepinephrine concentrations in rat brain assessed by gas chromatography. J Chromatogr 1981 Jun 19;210(3):505-11

Dotti A, Lostia O, Rubino IA, et al: The prolactin response in patients receiving neuroleptic therapy. The effect of fluphenazine decanoate. Prog Neuropsychopharmacol 1981;5(1):69-77

Dougherty GG Jr, Ellinwood EH Jr: Amphetamine behavioral toxicity: rotational behavior after chronic intrastriatal infusion. Biol Psychiatry 1981 May;16(5):479-88

Dourish CT, Cooper SJ: Single or repeated administration of small doses of apomorphine on water intake and activity in water-deprived rats. Neuropharmacology 1981 Mar;20(3):257-60

Downing RW, Rickels K: Hostility conflict and the effect of chlordiazepoxide on change in hostility level. Compr Psychiatry 1981 Jul-Aug;22(4):362-7

Drábiková K, Pečivová J, Nosál R: Účinok betaadrenolytík na uvoľňovanie 5-hydroxytryptamínu z izolovaných žírnych buniek. Bratisl Lek Listy 1981;76(1):52-60 (Eng. Abstr.) (Slo)

Drago F, Van Ree JM, Bohus B, et al: Endogenous hyperprolactinaemia enhances amphetamine- and apomorphine-induced stereotypy. Eur J Pharmacol 1981 Jun 19;72(2-3):249-53

Drew R, Siddik ZH, Mimnaugh EG, et al: Species and dose differences in the accumulation of imipramine by mammalian lungs. Drug Metab Dispos 1981 Jul-Aug;9(4):322-6

Duchemin AM: Aspects Biochimiques des Dépressions. Sem Hop Paris 1981 Apr 18-25;57(15-16):745-50 (Eng. Abstr.) (Fre)

Dudareva NA, Dashkevich VS, Salganik RI: Uvelichenie doli povtoriaiushchikhsia posledovatel'nostei DNK v transkriptsionno aktivnykh uchastkakh genoma krysy pri induktsii kortizolom i fenobarbitalom. Biokhimiia 1981 Jul;46(7):1258-66 (Eng. Abstr.) (Rus)

Dugas JE: Stability of chlorpromazine liquid in unit dose packaging [letter] Am J Hosp Pharm 1981 Sep;38(9):1276

Dulik DM, Soine WH: Color test for detection of 1-piperidinocyclohexanecarbonitrile (PCC) in illicit phencyclidine. Clin Toxicol 1981 Jun;18(6):737-42

Dumbrille-Ross A, Tang SW: Absence of high-affinity [3H]imipramine binding in platelets and cerebral cortex of fawn-hooded rats. Eur J Pharmacol 1981 Jun 10;72(1):137-8

Dumont C, Laurent J, Grandadam A, et al: Anorectic properties of a new long acting serotonin uptake inhibitor. Life Sci 1981 Apr 27; 28(17):1939-45

Dunnett SB, Björklund A, Stenevi U, et al: Behavioural recovery following transplantation of substantia nigra in rats subjected to 6-OHDA lesions of the nigrostriatal pathway. I. Unilateral lesions. Brain Res 1981 Jun 29;215(1-2):147-61

Durham HD, Frank GB: Dual action of meperidine on the frog neuromuscular junction: a prejunctional, opiate receptor-mediated depression of transmitter release and a postjunctional, nonopiate receptor effect on the endplate. Arch Int Pharmacodyn Ther 1981 May; 251(1):150-65

Durocher A, Chopin C, Gosselin B, et al: Rhabdomyolyses toxiques et médicamenteuses. Rev Med Interne 1980;1(2):223-6 (Eng. Abstr.) (Fre)

Duru C, Jacob M, Puech A, et al: Etude comparée de la vitesse de libération du phénobarbital à partir de formes galéniques sèches: appareil Erweka ZT3 et ballon de Poole. Pharm Acta Helv 1981;56(4-5):137-41 (Fre)

Düsing R, Wilke R, Kürber A, et al: Inner medullary osmolality and sodium concentration are decreased in rats during escape from DOCA-induced salt retention. Clin Sci 1981 Apr;60(4):467-9

Dutt MK: Influence of UV rays on Feulgen-type staining with azure A-SO2 prepared with normal hydrochloric acid and sodium thiosulphate. Microsc Acta 1981 Jul;84(4):339-44

DuVal JW, Saffouri B, Weir GC, et al: Stimulation of gastrin and somatostatin secretion from the isolated rat stomach by bombesin. Am J Physiol 1981 Sep;241(3):G242-7

Dyck LE: Release of radiolabeled dopamine, p-tyramine, and m-tyramine from rat striatal slices by some aminotetralins. Neurochem Res 1981 Apr;6(4):365-75

Dyer RG, Murugaiah K, Theodorou A, et al: During one year's neuroleptic treatment in rats striatal dopamine receptor blockade decreases but serum prolactin levels remain elevated. Life Sci 1981 Jan 12;28(2):167-74

Dzhaliashvili TA, Akhalkatsi RG, Iordanishvili GS, et al: Issledovanie vliianiia neprofarmakologicheskikh veshchestv na funktsional'nuiu aktivnost'golovnogo mozga krys. Ukr Biokhim Zh 1981 Mar-Apr; 53(2):109-14 (Eng. Abstr.) (Rus)

E

Early SL, Michaelis EK, Mertes MP: Pharmacological specificity of synaptosomal and synaptic membrane gamma-aminobutyric acid (GABA) transport processes. Biochem Pharmacol 1981 May 15; 30(10):1105-13

Easterbrook JS, Hibri NS: Epidurography using epinephrine and tomography. Radiology 1981 Sep;140(3):709-11

Eaton BM, Yudilevich DL: Uptake and asymmetric efflux of amino acids at maternal and fetal sides of placenta. Am J Physiol 1981 Sep; 241(3):C106-12

Ebner F, Fleig H, Trendelenburg U: The positive inotropic effect of (-)-noradrenaline and (+/-)-isoprenaline after chemical sympathectomy: evidence in favour of differences at a postsynaptic site. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):8-18

Eccleston D: Monoamines in affective illness. Is there a place for 5HT? Br J Psychiatry 1981 Mar;138:257-8

Echtenkamp SF, Davis JO, DeForrest JM, et al: Effects of indomethacin, renal denervation, and propranolol on plasma renin activity in conscious dogs with chronic thoracic caval constriction. Circ Res 1981 Aug; 49(2):492-500

Eckert M, Agricola H, Penzlin H: Immunocytochemical identification of proctolinlike immunoreactivity in the terminal ganglion and hindgut of the cockroach Periplaneta americana (L.). Cell Tissue Res 1981; 217(3):633-45

Eckstein R, Riess H, Sauer H, et al: Immunhämolytische Anämien mit Nierenversagen nach Nomifensineinnahme. Klin Wochenschr 1981 Jun

1;59(11):567-9 (Eng. Abstr.) (Ger)

Edelstein P, Schultz JR, Hirschowitz J, et al: Physostigmine and lithium response in the schizophrenias. Am J Psychiatry 1981 Aug; 138(8):1078-81

Eden S, Eriksson E, Martin JB, et al: Evidence for a growth hormone releasing factor mediating alpha-adrenergic influence on growth hormone secretion in the rat. Neuroendocrinology 1981 Jul;33(1):24-7

Edwards S, Castaneda RE, Ramirez L: Whole blood cholinesterase activity in cows in El Salvador. Vet Rec 1980 Nov 1;107(18):426

Egido J, Sanchez Crespo M, Sancho J, et al: Phenytoin in the treatment of IgA mesengial glomerulonephritis (Berger's disease) [letter] Clin Nephrol 1981 Mar;15(3):164-5

Ehinger B, Aberg L: Density of amine accumulating neurons in rabbit and guinea-pig retina. Acta Physiol Scand 1981 May;112(1):111-2

Ehlert FJ, Roeske WR, Yamamura HI: Dopaminergic regulation of muscarinic receptor binding in the corpus striatum. Proc West Pharmacol Soc 1981;24:93-5

Ehlert FJ, Roeske WR, Yamamura HI: Striatal muscarinic receptors: regulation by dopaminergic agonists. Life Sci 1981 May 21; 28(21):2441-8

Eison MS, Eison AS, Ellison G: The regional distribution of d-amphetamine and local glucose utilization in rat brain during continuous amphetamine administration. Exp Brain Res 1981; 43(3-4):281-8

Elam L, Barnett CA: Glucocorticoid induction of tyrosine aminotransferase in kidney cortex. Biochem Biophys Res Commun 1981 Jun 16;100(3):1143-7

ElAttar TM, Lin HS, Tira DE: Effect of epinephrine on prostaglandin E2 and cyclic AMP levels in gingiva of patients with chronic periodontitis. Prostaglandins Med 1981 Jun;6(6):601-12

Eldefrawi ME, Warnick JE, Schofield GG, et al: Interaction of imipramine with the ionic channel of the acetylcholine receptor of motor endplate and electric organ. Biochem Pharmacol 1981 Jun 1;30(11):1391-4

Elekes K: Monoamine precursor uptake in ganglia of a mollusc Anodonta cygnea L. (Bivalvia) An autoradiographic and ultrastructural study. Cell Tissue Res 1981;219(2):403-15

Elias KA, Blake CA: Effects of oestradiol, hypothalamic extracts and luteinizing hormone releasing hormone on rat anterior pituitary gland gonadotrophin release in vitro before and after the preovulatory luteinizing hormone surge at pro-oestrus. J Endocrinol 1981 Sep; 90(3):345-54

Elkin RG, Rogler JC, Featherston WR: Dietary phenylalanine and tyrosine interrelationships in the Sprague-Dawley rat. Proc Soc Exp Biol Med 1981 Jul;167(3):310-7

Ellins SR, Martin GC: Olfactory discrimination of lithium chloride by the coyote (Canis latrans). Behav Neural Biol 1981 Feb;31(2):214-24

Ellinwood EH Jr, Linnoila M, Angle HV, et al: Use of simple tasks to test for impairment of complex skills by a sedative. Psychopharmacology (Berlin) 1981;73(4):350-4

Elrod L Jr, Shada DM, Taylor VE: High-performance liquid chromatographic analysis of clorazepate dipotassium and monopotassium in solid dosage forms. J Pharm Sci 1981 Jul;70(7):793-5

Engberg G, Svensson TH, Rosell S, et al: A synthetic peptide as an antagonist of substance P. Nature 1981 Sep 17-23;293(5829):222-3

Engelhardt W, Schwille PO: Development of a sensitive somatostatin radioimmunoassay and its application to plasma of stressed and non-stressed rats. Horm Metab Res 1981 Jun;13(6):318-23

Ennis C, Kemp JD, Cox B: Characterisation of inhibitory 5-hydroxytryptamine receptors that modulate dopamine release in the striatum. J Neurochem 1981 Apr;36(4):1515-20

Enyeart J: Cyclic AMP, 5-HT, and the modulation of transmitter release at the crayfish neuromuscular junction. J Neurobiol 1981 Sep; 12(5):505-13

Epelbaum J, Tapia-Arancibia L, Kordon C: Noradrenaline stimulates somatostatin release from incubated slices of the amygdala and the hypothalamic preoptic area. Brain Res 1981 Jun 29;215(1-2):393-7

Erchegyi J, Coy DH, Nekola MV, et al: Luteinizing hormone-releasing hormone analogs with increased anti-ovulatory activity. Biochem Biophys Res Commun 1981 Jun 16;100(3):915-20

Eriksson E, Edén S, Modigh K: Importance of norepinephrine alpha 2-receptor activation for morphine-induced rat growth hormone secretion. Neuroendocrinology 1981 Aug;33(2):91-6

Eriksson L, Gordin A: Cardiovascular and behavior changes after ICV infusion of TRH in the conscious goat. Pharmacol Biochem Behav 1981 Jun;14(6):901-5

Erjavec F, Lembeck F, Florjanc-Irman T, et al: Release of histamine by substance P. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug; 317(1):67-70

Erskine DJ, Hutchison VH: Melatonin and behavioral thermoregulation in the turtle, Terrapene carolina triunguis. Physiol Behav 1981 Jun; 26(6):991-4

Erspamer V: Comparative histochemistry as a springboard for the discovery of biogenic amines and active peptides in molluscan tissues and amphibian skin. Basic Appl Histochem 1981;25(1):3-14

Espósito Avella M, Pinzón D, Troetsch O: Efecto del cloruro de litio en el metabolismo de los carbohidratos en los ratones. Rev Med Panama 1981 May;6(2):183-92 (Eng. Abstr.) (Spa)

Ettenberg A, Rogers J, Koob GF, et al: Endogenous opiates and fasting [letter] Science 1981 Sep 11;213(4513):1282

Evans RL: Alprazolam (Xanax, the Upjohn Company). Drug Intell Clin Pharm 1981 Sep;15(9):633-8

Eyal E, Nemet P, Korczyn AD, et al: [Comparison of bioavailability of pilocarpine] Harefuah 1980 Dec 15;99(12):445-7 (Eng. Abstr.) (Heb)

F

Faber J, Havrdová Z: Differential effect of REM stimulating and REM inhibiting drugs (reserpine and amitriptylin) on memory. Act Nerv Super (Praha) 1981 Jun;23(2):169-71

Faingold CL, Hoffmann WE, Stittsworth JD Jr: Pentylenetetrazol-induced enhancement of reticular formation auditory evoked potentials and acoustic startle responses in the cat. Neuropharmacology 1981 Aug; 20(8):787-9

Fairchild MD, Jenden DJ, Mickey MR, et al: Drug-specific EEG frequency spectra and their time courses produced in the cat by antidepressants and a benzodiazepine. Electroencephalogr Clin Neurophysiol 1981 Jul;52(1):81-8

Fanelli O, Teauta F: Carnitine optical isomers' action on the epinephrine stress induced in the isolated perfused rabbit heart. Pharmacology 1981; 22(6):371-7

Fang VS: Pharmacological difference of L-dopa, apomorphine, and bromocriptine against metoclopramide. Life Sci 1981 May 11; 28(19):2143-9

Farabollini F, Lupo di Prisco C, Dessi-Fulgheri F: Modifications of brain steroidogenesis and plasma steroids after p-chlorophenylalanine-methyl-ester treatment in male rats and rabbits. Pharmacol Biochem Behav 1981 Jun;14(6):911-4

Faraj BA, Carrano RA, Ali FM, et al: Studies on the effect of antidepressants on kinetics and metabolism of tyramine. J Pharmacol Exp Ther 1981 Sep;218(3):750-7

Faravelli C, Tonini R, Zaccara G, et al: Gli antidepressivi della terza generazione. Esperienza di 100 casi di depressione primaria trattati con viloxazina, nomifensina e mianserina. Minerva Psichiatr 1981 Apr-Jun; 22(2):79-83 (Eng. Abstr.) (Ita)

Farley JM, Yeh JZ, Watanabe S, et al: Endplate channel block by guanidine derivatives. J Gen Physiol 1981 Mar;77(3):273-93

Farrell GC, Gollan JL, Correia MA, et al: Heme enhances hexobarbital metabolism in perfused rat liver after drug-mediated destruction of cytochrome P-450. J Pharmacol Exp Ther 1981 Aug;218(2):363-7

Fasolo A, Gaudino G: Somatostatin immunoreactive neurons and fibers in the hypothalamus of the newt. Gen Comp Endocrinol 1981 Jun; 44(2):256-63

Favus MJ, Berelowitz M, Coe FL: Effects of somatostatin on intestinal calcium transport in the rat. Am J Physiol 1981 Sep;241(3):G215-21

Fedchenko SN: Strukturno-metabolicheskie integratsii éndokrinnykh kletok zheludka v usloviiakh narushennogo gormonal'nogo balansa. Arkh Anat Gistol Embriol 1981 Mar;80(3):68-77 (Eng. Abstr.) (Rus)

Feer H: Communication from the viewpoint of the European Regional Reference Center. Prog Neuropsychopharmacol 1981;5(2):197-200

Fehlmann M, Canivet B, Freychet P: Epidermal growth factor stimulates monovalent cation transport in isolated rat hepatocytes. Biochem Biophys Res Commun 1981 May 15;100(1):254-60

Fekete M, Várszegi M, Kádár T, et al: Effect of cholecystokinin octapeptide sulphate ester on brain monoamines in the rat. Acta Physiol Acad Sci Hung 1981;57(1):37-46

Felber W: Eine Studie über die Rezidivprophylaxe affektiver Erkrankungen mittels Lithium. Psychiatr Neurol Med Psychol (Leipz) 1981 Jun;33(6):330-2 (Ger)

Feldon J, Gray JA: The partial reinforcement extinction effect: influence of chlordiazepoxide in septal lesioned rats. Psychopharmacology (Berlin) 1981;74(3):280-9

Felten DL, Harrigan P, Burnett BT, et al: Fourth ventricular tanycytes: a possible relationship with monoaminergic nuclei. Brain Res Bull 1981 May;6(5):427-36

Ferguson PW, Clark CR, Gee SJ, et al: Phenobarbital treatments lower DDT body burden in rhesus monkeys. Arch Environ Contam Toxicol 1981;10(3):263-70

Ferrand I: Les tranquillisants. Soins Psychiatr 1981 Jan;(7):33-6 (Fre)

Few JD, Gawel MJ, Imms FJ, et al: The influence of the infusion of noradrenaline on plasma cortisol levels in man. J Physiol (Lond) 1980 Dec;309:375-89

Fiala ES, Kohl NE, Hecht SS, et al: The formation of azoxy-2-phenylethane during the biological oxidation of phenylethylamine by rabbit liver microsomes. Carcinogenesis 1981; 2(3):165-73

Fieber SS: Pseudocholinesterase—a clinical assessment. Crit Care Med 1981 Sep;9(9):660-1

File SE: Effects of a piperazine derivative piribedil, on exploration, locomotor activity and social behaviour in the rat. Prog Neuropsychopharmacol 1981;5(3):245-55

Filipovic N, Trkovnik M: Effect of single and repeated administration of delta 9-tetrahydrocannabinol on 5-hydroxytryptamine, noradrenaline, dopamine and tryptophan levels in the brain of Wistar rats. Arh Hig Rada Toksikol 1981;31(4):293-7

Fillion G, Fillion MP: Modulation of affinity of postsynaptic serotonin receptors by antidepressant drugs. Nature 1981 Jul 23;292(5821):349-51

Findlay JW, Butz RF, Williams BB, et al: Effect of monoamine oxidase inhibitors on codeine disposition and pentobarbitone sleep-times in the rat. J Pharm Pharmacol 1981 Jan;33(1):45-7

Findlay JW, Warren JT, Hill JA, et al: Stereospecific radioimmunoassays for d-pseudoephedrine in human plasma and their application to bioequivalency studies. J Pharm Sci 1981 Jun;70(6):624-31

Fink M, Irwin P: Pharmacoelectroencephalographic study of brotizolam, a novel hypnotic. Clin Pharmacol Ther 1981 Sep;30(3):336-42

Finley JC, Maderdrut JL, Petrusz P: The immunocytochemical localization of enkephalin in the central nervous system of the rat. J Comp Neurol 1981 Jun 1;198(4):541-65

Finley JC, Lindström P, Petrusz P: Immunocytochemical localization of beta-endorphin-containing neurons in the rat brain. Neuroendocrinology 1981 Jul;33(1):28-42

Fisch HU, Hammond KR, Joyce CR, et al: An experimental study of the clinical judgment of general physicians in evaluating and prescribing for depression. Br J Psychiatry 1981 Feb;138:100-9

Fischer HD, Rudolph E, Schmidt J, et al: Interaction at the synaptic level of fusaric acid with neurotransmitters. Acta Biol Med Ger 1980; 39(8-9):935-40

Fisher SK, Holz RW, Agranoff BW: Muscarinic receptors in chromaffin cell cultures mediate enhanced phospholipid labeling but not catecholamine secretion. J Neurochem 1981 Aug;37(2):491-7

Fitz-Patrick D, Patel YC: Evidence for somatostatin precursors in human stomach, placenta, and amniotic fluid. J Clin Endocrinol Metab 1981 Aug;53(2):372-6

Flaim SF, Craven RA: Diltiazem and verapamil inhibit norepinephrine-stimulated 45Ca uptake in rabbit aorta. Pharmacology 1981;22(5):286-93

Flaim SF, Field JM, Zelis R: Differential transmural constrictor response to norepinephrine in rabbit carotid artery. Gen Pharmacol 1981; 12(4):295-301

Fleming DM, Knox JD, Crombie DL: Debendox in early pregnancy and fetal malformation. Br Med J [Clin Res] 1981 Jul 11;283(6248):99-101

Flentge F, Postema F, Medema HM, et al: Acute choline administration in rat and mouse: no effect on dopamine metabolism in brain. Life Sci 1981 Jul 27;29(4):331-5

Flerov MN, Pasechnik VI, Glanik T: Izuchenie vol't-ampernykh kharakteristik ionnykh kanalov po garmonikam transmembrannogo toka. Biofizika 1981 Mar-Apr;26(2):277-83 (Eng. Abstr.) (Rus)

Flood JF, Landry DW, Jarvik ME: Cholinergic receptor interactions and their effects on long-term memory processing. Brain Res 1981 Jun 29; 215(1-2):177-85

Floud A, Fahn S: L-DOPA (L-3,4-dihydroxyphenylalanine) uptake by human red blood cells. Biochim Biophys Acta 1981 Jul 20;645(2):165-9

Fontaine-Perus J, Chanconie M, Polak JM, et al: Origin and development of VIP and substance P containing neurons in the embryonic avian gut. Histochemistry 1981;71(3):313-23

Forsman L: Habitual catecholamine excretion and its relation to habitual distress. Biol Psychol 1980 Sep;11(2):83-97

Forsman L: Note on estimating catecholamines in urine sampled after 75-min periods of mental work and inactivity. J Psychosom Res 1981; 25(3):223-5

Fowler CJ, Oreland L: Substrate- and stereoselective inhibitor of human brain monoamine oxidase by 4-dimethylamino-alpha, 2-dimethylphenethylamine (FLA 336). J Pharm Pharmacol 1981 Jun; 33(6):403-6

Fowler CJ, Oreland L, Callingham BA: The acetylenic monoamine oxidase inhibitors clorgyline, deprenyl, pargyline and J-508: their properties and applications. J Pharm Pharmacol 1981 Jun;33(6):341-7 (83 ref.)

Fraeyman NH, De Potter WP, Singh P, et al: The effect of intracerebroventricularly administered dibutyryl adenosine 3',5'-cyclic monophosphate on cerebrospinal fluid and serum dopamine-beta-hydroxylase in rabbits. Biochem Pharmacol 1981 Jul 1;30(13):1765-9

Frances A, Clarkin J: Differential therapeutics: a guide to treatment selection. Hosp Community Psychiatry 1981 Aug;32(8):537-46

Frances H, Maurin Y, Lecrubier Y, et al: Effect of chronic lithium treatment on isolation-induced behavioral and biochemical effects in mice. Eur J Pharmacol 1981 Jul 10;72(4):337-41

Francesconi R, Mager M: Chronic chlorpromazine administration in rats: effects on ability to work in the heat. J Appl Physiol 1981 Mar; 50(3):509-12

Francesconi R, Mager M: Thermoregulatory effects of centrally administered bombesin, bradykinin, and methionine-enkephalin. Brain Res Bull 1981 Jul;7(1):63-8

Frankfurt M, Lauder JM, Azmitia EC: The immunocytochemical localization of serotonergic neurons in the rat hypothalamus. Neurosci Lett 1981 Jul 17;24(3):227-32

Franks S, Horrocks PM, Lynch SS, et al: Treatment of hyperprolactinaemia with pergolide mesylate: acute effects and preliminary evaluation of long-term treatment. Lancet 1981 Sep 26; 2(8248):659-61

Franquinet R, Martelly I: Effects of serotonin and catecholamines on RNA synthesis in planarians; in vitro and in vivo studies. Cell Differ 1981 Aug;10(4):201-9

Fratta W, Rossetti Z, Gessa GL: Rapid depletion and restoration of striatal met-enkephalin after ketamine. Life Sci 1981 Jul 6;29(1):93-7

Fratta W, Rossetti ZL, Poggioli R, et al: Reciprocal antagonism between ACTH1-24 and beta-endorphin in rats. Neurosci Lett 1981 Jun 12; 24(1):71-4

Frawley LS, Neill JD: Stimulation of prolactin secretion in rhesus monkeys by vasoactive intestinal polypeptide. Neuroendocrinology 1981 Aug; 33(2):79-83

Fredholm BB, Sollevi A: The release of adenosine and inosine from canine subcutaneous adipose tissue by nerve stimulation and noradrenaline. J Physiol (Lond) 1981;313:351-67

Freedman SB, Poat JA, Woodruff GN: Effect of guanine nucleotides on dopaminergic agonist and antagonist affinity for [3H]sulpiride binding sites in rat striatal membrane preparations. J Neurochem 1981 Sep; 37(3):608-12

Freeman BM, Manning AC: Stressor effects of handling on the immature fowl. Res Vet Sci 1979 Mar;26(2):223-6

Frenkl R, Szeberényi S, Csákváry G: Enzyme inducer effects after liver denervation in the rat. Acta Physiol Acad Sci Hung 1981;57(1):47-50

Fried G: Noradrenaline release and uptake in isolated small dense cored vesicles from rat seminal ducts. Acta Physiol Scand 1981 May; 112(1):41-6

Frieder B, Rapport MM: Enhancement of depolarization-induced release of gamma-aminobutyric acid from brain slices by antibodies to ganglioside. J Neurochem 1981 Sep;37(3):634-9

Frost BR, Frewin DB: Vascular responses to REN-293 (2-amino-3[3, 5-dihydroxyphenyl]-1-propanol hydrochloride)--a new sympathomimetic agent. Aust J Exp Biol Med Sci 1981 Apr;59(Pt 2):179-82

Fujita H, Endo A, Suzuki K: Inactivation of bacteriophage lambda by near-ultraviolet irradiation in the presence of chlorpromazine. Photochem Photobiol 1981 Feb;33(2):215-22

Fujitani T, Kanatani K, Inoue K, et al: [Norepinephrine content in the inferior turbinate of the patients with nasal allergy (author's transl)] Nippon Jibiinkoka Gakkai Kaiho 1981 Feb;84(2):168-73 (Eng. Abstr.) (Jpn)

Fujiwara H, Uemoto M, Tanaka C: Stimulation of the rat dorsal raphe in vivo releases labeled serotonin from the parietal cortex. Brain Res 1981 Jul 20;216(2):351-60

Fukuda M, Kuwayama Y, Shiosaka S, et al: Demonstration of a substance P-like immunoreactivity in retinal cells of the rat. Neurosci Lett 1981 May 29;23(3):239-42

Fuller RW, Hemrick-Luecke SK, Perry KW: Influence of harmaline on the ability of pargyline to alter catecholamine metabolism in rats. Biochem Pharmacol 1981 Jun 1;30(11):1295-8

Fuller RW, Hemrick-Luecke S, Toomey RE, et al: Properties of 8,9-dichloro-2,3,4,5-tetrahydro-1H-2-benzazepine, an inhibitor of norepinephrine N-methyltransferase. Biochem Pharmacol 1981 Jun 1; 30(11):1345-52

Fuller RW, Perry KW: Amfonelic acid antagonism of dopamine and norepinephrine depletion by alpha-methyl-m-tyrosine in rat brain. Biochem Pharmacol 1981 Jul 15;30(14):2025-6

Fuller RW, Snoddy HD, Mason NR, et al: Substituted piperazines as central serotonin agonists: comparative specificity of the postsynaptic actions of quipazine and m-trifluoromethylphenylpiperazine. J Pharmacol Exp Ther 1981 Sep;218(3):636-41

Fuller RW, Hemrick-Luecke SK, Perry KW: Lowering of dopamine metabolites in rat brain by harmaline. J Pharm Pharmacol 1981 Apr; 33(4):255-6

Fuller RW, Perry KW: Elevation of 3,4-dihydroxyphenylacetic acid concentration by L-5-hydroxytryptophan in control and fluoxetine-pretreated rats. J Pharm Pharmacol 1981 Jun;33(6):406-7

Funk KF, Schmidt J, Westermann KH: Zentral Transmitterdepletion durch Reserpin und motorisches Verhalten der Ratte. Acta Biol Med Ger 1980;39(8-9):923-7 (Eng. Abstr.) (Ger)

Funovics J, Hölbling N, Rauhs R, et al: The effect of SST, glucagon, calcitonin and PGE1 on exocrine pancreatic secretion in the unrestrained dog in long-term experiments. Eur Surg Res 1981; 13(3):213-26

Furlanut M, Delucca MG, Dilberis G, et al: Rapid and sensitive high-pressure liquid chromatographic method for monitoring carbamazepine levels in serum. Br J Clin Pharmacol 1981 Apr; 11(4):393-5

Fuxe K, Agnati LF, Köhler C, et al: Characterization of normal and supersensitive dopamine receptors: effects of ergot drugs and neuropeptides. J Neural Transm 1981;51(1-2):3-37

G

Gabana MA, Varotto M, Saladini M, et al: Influenze farmacologiche sul

AUTHOR SECTION

livello e trasporto cerebrale del GABA. --II) Effetto di alcani psicofarmaci sul livello e accumulo cerebrale del GABA. Boll Soc Ital Biol Sper 1981 Apr 30;57(8):909-13 (Eng. Abstr.) (Ita)

Gage FH, Springer JE: Behavioral assessment of norepinephrine and serotonin function and interaction in the hippocampal formation. Pharmacol Biochem Behav 1981 Jun;14(6):815-21

Gähwiler BH: Development of acute tolerance during exposure of hippocampal explants to an opioid peptide. Brain Res 1981 Jul 27;217(1):196-200

Gähwiler BH, Herrling PL: Effects of opioid peptides on synaptic potentials in explants of rat hippocampus. Regul Pept 1981 Feb;1(5):317-26

Gairin JE, Haran R, Mazarguil H, et al: (D-Ala2, N-Val5), (D-Ala2, Met5) enkephalins and enkephalinamides. Correlation between biological activity and NMR features. FEBS Lett 1981 Jun 1;128(1):51-4

Gál EM, Whitacre DH: Biopterin. VII. Inhibition of synthesis of reduced biopterins and its bearing on the function of cerebral tryptophan-5-hydroxylase in vivo. Neurochem Res 1981 Mar;6(3):233-41

Gallager DW, Mallorga P, Swaiman KF, et al: Effects of phenytoin on [3H]diazepam binding in dissociated primary cortical cell culture. Brain Res 1981 Aug 10;218(1-2):319-30

Gallanosa AG, Spyker DA, Shipe JR, et al: Human xylazine overdose: a comparative review with clonidine, phenothiazines, and tricyclic antidepressants. Clin Toxicol 1981 Jun;18(6):663-78 (38 ref.)

Gamse R, Lackner D, Gamse G, et al: Effect of capsaicin pretreatment on capsaicin-evoked release of immunoreactive somatostatin and substance P from primary sensory neurons. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):38-41

Ganina SS, Mel'nikova ZL, Iukhanova NA, et al: Primenenie tempal'gina dlia premedikatsii pri stomatologicheskikh vmeshatel'stv. Stomatologiia (Mosk) 1981 May-Apr;60(2):36-8 (Eng. Abstr.) (Rus)

Garattini S, Valzelli L: Is the isolated animal a possible model for phobia and anxiety? Prog Neuropsychopharmacol 1981;5(2):159-65 (56 ref.)

Gardner CR, Richards MH, Grove J: Effects of GABA metabolism on [3H]-GABA transport in synaptosomal preparations from rat cerebral cortex. Adv Biochem Psychopharmacol 1981;29:143-50

Garrigou D, Broekkamp CL, Lloyd KG: Involvement of the amygdala in the effect of antidepressants on the passive avoidance deficit in bulbectomised rats. Psychopharmacology (Berlin) 1981;74(1):66-70

Garson OM, Latimer NZ, Chiu E, et al: Chromosome studies of patients on long-term lithium therapy for psychiatric disorders. Med J Aust 1981 Jul 11;2(1):37-9

Garuti L, Ferranti A, Giovanninetti G, et al: Richerche su sostanze ad attività antivirale. Nota XVIII - bis-amidinoidrazoni di dialdeidi aromatiche N-eterocicliche. Farmaco [Sci] 1981 Jun;36(6):393-9 (Eng. Abstr.) (Ita)

Gary NE, Byra WM, Eisinger RP: Carbamazepine poisoning: treatment by hemoperfusion. Nephron 1981;27(4-5):202-3

Gauchy C, Kemel ML, Glowinski J, et al: In vivo release of newly synthesized GABA in the basal ganglia of the cat. Adv Biochem Psychopharmacol 1981;29:183-91

Gaudin-Chazal G, Segu L, Seyfritz N, et al: Visualization of serotonin neurones in the nodose ganglia of the cat. An autoradiographic study. Neuroscience 1981;6(6):1027-37

Gauthier M, Soumireu-Mourat B: 6-Hydroxydopamine and radiofrequency lesions of the lateral entorhinal cortex facilitate an operant appetitive conditioning task in mice. Neurosci Lett 1981 Jul 2;24(2):193-7

Gavaret JM, Cahnmann HJ, Nunez J: Thyroid hormone synthesis in thyroglobulin. The mechanism of the coupling reaction. J Biol Chem 1981 Sep 10;256(17):9167-73

el-Gawhary NE, Ghaleb HA, Goda NA, et al: Interaction between aminophylline and beta adrenergic blockers 'propranolol' & 'practolol' on the myocardium and tracheal spirals in experimental animals. J Egypt Med Assoc 1979;62(1-2):171-83

Gear AR: Preaggregation reactions of platelets. Blood 1981 Sep;58(3):477-90

Gebauer H: GABA transport in the rat thyroid. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):61-6

Genazzani AR, Facchinetti F, Parrini D: beta-lipotrophin and beta-endorphin plasma levels during pregnancy. Clin Endocrinol (Oxf) 1981 Apr;14(4):409-18

Gentsch C, Lichtsteiner M, Feer H: Locomotor activity, defecation score and corticosterone levels during an openfield exposure: a comparison among individually and group-housed rats, and genetically selected rat lines. Physiol Behav 1981 Jul;27(1):183-6

George CF: Drug metabolism by the gastrointestinal mucosa. Clin Pharmacokinet 1981 Jul-Aug;6(4):259-74

Gerner RH, Hare TA: CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Am J Psychiatry 1981 Aug;138(8):1098-101

Gerner RH, Wolff SM, Fauci AS, et al: Lithium carbonate for recurrent fever and neutropenia. JAMA 1981 Oct 2;246(14):1584-6

Gever LN: Drug alert: two forms of dilantin. Nursing (Horsham) 1981 Sep;11(9):78

Ghebregzabher M, Rufini S, Castellucci MG, et al: Analysis of some tryptophan and phenylalanine metabolites in urine by a straight-phase high-performance liquid chromatographic technique. J Chromatogr 1981 Feb 13;222(2):191-201

Ghosh SP, Chatterjee TK, Ghosh JJ: Antiandrogenic effect of delta-9-tetrahydrocannabinol in adult castrated rats. J Reprod Fertil 1981 Jul;62(2):513-7

Gianoulakis C, Drouin JN, Seidah NG, et al: Effect of chronic morphine treatment on beta-endorphin biosynthesis by the rat neurointermediate lobe. Eur J Pharmacol 1981 Jul 10;72(4):313-21

Gibson GE, Peterson C, Jenden DJ: Brain acetylcholine synthesis declines with senescence. Science 1981 Aug 7;213(4508):674-6

Gibson GE, Peterson C, Sansone J: Decreases in amino acids and acetylcholine metabolism during hypoxia. J Neurochem 1981 Jul;37(1):192-201

Gibson GT, Colley DP, McMichael AJ, et al: Congenital anomalies in relation to the use of doxylamine/dicyclomine and other antenatal factors: an ongoing prospective study. Med J Aust 1981 Apr 18;1(8):410-4

Gibson SJ, Polak JM, Bloom SR, et al: The distribution of nine peptides in rat spinal cord with special emphasis on the substantia gelatinosa and on the area around the central canal (lamina X). J Comp Neurol 1981 Sep 1;201(1):65-79

Gidley MJ, Hall LD, Sanders JK, et al: Acetaldehyde--enkephalins: structure proof and some conformational deductions from one- and two-dimensional proton nuclear magnetic resonance spectra. Biochemistry 1981 Jun 23;20(13):3880-3

Giguere V, Cote J, Labrie F: Characteristics of the alpha-adrenergic stimulation of adrenocorticotropin secretion in rat anterior pituitary cells. Endocrinology 1981 Sep;109(3):757-62

Gilles PA, Karavolas HJ: Effect of 20 alpha-dihydroprogesterone, progesterone, and their 5 alpha-reduced metabolites on serum gonadotropin levels and hypothalamic LHRH content. Biol Reprod 1981 Jun;24(5):1088-97

Gillespie JS, Martin W: A smooth muscle inhibitory material from the bovine retractor penis and rat anococcygeus muscles. J Physiol (Lond) 1980 Dec;309:55-64

Gillespie MN, Niehaus KE, Rodger IW, et al: Sodium-dependent relaxation in arterial smooth muscle. Clin Exp Pharmacol Physiol 1981 May/June;8(3):209-14

Gillespie TJ, Sipes IG: Sensitive gas chromatographic determination of trifluoperazine in human plasma. J Chromatogr 1981 Apr 10;223(1):95-102

Gillham B, Beckford U, Insall RL, et al: Dynamics of the formation and release of corticotrophin releasing activity by the rat hypothalamus in vitro. J Endocrinol 1981 Aug;90(2):201-10

Gillman PK, Bartlett JR, Bridges PK, et al: Indolic substances in plasma, cerebrospinal fluid, and frontal cortex of human subjects infused with saline or tryptophan. J Neurochem 1981 Aug;37(2):410-7

Girod C, Dubois MP, Durand N: Sur la mise en évidence imunocytochimique de fibres à somatostatine dans la neurohypophyse du singe Macacus irus. C R Trav Lab Carlsberg 1981;175(3):347-51 (Eng. Abstr.) (Fre)

Gispen WH, Isaacson RL: ACTH-induced excessive grooming in the rat. Pharmacol Ther [B] 1981;12(1):209-46 (152 ref.)

Gisselmann A, Marin A: Psychose maniaco-dépressive. Efficacité du lithium sur certains troubles du métabolisme glucidique. Nouv Presse Med 1981 Jun 6;10(25):2121 (Fre)

Gitlin M: Questioning a contraindication of propranolol [letter] Am J Psychiatry 1981 Sep;138(9):1261-2

Glass MR, Rudd BT, Lynch SS, et al: Oestrogen-gonadotrophin feedback mechanisms in the puerperium. Clin Endocrinol (Oxf) 1981 Mar;14(3):257-67

Glass RM, Uhlenhuth EH, Hartel FW, et al: Cognitive dysfunction and imipramine in outpatient depressive. Arch Gen Psychiatry 1981 Sep;38(9):1048-51

Gledhill B, Donovan BT: Repetitive treatment with gonadotrophin releasing factor or a long-acting analogue upon gonadotrophin secretion in the ferret. J Endocrinol 1981 Aug;90(2):275-83

Glembotski CC: Subcellular fractionation studies on the post-translational processing of pro-adrenocorticotropic hormone/endorphin in rat intermediate pituitary. J Biol Chem 1981 Jul 25;256(14):7433-9

Glennon RA, Salley JJ Jr, Steinsland OS, et al: Synthesis and evaluation of novel alkylpiperazines as potential dopamine antagonists. J Med Chem 1981 Jun;24(6):678-83

Glick SD, Weaver LM, Meibach RC: Amphetamine enhancement of reward asymmetry. Psychopharmacology (Berlin) 1981;73(4):323-7

Glitsch HG, Kampmann W, Pusch H: Activation of active Na transport in sheep Purkinje fibres by external K or Rb ions. Pflugers Arch 1981 Jul;391(1):28-34

Gloger S, Grunhaus L, Birmacher B, et al: Treatment of spontaneous panic attacks with chlomipramine. Am J Psychiatry 1981 Sep;138(9):1215-7

Glossmann H, Presek P, Eigenbrodt E: Quercetin inhibits tyrosine phosphorylation by the cyclic nucleotide-independent, transforming protein kinase, pp60src. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):100-2

AUTHOR SECTION

Glover V, Bhattacharya SK, Sandler M, et al: Benzodiazepines reduce stress-augmented increase in rat urine monoamine oxidase inhibitor. Nature 1981 Jul 23;292(5821):347-9

Glow RA: Treatment alternatives for hyperactive children - a comment on 'problem children' and stimulant drug treatment. Aust NZ J Psychiatry 1981 Jun;15(2):123-8

Gnilitskaia VB, Belkin SG, Zhizhina EA: Fliuorimetricheskoe opredelenie kontsentratsii khinidina v krovi. Lab Delo 1981;(8):511 **(Rus)**

Godukhin OV, Zharikova AD, Zakharova LI: Rol' dofaminovykh retseptorov v reguliatsii glutamatergicheskoi sinapticheskoi peredachi v neostriatume mozga krys. Fiziol Zh SSSR 1981 Mar;67(3):384-9 (Eng. Abstr.) **(Rus)**

Goebel RJ, Currie BL, Bowers CY: Potential thyroliberin affinity labels. 1. Chloroacetyl-substituted phenylalanylpyrrolidines. J Med Chem 1981 Apr;24(4):366-70

Goldman ME, Gundersen RE, Erickson CK, et al: High performance liquid chromatographic analysis of catecholamines in growing and non-growing Tetrahymena pyriformis. Biochim Biophys Acta 1981 Aug 17;676(2):221-5

Golovleva LA, Finkel'shtein ZI, Popovich NA, et al: Prevrashchenie ordrama mikroorganizmami. Izv Akad Nauk SSSR [Biol] 1981 May-Jun;(3):348-58 (Eng. Abstr.) **(Rus)**

Golubev VN: Kationnaia spetsifichnost' zhidkikh membran, modifitsirovannykh gramitsidinom. Biofizika 1981 Mar-Apr;26(2):360-1 (Eng. Abstr.) **(Rus)**

Gomes UC, McCarthy BW, Shanley BC: Effect of neuroleptics on indoleamine-N-methyltransferase activity and brain metabolism of bufotenin. Biochem Pharmacol 1981 Mar 15;30(6):571-5

Gomolin I: Meprobamate [news] Clin Toxicol 1981 Jun;18(6):757-60

González Martínez de Aárate JL, Saiz Martínez-Acitores J, Sánchez García A, et al: Efecto de la nomifensina sobre el metabolismo oxidativo de cerebro de rata 'in vitro'. Arch Neurobiol (Madr) 1981 Mar-Apr; 44(2):109-16 (Eng. Abstr.) **(Spa)**

González DH, Page JB: Cuban women, sex role conflicts and the use of prescription drugs. J Psychoactive Drugs 1981 Jan-Mar;13(1):47-51

Goodale DB: The role of substance P in simultaneously mediating oral pain and inflammation. Anesth Prog 1981 Mar-Apr;28(2):41-3

Goode DJ, Meltzer HY, Fang VS: Daytime variation in serum prolactin level in patients receiving oral and depot antipsychotic medication. Biol Psychiatry 1981 Jul;16(7):653-62

Goodhardt M, Guellaen G, Hanoune J: Specific antibodies against the irreversible alpha-adrenergic antagonist, phenoxybenzamine. Biochem Pharmacol 1981 Jun 15;30(12):1685-92

Goodrich C, Wilk C: Temperature preferences and the effect of changes in serotonin in maturing mice. Physiol Behav 1981 Jun;26(6):1041-7

Gopalam KB, Rao PR: Genetic studies on Vysyas of Andhra Pradesh, S. India: A1A2BO, Rh (O) D, transferrin, group specific component, haptoglobin and pseudocholinesterase types. Acta Anthropogenet 1981; 5(3):175-80

Gordon WF: Elderly depressives: treatment and follow-up. Can J Psychiatry 1981 Mar;26(2):110-3

Górka Z, Wojtasik E: The effect of antidepressants on behavioral despair in rats. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):463-8

Górka Z, Zacny E: The effect of single and chronic administration of imipramine on clonidine-induced hypothermia in the rat. Life Sci 1981 Jun 22;28(25):2847-54

Gorski RA, Yanase M: Estrogen facilitation of lordosis behavior in the female rat. Exp Brain Res 1981;Suppl 3:222-37

Govoni S, Hanbauer I, Hexum TD, et al: In vivo characterization of the mechanisms that secrete enkephalin-like peptides stored in dog adrenal medulla. Neuropharmacology 1981 Jul;20(7):639-45

Goyal RK, Verma SC: Pharmacological investigations into the effects of histamine and histamine analogs on guinea pig and rat uterus. Agents Actions 1981 Jul;11(4):312-7

Grab DJ, Carlin RK, Siekevitz P: Function of a calmodulin in postsynaptic densities. II. Presence of a calmodulin-activatable protein kinase activity. J Cell Biol 1981 Jun;89(3):440-8

Granholm AC, Seiger A: Thyroid hormone dependency in immature but not mature grafted locus coeruleus neurons. Evidence from intraocular innervation of iris transplants. Med Biol 1981 Feb;59(1):51-7

Granner D, Noguchi T, Diesterhaft M: Evidence for a dual effect of dibutyryl cyclic AMP on the synthesis of tyrosine aminotransferase in rat liver. Adv Cyclic Nucleotide Res 1981;14:529-37

Graves DA: Phenytoin by volume-control set [letter] Am J Hosp Pharm 1981 Aug;38(8):1119, 1121

Gray JA, Davis N, Feldon J, et al: Animal models of anxiety. Prog Neuropsychopharmacol 1981;5(2):143-57 (40 ref.)

Graybiel A, Cramer DB, Wood CD: Experimental motion sickness: efficacy of transdermal scopolamine plus ephedrine. Aviat Space Environ Med 1981 Jun;52(6):337-9

Grecu I, Barbu S, Ghizdavu L: Mise en valeur de plusieurs bentonites á des fins pharmaceutiques. III. Étude de l'adsorption sur des bentonites du nitrazepan et de l'oxazepam. Ann Pharm Fr 1980;38(6):501-6 (Eng. Abstr.) **(Fre)**

Greenberg MI, Roberts JR, Baskin SI: Use of endotracheally administered epinephrine in a pediatric patient. Am J Dis Child 1981 Aug; 135(8):767-8

Greenberg RS: Determination of fenvalerate, a synthetic pyrethroid, in grapes, peppers, apples, and cottonseeds by gas-liquid chromatography. J Agric Food Chem 1981 Jul-Aug;29(4):856-60

Greenblatt DJ, Woo E: The specificity of the extraction fluorescence assay for serum or plasma quinidine. J Clin Pharmacol 1981 Aug-Sep; 21(8-9):333-6 (17 ref.)

Gregson RP, Lohr RR, Marwood JF, et al: 3-Hydroxy-4-methoxyphenethylamine, the cardioactive constituent of a soft coral. Experientia 1981 May 15;37(5):493-4

Greil W: Pharmakokinetik und Toxikologie des Lithiums. Bibl Psychiatr 1981;(161):69-103 (147 ref.) (Eng. Abstr.) **(Ger)**

Grella P, Meneghetti G, Cecchetto A, et al: Bromocriptina e fertilità puerperale. Riv Ital Ginecol 1980;59(2-3):223-31 (Eng. Abstr.) **(Ita)**

Gremo F, Vernadakis A: Preferential accumulation of [3H] corticosterone in chick brain during embryonic development. Neurochem Res 1981 Apr;6(4):343-51

Gresik EW, Schenkein I, van der Noen H, et al: Hormonal regulation of epidermal growth factor and protease in the submandibular gland of the adult mouse. Endocrinology 1981 Sep;109(3):924-9

Griffin N, Draper RJ, Webb MG: Addiction to tranylcypromine. Br Med J [Clin Res] 1981 Aug 1;283(6287):346

Grigor'eva GM: Propionilkholinesterazy mozga briukhonogikh molliuskov. Vzaimodeistvie a substratami i ingibitorami. Biokhimiia 1980 Dec;45(12):2176-88 (Eng. Abstr.) **(Rus)**

Grimm VE, Hershkowitz M: The effect of chronic diazepam treatment on discrimination performance and 3H-flunitrazepam binding in the brains of shocked and nonshocked rats. Psychopharmacology (Berlin) 1981;74(2):132-6

Grimmelikhuijzen CJ, Carraway RE, Rökaeus A, et al: Neurotensin-like immunoreactivity in the nervous system of hydra. Histochemistry 1981; 72(2):199-209

Grimmelikhuijzen CJ, Balfe A, Emson PC, et al: Substance P-like immunoreactivity in the nervous system of hydra. Histochemistry 1981; 71(3):325-33

Grinde B, Seglen PO: Effects of amino acid analogues on protein degradation in isolated rat hepatocytes. Biochim Biophys Acta 1981 Aug 5;676(1):43-50

Gromova EA, Semenova TP, Li ON, et al: Effect of injury to the serotoninergic and noradrenergic brain systems on food and defensive conditioned reflexes in rats. Neurosci Behav Physiol 1981 Jan-Feb; 11(1):10-5

Gronert GA, Michenfelder JD, Sharbrough FW, et al: Canine cerebral metabolic tolerance during 24 hours deep pentobarbital anesthesia. Anesthesiology 1981 Aug;55(2):110-3

Gross R, Hackenberg HM, Hackenthal E, et al: Interaction between perfusion pressure and sympathetic nerves in renin release by carotid baroreflex in conscious dogs. J Physiol (Lond) 1981;313:237-50

Grota LJ: Serotonin regulation of corticoid secretion in infant rats. Dev Psychobiol 1981 May;14(3):221-8

Grove J, Schechter PJ, Tell G, et al: Increased gamma-aminobutyric acid (GABA), homocarnosine and beta-alanine in cerebrospinal fluid of patients treated with gamma-vinyl GABA (4-amino-hex-5-enoic acid). Life Sci 1981 May 21;28(21):2431-9

Guensberger E, Molcan J, Caplová T, et al: Strategie der Therapie depressiver Zustände mit Psychopharmaka. Agressologie 1979; 20(D):315-8 (Eng. Abstr.) **(Ger)**

Guillemant J, Guillemant S: Protein-bound cyclic AMP and steroidogenesis in the adrenal gland of the rat. J Endocrinol 1981 Jul; 90(1):77-82

Guillemin R: Hypothalamic hypophysiotrophic peptides, known and unknown. The Sir Henry Dale lecture for 1980. J Endocrinol 1981 Jul;90(1):3p-10p (38 ref.)

Guimarães S, Paiva MQ: Two different biophases for adrenaline released by electrical stimulation or tyramine from the sympathetic nerve endings of the dog saphenous vein. Naunyn Schmiedebergs Arch Pharmacol 1981 Jun;316(3):200-4

Gundlach AL, Beart PM: Effect of GABAergic drugs on dopamine catabolism in the nigrostriatal and mesolimbic dopaminergic pathways of the rat. J Pharm Pharmacol 1981 Jan;33(1):41-3

Gundlach AL, Beart PM: Differential effects of IV and IP muscimol on central dopamine metabolism. Psychopharmacology (Berlin) 1981; 74(1):71-3

Gupta C, Mills NC, Bullock LP, et al: The effects of testosterone and progestins on the rate of beta-glucuronidase synthesis in mouse kidney as studied with an immunoprecipitation assay. Int J Androl 1981 Jun; 4(3):342-54

Gut I, Hátle K, Zílková L: Effect of phenobarbital pretreatment on benzene biotransformation in the rat. II. 9,000 g supernatant and isolated perfused liver versus living rat. Arch Toxicol 1981 Mar;47(1):13-24

Guttmacher S, Lehmann H, Sabor S: Rogers vs. Okin: the public's reaction. Ann NY Acad Sci 1981;368:133-6

Guyotat J: La pratique psychiatrique telle qu'elle apparaît à travers le groupe Balint. Schweiz Arch Neurol Neurochir Psychiatr 1981; 128(2):251-61 (Eng. Abstr.) **(Fre)**

György L, Orr Z, Folly G, et al: The influence of dopamine and dopaminergic agonists on the contractions of field stimulated rat vas deferens. Arch Int Pharmacodyn Ther 1981 Mar;250(1):55-64

H

Haber S, Elde R: Correlation between Met-enkephalin and substance P immunoreactivity in the primate globus pallidus. Neuroscience 1981; 6(7):1291-7

Hackman MR, Brooks MA: Differential pulse amperometric detection of drugs in plasma using a dropping mercury electrode as a high-performance liquid chromatographic detector. J Chromatogr 1981 Feb 13;222(2):179-90

Hackman RM, Graves HB: Corticosterone levels in mice exposed to high-intensity electric fields. Behav Neural Biol 1981 Jun;32(2):201-13

Hacksell U, Arvidsson LE, Svensson U, et al: Monophenolic 2-(dipropylamino)indans and related compounds: central dopamine-receptor stimulating activity. J Med Chem 1981 Apr; 24(4):429-34

Hadziselimovic F, Girard J, Höcht B, et al: Effect of LH-RH treatment on hypothalamo-pituitary-gonadal axis and Leydig cell ultrastructure in cryptorchid boys. Horm Res 1980;13(6):358-66

Al-Hakiem MH, White GW, Smith DS, et al: Direct determination of propranolol in serum or plasma by fluoroimmunoassay. Ther Drug Monit 1981;3(2):159-65

Hall RC, Feinsilver DL, Holt RE: Anticholinergic psychosis: differential diagnosis and management. Psychosomatics 1981 Jul;22(7):581-3, 587

Hallam TJ, Scrutton MC, Wallis RB: Responses of rabbit platelets to adrenaline induced by other agonists. Thromb Res 1981 Feb-Mar; 21(4-5):413-24

Halle W, Hecker D: Zum histochemischen Nachweis von beta-Glucuronidase und Leucinaminopeptidase in kultivierten Gefässendothelzellen. Acta Histochem (Jena) 1981;68(2):188-92 (Eng. Abstr.) **(Ger)**

Halleck SL: Covert values in the treatment of psychosis. Am J Psychother 1981 Apr;35(2):173-86

Halstrøm J, Qasim MA, Brunfeldt K, et al: N-(9-Xanthenyl)amino acid N-carboxyanhydrides in the solid-phase synthesis of a Lys-Lys-linked cyclic leucine-enkephalin. Hoppe Seylers Z Physiol Chem 1981 Jun; 362(6):593-9

Hamada T, Tamate H: Intramuscular injections of 1,2-propenediol can stimulate rumen papillar development of milk-fed kids. Experientia 1981 Jun;37(6):579-80

Hamberger A, Jacobson I, Lindroth P, et al: Neuron-glia interactions in the biosynthesis and release of transmitter amino acids. Adv Biochem Psychopharmacol 1981;29:509-18 (29 ref.)

Hamed AT, Lokhandwala MF, Jandhyala BS: Effect of bromocriptine on cardiac function and coronary blood flow. J Cardiovasc Pharmacol 1981 May-Jun;3(3):636-46

Hamlet MA, Rorie DK, Tyce GM: Release of endogenous catecholamines from slices of hypothalamus of rats. Brain Res 1981 Aug 3;217(2):315-25

Hammonds RG Jr, Ling N, Puett D: Interaction of tritiated beta-endorphin with rat brain membranes. Anal Biochem 1981 Jun;114(1):75-84

Han JS: [Concerning the quantum theory of acetylcholine release] Sheng Li Ko Hsueh Chin Chan 1980 Mar;11(3):255-8 **(Chi)**

Hancox AJ, Scrimshire DA: A proposed model for the synthesis, storage and release of acetylcholine at the neuromuscular junction. J Biomed Eng 1981 Jul;3(3):183-95

Hansen S, Stanfield EJ, Everitt BJ: The effects of lesions of lateral tegmental noradrenergic neurons on components of sexual behavior and pseudopregnancy in female rats. Neuroscience 1981;6(6):1105-17

Hanson GR, Alphs L, Wolf W, et al: Haloperidol-induced reduction of nigral substance P-like immunoreactivity: a probe for the interactions between dopamine and substance P neuronal systems. J Pharmacol Exp Ther 1981 Aug;218(2):568-74

Harder DR: Membrane activation of smooth muscle from rabbit basilar artery by dopamine. Pfluegers Arch 1981 Jun;390(3):296-8

Hargrove JL, Granner DK: Physical properties, limited proteolysis, and acetylation of tyrosine aminotransferase from rat liver. J Biol Chem 1981 Aug 10;256(15):8012-7

Harmar A, Keen P: Chemical characterization of substance P-like immunoreactivity in primary afferent neurones. Brain Res 1981 Sep 7; 220(1):203-7

Harris KH, Murphy BD: Prolactin in maintenance of the corpus luteum of early pseudopregnancy in the golden hamster. J Endocrinol 1981 Aug;90(2):145-50

Harris RR, Mackenzie IC: The effects of alpha and beta adrenergic agonists and cyclic adenosine 3':5'-monophosphate on epidermal metabolism. J Invest Dermatol 1981 Oct;77(4):337-40

Harrison RN, Mackay AD, Shepherd HA: Fibre-optic gastroscopy and intravenous diazepam: their combined effect on arterial oxygen saturation. Pharmatherapeutica 1981;2(9):565-7

Hartling OJ, Svendsen TL, Trap-Jensen J: Systemic and forearm haemodynamic and metabolic effects of racemic propranolol or D-propranolol in healthy subjects. Clin Sci 1981 Jun;60(6):675-9

Hartmann RJ, Geller I: Effects of buspirone on conflict behavior of laboratory rats and monkeys. Proc West Pharmacol Soc 1981;24:179-81

Harty RF, Maico DG, McGuigan JE: Somatostatin inhibition of basal and carbachol-stimulated gastrin release in rat antral organ culture. Gastroenterology 1981 Oct;81(4):707-12

Harvey JA, Gormezano I: Effects of haloperidol and pimozide on classical conditioning of the rabbit nictitating membrane response. J Pharmacol Exp Ther 1981 Sep;218(3):712-9

Harvey S, Sterling RJ, Phillips JG: Diminution of thyrotrophin releasing hormone-induced growth hormone secretion in adult domestic fowl (Gallus domesticus). J Endocrinol 1981 Jun;89(3):405-10

Hasday JD, Karch FE: Benzodiazepine prescribing in a family medicine center JAMA 1981 Sep 18;246(12):1321-5

Hashimoto K, Ohno N, Aoki Y, et al: A different distribution of corticotropin releasing factor and arginine vasopressin contents in the hypothalamic nuclei after estrogen administration. Acta Med Okayama 1981 Feb;35(1):37-43

Hashimoto K, Ohno N, Yunoki S, et al: Characterization of corticotropin releasing factor (CRF) and arginine vasopressin in median eminence extracts on sephadex gel-filtration. Endocrinol Jpn 1981 Feb;28(1):1-7

Hata T, Kita T, Yoneda R, et al: Effects of exogenous stimuli and centrally acting drugs on galvanic skin responses in rats. Jpn J Pharmacol 1981 Feb;31(1):23-31

Hatano Y, Kohli JD, Goldberg LI, et al: Relative contracting and relaxing potencies of a series of prostaglandins on isolated canine mesenteric artery strips. Prostaglandins 1981 Apr;21(4):515-29

Haubrich DR, Gerber NH, Pfluéger AB: Deanol affects choline metabolism in peripheral tissues of mice. J Neurochem 1981 Aug;37(2):476-82

Hazum E: Photo-affinity inactivation of gonadotropin releasing hormone receptors. FEBS Lett 1981 Jun 1;128(1):111-3

Headley PM, Desarmenien M, Santangelo F, et al: Direct action of pentobarbitone in potentiating the responses to GABA of rat dorsal root ganglion neurones in vitro. Neurosci Lett 1981 Jul 17;24(3):273-80

Heath H 3d: Biogenic amines and the secretion of parathyroid hormone and calcitonin. Endocr Rev 1980 Fall;1(4):319-38 (141 ref.)

Hedner J, Hedner T, Bergman B, et al: Respiratory depression by GABA-ergic drugs in the preterm rabbit. J Dev Physiol 1980 Dec; 2(6):401-7

Hedner J, Almgren O, Jonason J, et al: Neuronal and extraneuronal uptake of 3H-noradrenaline in rat portal vein in vitro. Acta Physiol Scand 1981 Feb;111(2):171-7

Hedner T, Bergman B, Holmgren M: Adrenal catecholamines during and following hypoxia in neonatal rats. Med Biol 1980 Aug;58(4):228-31

Hedner T: Endogena opioider i centrala nervsystemet. Lakartidningen 1981 Jul 22;78(30-31):2689-93 (Eng. Abstr.) **(Swe)**

Heide L, Leistner E: Enzymatic synthesis of the coenzyme A ester of o-succinylbenzoic acid, an intermediate in menaquinone (vitamin K2) biosynthesis. FEBS Lett 1981 Jun 15;128(2):201-4

Heidemann DR: High-pressure liquid chromatographic determination of methscopolamine nitrate, phenylpropanolamine hydrochloride, pyrilamine maleate, and pheniramine maleate in tablets. J Pharm Sci 1981 Jul;70(7):820-2

Heikkila RE, Babington RG, Houlihan WJ: Pharmacological studies with several analogs of mazindol: correlation between effects on dopamine uptake and various in vivo responses. Eur J Pharmacol 1981 May 8; 71(2-3):277-86

Heikkila RE: Differential effects of several dopamine uptake inhibitors and releasing agents on locomotor activity in normal and in reserpinized mice. Life Sci 1981 Apr 27;28(17):1867-73

Helia O, Vargova E, Jindra A: Reduction of octoclothepine-N-oxide by rat liver microsomes. Eur J Drug Metab Pharmacokinet 1981;6(2):155-8

Helle KB, Serck-Hassen G, Jørgensen G, et al: Neurotensin-induced contractions in venous smooth muscle. J Auton Nerv Syst 1980 Jul; 2(2):143-55

Helman CG: Patients' perceptions of psychotropic drugs. J R Coll Gen Pract 1981 Feb;31(223):107-12

Helmeste DM, Seeman P, Coscina DV: Relation between brain catecholamine receptors and dopaminergic stereotypy in rat strains. Eur J Pharmacol 1981 Feb 19;69(4):465-70

Hemminki E, Pesonen T, Hansen EH: Number and type of psychotropic drugs on the Scandinavian market in 1950-1977. Drug Intell Clin Pharm 1981 Jan;15(1):27-37

Henderson JD, Dayton PG, Israili ZH, et al: A nonmetabolized analogue of phenytoin. J Med Chem 1981 Jul;24(7):843-7

Henderson V, Fisher JW, D'Allessandris R: Toxic and teratogenic effects of hydrazine on fathead minnow (pimephales promelas) embryos. Bull Environ Contam Toxicol 1981 Jun;26(6):807-12

Hendry SH, Jones EG: Sizes and distributions of intrinsic neurons incorporating tritiated GABA in monkey sensory-motor cortex. J Neurosci 1981 Apr;1(4):390-408

Henri L, Groleau M: Retroperitoneal fibrosis after treatment with propranolol [letter] Drug Intell Clin Pharm 1981 Sep;15(9):696

Henry JA, Iliopoulou A, Kaye CM, et al: Changes in plasma concentrations of acebutolol, propranolol and indomethacin during physical exercise. Life Sci 1981 Apr 27;28(17):1925-9

Herdt TH, Stevens JB, Linn J, et al: Influence of ration composition and energy balance on blood beta-hydroxybutyrate (ketone) and plasma

glucose concentrations of dairy cows in early lactation.
Am J Vet Res 1981 Jul;42(7):1177-80

Hermann T, Mokrosz J, Bojarski J: Kinetics and mechanism of decomposition of some derivatives of 5-allylbarbituric acid. Part V. The course of hydrolysis of 5 allyl-5-(2'-hydroxypropyl)barbituric acid. Pol J Pharmacol Pharm 1980;32(5):807-13

Hermans WP, Debets MH, van Leeuwen EC, et al: Time-related secretion of gonadotrophins after a single injection of steroid-free bovine follicular fluid in prepubertal and adult female rats. J Endocrinol 1981 Jul;90(1):69-76

Hernández LL, Powell DA: Forebrain norepinephrine and serotonin concentrations and cardiac conditioning in normal rabbits and rabbits with septal lesions. Brain Res Bull 1981 Jun;6(6):479-86

Hertrich O: Depression - Somatisierung - Suizid. Teil 2: Larvierte Depression, Suizid. Fortschr Med 1981 Jul 2;99(25):973-7 (Ger)

Hertz L, Mukerji S, Richardson JS: Down-regulation of beta-adrenergic activity in astroglia by chronic treatment with an antidepressant drug. Eur J Pharmacol 1981 Jun 19;72(2-3):267-8

Herve D, Simon H, Blanc G, et al: Opposite changes in dopamine utilization in the nucleus accumbens and the frontal cortex after electrolytic lesion of the median raphe in the rat. Brain Res 1981 Jul 20;216(2):422-8

Hesse B, Kanstrup IL, Christensen NJ, et al: Reduced norepinephrine response to dynamic exercise in human subjects during O2 breathing. J Appl Physiol 1981 Jul;51(1):176-8

Heuzenroeder MW, Reeves P: The tsx protein of Escherichia coli can act as a pore for amino acids. J Bacteriol 1981 Sep;147(3):1113-6

Hiai S, Yokoyama H, Oura H: Effect of escin on adrenocorticotropin and corticosterone levels in rat plasma. Chem Pharm Bull (Tokyo) 1981 Feb;29(2):490-4

Hidaka H: Biopharmacological assessment of calmodulin function: utility of calmodulin antagonist naphthalenesulfonamide.
Proc West Pharmacol Soc 1981;24:203-8

Hierowski MT, Waring AJ, Schally AV: Synthesis and degradation of cyclic nucleotides in the pituitary gland, ovary and testis of rats treated with D-Trp6-luteinizing hormone-releasing hormone.
Biochim Biophys Acta 1981 Jul;675(2):232-8

Higgins D, Iacovitti L, Joh TH, et al: The immunocytochemical localization of tyrosine hydroxylase within rat sympathetic neurons that release acetylcholine in culture. J Neurosci 1981 Feb;1(2):126-31

Hilditch A, Drew GM: Characteristics of the dopamine receptors in the rabbit isolate splenic artery. Eur J Pharmacol 1981 Jul 10;72(4):287-96

Hillier SG, Reichert LE Jr, van Hall EV: Modulation of FSH-controlled steroidogenesis in rat granulosa cells: direct in-vitro effects of LHRH and ICI-118630. Mol Cell Endocrinol 1981 Aug;23(2):193-205

Hirano T, Niijima A: Two populations of nerve fibers in the adrenal nerve. J Auton Nerv Syst 1980 May;2(1):81-6

Hirata M, Aso Y, Hsu KY, et al: Metabolism of isoniazid and free hydrazine formation in isolated rat hepatocytes. J Pharmacobiodyn 1981 Feb;4(2):145-7

Hirsch JD, Lydigsen JL: Binding of beta-carboline-3-carboxylic acid ethyl ester to mouse brain benzodiazepine receptors in vivo.
Eur J Pharmacol 1981 Jul 10;72(4):357-60

Hirst BH, Shaw B, Meyers CA, et al: Structure-activity studies with somatostatin: the role of tryptophan in position 8. Regul Pept 1980 Oct; 1(2):97-113

Hirst GD, Neild TO: Localization of specialized noradrenaline receptors at neuromuscular junctions on arterioles of the guinea-pig.
J Physiol (Lond) 1981;313:343-50

Hisayama T, Takayanagi I, Kasuya Y: Effects of cocaine on Ca-mobility in microsomal fraction from rat vas deferens. Jpn J Pharmacol 1981 Feb;31(1):1-6

Hishida A, Honda N: [Catecholamines and potassium metabolism]
Nippon Rinsho 1981 Feb;39(2):304-9 (29 ref.) (Jpn)

Hjeresen DL, Kaune WT, Decker JR, et al: Effects of 60-Hz electric fields on avoidance behavior and activity of rats.
Bioelectromagnetics 1980;1(3):299-312

Ho K, Lloyd BL, Taylor RR: Cardiac beta-adrenoreceptors in the thyroxine-treated dog. Clin Exp Pharmacol Physiol 1981 Mar-Apr; 8(2):183-7

Ho KJ, Ho LH: Inhibitory effect of bile acids on the activity of human beta-glucuronidase at its optimal pH. Proc Soc Exp Biol Med 1981 Jul;167(3):304-9

Hochberg Z, Weiss J, Richman RA: Inhibin-like activity in extracts of rabbit placentae. Placenta 1981 Jul-Sep;2(3):259-64

Hoehler FK, Sandman CA: Effects of alpha-MSH and beta-endorphin on startle reflex in rat. Peptides (Fayetteville) 1981;2 Suppl 1:137-41

Hoes MJ, Kreutzer EK, Sijben N: Xanthurenic acid excretion in urine after oral intake of 5 grams L-tryptophan by healthy volunteers: standardisation of the reference values. J Clin Chem Clin Biochem 1981 May;19(5):259-64

Hoffman DW, Marchi M, Giacobini E: Norepinephrine uptake in aging adrenergic nerve terminals. Neurobiol Aging 1980 Summer;1(1):65-8

Hoffman EW: Phenytoin-induced interstitial nephritis. South Med J 1981 Sep;74(9):1160-1

Hoffman GE, Sladek JR Jr: Age-related changes in dopamine, LHRH and somatostatin in the rat hypothalamus. Neurobiol Aging 1980 Summer;1(1):27-37

Hofmann W, Herrmann WM, Kubicki S: Die Analyse akustisch evozierter Potentiale. Darstellung eines objektiven, voll automatisierten Auswertungsverfahrens. EEG EMG 1981 Jun;12(2):84-9 (Eng. Abstr.) (Ger)

Hofstein R, Bernett B, Samuel D: The effect of anti-synaptosomal membrane antibodies of neurotransmitter uptake. J Neurochem 1981 Jul;37(1):14-21

Holder AT, Preece MA, Wallis M: Effect of glucocorticoids, butanol extraction of serum and adrenalectomy on somatomedin levels in the rat. J Endocrinol 1981 Sep;90(3):411-20

Holland PJ: Lithium capsule. Am Fam Physician 1981 Sep;24(3):147-8

Hollister LE: Current antidepressant drugs: their clinical use. Drugs 1981 Aug;22(2):129-52 (93 ref.)

Hollister LE, Davis KL, Berger PA: Apomorphine in schizophrenia.
Commun Psychopharmacol 1980;4(4):277-81

Höllt V, Haarmann I, Herz A: Long-term treatment of rats with morphine reduces the activity of messenger ribonucleic acid coding for the beta-endorphin/ACTH precursor in the intermediate pituitary.
J Neurochem 1981 Sep;37(3):619-26

Holt RJ, Gaskins JD: Prescription of neuroleptic drugs by family practice residents [letter] Am J Psychiatry 1981 Aug;138(8):1129

Holzer P, Emson PC, Holzbauer M, et al: Tissue distribution of substance P in the domestic pig during postnatal development. Brain Res 1981 Jun;227(3):455-9

Holzer P, Emson PC, Iversen LL, et al: Regional differences in the response to substance P on the longitudinal muscle and the concentration of substance P in the digestive tract of the guinea-pig.
Neuroscience 1981;6(7):1433-41

Hong WH, Szalczewski DH: Characteristics of equilibrium reaction of zolazepam. J Pharm Sci 1981 Jun;70(6):691-3

Honma T, Sudo A, Miyagawa M, et al: Effects of exposure to trichloroethylene and tetrachloroethylene on the contents of acetylcholine, dopamine, norepinephrine and serotonin in rat brain.
Ind Health 1980;18(4):171-8

Hooley RD, Schams D, Findlay JK: Immunoreactive growth hormone levels during the hormonal induction of lactation and during hand-milking in ewes. J Endocrinol 1981 Jun;89(3):437-42

Hooper WD, Kunze HE, Eadie MJ: Qualitative and quantitative studies of methylphenobarbital metabolism in man. Drug Metab Dispos 1981 Jul-Aug;9(4):381-5

Hooper WD, Kunze HE, Eadie MJ: Simultaneous assay of methylphenobarbital and phenobarbital in plasma using gas chromatography—mass spectrometry with selected ion monitoring.
J Chromatogr 1981 May 8;223(2):426-31

Hopkins SJ: Chlorpromazine: it leaves me cold! Nurs Mirror 1981 Aug 12;153(7):34-5

Hopper K: Right to refuse what? Images, ambiguities and possibilities in Rogers v. Okin. Ann NY Acad Sci 1981;368:137-40

Horáček J, Kadlec O: Endorfiny — nové regulační peptidy.
Cas Lek Cesk 1981 Jun 25;120(25):753-5 (Eng. Abstr.) (Cze)

Horie T, Sugiyama Y, Awazu S, et al: The correlation between drug binding to the human erythrocyte and its hemolytic activity.
J Pharmacobiodyn 1981 Feb;4(2):116-22

Horita A, Carino MA: A comparison of the pharmacological properties of TRH and MK-771. Proc West Pharmacol Soc 1981;24:347-8

Horrocks WD Jr, Snyder AP: Measurement of distance between fluorescent amino acid residues and metal ion binding sites. Quantitation of energy transfer between tryptophan and terbium(III) or europium(III) in thermolysin. Biochem Biophys Res Commun 1981 May 15; 100(1):111-7

Horsthemke B, Knisatschek H, Rivier J, et al: Degradation of luteinizing hormone - releasing hormone and analogs by adenohypophyseal peptidases. Biochem Biophys Res Commun 1981 May 29;100(2):753-9

Hosford DA, Haigler HJ, Turner RS: Methionine-enkephalin and morphine: amount ejected microiontophoretically.
J Neurosci Methods 1981 Aug;4(2):135-9

Hösli L, Hösli E, Zehntner C, et al: Effects of substance P on neurones and glial cells in cultured rat spinal cord. Neurosci Lett 1981 Jul 2; 24(2):165-8

Hubbard JW, Bailey K, Midha KK, et al:
3-O-methyl-alpha-methyldopamine, a urinary metabolite of p-methoxyamphetamine in dog and monkey. Drug Metab Dispos 1981 May-Jun;9(3):250-4

Hue L, Blackmore PF, Exton JH: Fructose 2,6-bisphosphate. Hormonal regulation and mechanism of its formation in liver. J Biol Chem 1981 Sep 10;256(17):8900-3

Huet PM, Pomier-Layrargues G, Duguay L, et al: Blood-brain transport of tryptophan and phenylalanine: effect of portacaval shunt in dogs. Am J Physiol 1981 Aug;241(2):G163-9

Hughes CL Jr, Everett JW, Tyrey L: Delta 9-tetrahydrocannabinol suppression of prolactin secretion in the rat: lack of direct pituitary effect. Endocrinology 1981 Sep;109(3):876-80

Huhtaniemi IT, Catt KJ: Induction and maintenance of gonadotropin and lactogen receptors in hypoprolactinemic rats. Endocrinology 1981 Aug;

AUTHOR SECTION

109(2):483-90

Huizer H, Theeuwen AB, Verweij AM, et al: Impurities in illicit amphetamine. J Forensic Sci Soc 1981 Jul;21(3):225-32

Huland H, Augustin HJ, Baumgarten HG, et al: Effect of dopamine on renal haemodynamics in the denervated dog kidney. Urol Res 1981 Mar 17;9(1):5-11

Hullin DA, Elder GH, Laurence KM, et al: Amniotic fluid cholinesterase measurement as a rapid method for the exclusion of fetal neural tube defects. Lancet 1981 Aug 15;2(8242):325-7

Hume J, Katzung BG: Physiological role of endogenous amines in the modulation of ventricular automaticity in the guinea-pig.
J Physiol (Lond) 1980 Dec;309:275-86

Hunter T, Cooper JA: Epidermal growth factor induces rapid tyrosine phosphorylation of proteins in A431 human tumor cells. Cell 1981 Jun; 24(3):741-52

Huot S, Robin M, Palfreyman MG: Effect of gamma-vinyl GABA alone or associated with diazepam on a conflict test in the rat.
Adv Biochem Psychopharmacol 1981;29:45-52

Huston G, Martin VI, Al-Dujaili EA, et al: Evaluation of the mineralocorticoid activity of 18-hydroxycorticosterone. Clin Sci 1981 Aug;61(2):201-6

Hwu HG, Ardekani AB, Helzer JE: A longitudinal record study of renal function in patients treated with lithium. J Affective Disord 1981 Jun; 3(2):101-9

Hylden JL, Wilcox GL: Intrathecal substance P elicits a caudally-directed biting and scratching behavior in mice. Brain Res 1981 Jul 27; 217(1):212-5

Hynes MD, Lal H: Chronic haloperidol treatment fails to alter the anorexic actions of dopaminergic agonists and cholinergic drugs.
Prog Neuropsychopharmacol 1981;5(3):271-5

I

Iakhnitsa IA, Bulgakova NV, Piliavskiĭ AI: Vliianie veshchestv, potentsiruiushchikh ili ugnetaiushchikh aktivnost' neironov golubogo piatna, na nekotorye vidy spinal'nogo tormozheniia u koshki.
Neirofiziologiia 1981;13(3):247-58 (Eng. Abstr.) **(Rus)**

Idova GV, Cheido MA: Uchastie razlichnykh kletochnykh populiatsiĭ v immunnom otvete (IgM i IgG) pri deistvii biogennogo amina serotonina. Vestn Akad Med Nauk SSSR 1981;(5):39-41 (Eng. Abstr.) **(Rus)**

Ikeda F, Kono T, Oseko F, et al: Effects of diltiazem hydrochloride on pressor and steroidogenic actions of angiotensins and norepinephrine in man. Endocrinol Jpn 1980 Dec;27(6):779-84

Iliopoulou A, Kaspi T, Blackett A, et al: Clinical pharmacological studies with LM 5008, a new antidepressant. Pharmatherapeutica 1981; 2(9):613-21

Imamoto K, Nagai T, Kimura H, et al: Effect of neonatal administrations of 6-OHDA on the brain development. I. Alteration in the striatum. Arch Histol Jpn 1980 Oct;43(4):347-64

Imandt L, Tijhuis D, Wessels H, et al: Lithium inhibits adenylate cyclase of human platelets. Thromb Haemost 1981 Apr 30;45(2):142-5

Imperato A, Porceddu ML, Morelli M, et al: Role of dorsal mesencephalic reticular formation and deep layers of superior colliculus as out-put stations for turning behaviour elicited from the substantia nigra pars reticulata. Brain Res 1981 Jul 20;216(2):437-43

Imura H, Nakai Y, Nakao K, et al: [ACTH, endorphins and related peptides (author's transl)] Tanpakushitsu Kakusan Koso 1981 Feb; 26(2):90-101 (56 ref.) **(Jpn)**

Ingram DK, London ED, Goodrick CL: Age and neurochemical correlates of radial maze performance in rats. Neurobiol Aging 1981 Spring; 2(1):41-7

Inoue K, Mizokami K, Sunouchi M, et al: [Development of hexobarbital radiometry and its application (author's transl)]
Eisei Shikenjo Hokoku 1980;98:56-62 (Eng. Abstr.) **(Jpn)**

Inoue M, Shibata M, Kondo Y, et al: Role of tryptophanyl and tyrosyl residues of flavoproteins in binding with flavin coenzymes. X-ray structural studies using model complexes. Biochemistry 1981 May; 20(10):2936-45

Irwin M, Belendiuk K, McCloskey K, et al: Tryptophan metabolism in children with attentional deficit disorder. Am J Psychiatry 1981 Aug; 138(8):1082-5

Isberg RS: A comparison of phenelzine and imipramine in an obsessive-compulsive patient. Am J Psychiatry 1981 Sep;138(9):1250-1

Ishigooka J, Tanaka K, Suzuki Y, et al: Selective inhibitory effects of chlorpromazine and imipramine on platelet aggregation.
Int Pharmacopsychiatry 1980;15(5):270-80

Ismailov AD, Baranova NA, Danilov VS, et al: Ingibirovanie bakterial'noi liuminestsentsii substratami tsitokhroma P-450. Biokhimiia 1981 Feb; 46(2):234-9 (Eng. Abstr.) **(Rus)**

Israël M, Manaranche R, Morel N, et al: Redistribution of intramembrane particles related to acetylcholine release by cholinergic synaptosomes. J Ultrastruct Res 1981 May;75(2):162-78

Ito S, Iwanaga T, Yamada Y, et al: Immunohistological demonstration of ACTH-like immunoreactivity in the foetal adrenal medulla in the 23rd week of gestation. Acta Endocrinol (Copenh) 1981;97(3):412-8

Ito Y, Kitamura K, Kuriyama H: Nitroglycerine and catecholamine actions on smooth muscle cells of the canine coronary artery.
J Physiol (Lond) 1980 Dec;309:171-83

Itoh M, Mizukoshi H, Fuke K, et al: Tryptophan fluorescence of human hemoglobin. I. Significant change of fluorescence intensity and lifetimes in the T - R transition. Biochem Biophys Res Commun 1981 Jun 16; 100(3):1259-65

Itoh Z, Aizawa I, Nakamura T: [Effect of dopamine and its antagonists on contractile activity of the lower esophageal sphincter and the stomach (author's transl)] Nippon Heikatsukin Gakkai Zasshi 1980 Jun; 16(2):99-107 (Eng. Abstr.) **(Jpn)**

Iwamoto ET: Studies on axonal transport in dopaminergic neurons: effect of neuropharmacologic lesions. Life Sci 1981 May 11;28(19):2179-86

Izumikawa F: Release mechanisms of 5-HT from the gastrointestinal tract in rats. Nippon Geka Hokan 1980 Sep 1;49(5):572-94

J

Jackman GP, McLean AJ, Jennings GL, et al: No stereoselective first-pass hepatic extraction of propranolol. Clin Pharmacol Ther 1981 Sep; 30(3):291-6

Jackson IM: Evolutionary significance of the phylogenetic distribution of the mammalian hypothalamic releasing hormones. Fed Proc 1981 Sep;40(11):2545-52

Jacobi JM, Lloyd HM: Modulation by dopamine antagonists of DNA synthesis in the pituitary gland of the male rat. Neuroendocrinology 1981 Aug;33(2):97-100

Jagiello-Wójtowicz E: Central action of phenylethylamine in rats.
Pol J Pharmacol Pharm 1981 Jan-Feb;33(1):59-71

Jagiello-Wójtowicz E: Central action of adrenaline. Acta Physiol Pol 1981 Mar-Apr;32(2):169-80

Jahnke GD, Lazarus LH, DiAugustine RP, et al: Peptide hormone degradation by a rat mast cell chymase-heparin complex. Life Sci 1981 Jul 27;29(4):397-403

Jain VK: Phototransfer, sensitization and re-estimation of dose in lithium fluoride TLD. Health Phys 1981 Aug;41(2):363-70

Jakobs KH, Aktories K, Schultz G: Inhibition of adenylate cyclase by hormones and neurotransmitters. Adv Cyclic Nucleotide Res 1981; 14:173-87

Jambart S, Draoui F, Hamon P, et al: Interférence du méprobamate avec le dosage des hormones cortico-surrénales. Nouv Presse Med 1981 May 2;10(20):1643-4 (Eng. Abstr.) **(Fre)**

James MO, Little PJ: Polyhalogenated biphenyls and phenobarbital: evaluation as inducers of drug metabolizing enzymes in the sheepshead, Archosargus probatocephalus. Chem Biol Interact 1981 Aug; 36(2):229-48

James R, Küpfer A, Villeneuve JP, et al: Induction of drug-metabolizing enzymes by the enantiomers of normephenytoin in the rat.
Drug Metab Dispos 1981 May-Jun;9(3):297-302

Jan LY, Jan YN: Role of an LHRH-like peptide as a neurotransmitter is sympathetic ganglia of the frog. Fed Proc 1981 Sep;40(11):2560-4

Al-Janabi II, Anber SA, Fikrat HT: In vitro detection of possible in vivo drug interactions. Part 2: A study of the effect of hydrochlorothiazide and frusemide on the partition coefficient and solubility characteristics of propranolol hydrochloride. Pharmazie 1981;36(7):485-8

Janicki P, Szreniawski Z: Effect of estazolam on the caudate spindle in the cat. Act Nerv Super (Praha) 1981 Jun;23(2):172-3

Janiec W, Pytlik M, Piekarska T: The influence of psychotropic drugs on the phosphodiesterase activity in the rat brain meninges.
Pol J Pharmacol Pharm 1980 May-Jun;32(3):297-303

Jankowski A, Siemion IZ, Szewczuk Z: The investigation of [(4'-amino)-PHE]4-enkephalin conformation in water by the spectrofluorimetric procedure. Acta Biochim Pol 1981;28(1):11-20

Janssens LA: De behandeling van schijndracht bij de teef met bromocriptine (Parlodel). Tijdschr Diergeneeskd 1981 Aug 1; 106(15):767-70 (Eng. Abstr.) **(Dut)**

Järbe TU: Cocaine cue in pigeons: time course studies and generalization to structurally related compounds (norcocaine, WIN 35,428 and 35,065-2) and (+)-amphetamine. Br J Pharmacol 1981 Aug; 73(4):843-52

Javaid JI, Davis JM: GLC analysis of phenylalkyl amines using nitrogen detector. J Pharm Sci 1981 Jul;70(7):813-5

Jeftinija S, Semba K, Randic M: Norepinephrine reduces excitability of single cutaneous primary afferent C-fibers in the cat spinal cord.
Brain Res 1981 Aug 31;219(2):456-63

Jenike MA: Rapid response of severe obsessive-compulsive disorder to tranylcypromine. Am J Psychiatry 1981 Sep;138(9):1249-50

Jimerson DC, Markey SP, Oliver JA, et al: Simultaneous measurement of plasma 4-hydroxy-3-methoxyphenylethylene glycol and
3,4-dihydroxyphenylethylene glycol by gas chromatography mass spectrometry. Biomed Mass Spectrom 1981 Jun;8(6):256-9

Jochemsen R, Breimer DD: Assay of triazolam in plasma by capillary gas chromatography. J Chromatogr 1981 May 8;223(2):438-44

Johnson AL, Hollister LE, Berger PA: The anticholinergic intoxication syndrome: diagnosis and treatment. J Clin Psychiatry 1981 Aug;

AUTHOR SECTION

42(8):313-7

Johnson FN: John F.J. Cade, 1912 to 1980: a reminiscence. Pharmacopsychiatria 1981 Jul;14(4):148-9

Johnson JH, Davis CL: Increased pituitary sensitivity to luteinizing hormone releasing hormone at puberty: an event of proestrus. Proc Soc Exp Biol Med 1981 Jul;167(3):434-7

Johnson LC, Spinweber CL: Effect of a short-acting benzodiazepine on brain electrical activity during sleep. Electroencephalogr Clin Neurophysiol 1981 Jul;52(1):89-97

Jones GL, Amato RJ, Wimbish GH, et al: Comparison of anticonvulsant potencies of cyheptamide, carbamazepine, and phenytoin. J Pharm Sci 1981 Jun;70(6):618-20

Jones PB, Hsueh AJ: Direct effects of gonadotropin releasing hormone and its antagonist upon ovarian functions stimulated by FSH, prolactin, ans LH. Biol Reprod 1981 May;24(4):747-59

Jones RC: The fate of conceptuses in rats receiving an intrauterine injection of luteinizing hormone-releasing hormone (LRH) prior to implantation. Int J Fertil 1981;26(2):120-3

Joseph JA, Filburn CR, Roth GS: Development of dopamine receptor denervation supersensitivity in the neostriatum of the senescent rat. Life Sci 1981 Aug 10;29(6):575-84

Joseph SA, Piekut DT, Knigge KM: Immunocytochemical localization of luteinizing hormone-releasing hormone (LHRH) in Vibratome-sectioned brain. J Histochem Cytochem 1981 Feb; 29(2):247-54

Joshi VV, Balsara JJ, Jadhav JH, et al: Effect of L-histidine and chlorcyclizine on apomorphine-induced climbing behaviour and methamphetamine stereotypy in mice. Eur J Pharmacol 1981 Feb 19; 69(4):499-502

Joyce JN, Davis RE, Van Hartesveldt C: Behavioral effects of unilateral dopamine injection into dorsal or ventral striatum. Eur J Pharmacol 1981 Jun 10;72(1):1-10

Jurkowlaniec E, Bialowąs J: Rewarding effect of noradrenergic stimulation of the amygdala in food deprived rats. Physiol Behav 1981 Jul;27(1):27-31

Jutisz M, Kraicer J, Ribot G: Characterization of corticotropin-releasing factor activity from sheep hypothalamic extracts. Life Sci 1981 Jun 15;28(24):2761-8

K

Kabes J, Balon R, Papežová H: Výsledky klinického zkoušeni nomifensinu. Cesk Psychiatr 1981 Feb;77(1):42-9 (Eng. Abstr.) (Cze)

Kabes J, Dostal T, Náhunek K, et al: Multicentre study with viloxazine (Vivalan) in depressed patients. Int Pharmacopsychiatry 1980; 15(4):228-39

Kachi T, Banerji TK, Quay WB: The invagination complex in nerve endings on adrenomedullary adrenaline cells: quantitative ultrastructural description, and analysis of changes with time-of-day and their modification by sham-surgery and pinealectomy. J Auton Nerv Syst 1980 Oct;2(3):241-58

Kadir HA, Knowles CO: Inhibition of rat brain monoamine oxidase by insecticides, acaricides and related compounds. Gen Pharmacol 1981; 12(4):239-47

Käiväräinen AI, Rozhkov SP, Sykulev YuK, et al: Hapten-induced changes in pig anti-dansyl antibodies revealed by EPR spectra of spin-labelled antibodies. Immunol Lett 1981 Apr;3(1):5-11

Kaiya H, Tamura Y, Adachi S, et al: Substance P-like immunoreactivity in plasma of psychotic patients and effects of neuroleptics and electroconvulsive therapy. Psychiatry Res 1981 Aug;5(1):11-21

Kalandarov S, Bychkov VP, Frenkel' ID, et al: O vozmozhnosti ispol'zovaniia alimentarnykh sredtsv dlia korrektsii adrenokortikal'noĭ sistemy. Kosm Biol Aviakosm Med 1981 Jun-Jul;15(4):19-22 (Eng. Abstr.) (Rus)

Kalivas PW, Horita A: Neuroanatomical dissociation of thyrotropin-releasing hormone induced shaking behavior and thermogenic mechanisms. Regul Pept 1981 Feb;1(5):335-45

Kalix P: Cathinone, an alkaloid from khat leaves with an amphetamine-like releasing effect. Psychopharmacology (Berlin) 1981; 74(3):269-70

Kalliecharan R: The influence of exogenous ACTH on the levels of corticosterone and cortisol in the plasma of young chicks (Gallus domesticus). Gen Comp Endocrinol 1981 Jun;44(2):249-51

Kalra PS, Simpkins JW, Kalra SP: Hyperprolactinemia counteracts the testosterone-induced inhibition of the preoptic area dopamine turnover. Neuroendocrinology 1981 Aug;33(2):118-22

Kalra SP, Chen CL, Kumar MS: Differential response to methionine-enkephalin in basal hypothalamus and preoptic area following hypothalamic deafferentation. Brain Res 1981 Jun 29; 215(1-2):410-3

Kamase H: The diurnal variations of monoamine oxidase activity in discrete nuclei of rat brain. Folia Psychiatr Neurol Jpn 1980; 34(4):481-92

Kameyama T, Ukai M: Multi-dimensional analyses of behavior in mice treated with alpha-endorphin. Neuropharmacology 1981 Mar; 20(3):247-50

Kamiya H, Takano Y, Sakurai Y, et al: Effect of imipramine on high potassium evoked 3H-dopamine release in the rat striatum. Res Commun Chem Pathol Pharmacol 1981 Jul;33(1):49-60

Kammerer RC, Schmitz DA, Distefano EW, et al: The metabolism of phencyclidine by rabbit liver preparations. Drug Metab Dispos 1981 May-Jun;9(3):274-8

Kan JP, Strolin Benedetti M: Characteristics of the inhibition of rat brain monoamine oxidase in vitro by MD780515. J Neurochem 1981 Apr; 36(4):1561-71

Kandasamy SB, Kirlin WG, Kaul PN: Prostacyclin-induced hypothermia: involvement of central histamine H2-receptors. Life Sci 1981 Jun 1; 28(22):2553-60

Kaneno S, Shimazono Y: Decreased in vivo [3H]spiroperidol binding in rat brain after repeated methamphetamine administration. Eur J Pharmacol 1981 Jun 10;72(1):101-5

Kang ES, Gates RE: Direct phosphorylation effects of epinephrine on the plasma membranes of intact rat fat cells. Dev Pharmacol Ther 1981; 2(1):55-66

Kanner BI, Kifer L: Efflux of gamma-aminobutyric acid by synaptic plasma membrane vesicles isolated from rat brain. Biochemistry 1981 Jun 9;20(12):3354-8

Kanter KR, Jaffin JH, Ehrlichman RJ, et al: Superiority of perfluorocarbon cardioplegia over blood or crystalloid cardioplegia. Circulation 1981 Aug;64(2 Pt 2):75-80

Kanter KR, Flaherty JT, Bulkley BH, et al: Beneficial effects of adding propranolol to multidose potassium cardioplegia. Circulation 1981 Aug; 64(2 Pt 2):84-90

Kao KJ, Sommer JR, Pizzo SV: Modulation of platelet shape and membrane receptor binding by Ca2+-calmodulin complex. Nature 1981 Jul 2;292(5818):82-4

Kapatos G, Kaufman S, Weller JL, et al: Biosynthesis of biopterin: adrenergic cyclic adenosine monophosphate-dependent inhibition in the pineal gland. Science 1981 Sep 4;213(4512):1129-31

Kapetanovic IM, Kupferberg HJ: Inhibition of microsomal phenobarbital metabolism by valproic acid. Biochem Pharmacol 1981 Jun 1; 30(11):1361-3

Kaplan KL, Dauzier MJ, Rose S: ADP and epinephrine-induced release of platelet fibrinogen. Blood 1981 Oct;58(4):797-802

Kapp W: Pharmakologische und toxikologische Aspekte zu Benzodiazepinen. Anaesth Intensivther Notfallmed 1981 Jun;16(3):125-7 (Eng. Abstr.) (Ger)

Karacan I, Orr W, Roth T, et al: Dose-related effects of flurazepam on human sleep-walking patterns. Psychopharmacology (Berlin) 1981; 73(4):332-9

Karashima T: Isoprenaline- and noradrenaline-induced hyperpolarization of guinea-pig liver cells. Br J Pharmacol 1981 Aug;73(4):867-77

Karczmar AG, Kindel GH: Acetylcholine turnover and aggression in related three strains of mice. Prog Neuropsychopharmacol 1981; 5(1):35-48

Karelson EI, Tarve US, Tiakhepyl'd LIa: Vliianie psikhotropnykh sredstv na Ca-aktiviruemye ATF-azy mozga in vitro. Biull Eksp Biol Med 1981 May;91(5):576-8 (Eng. Abstr.) (Rus)

Karlish SJ, Pick U: Sidedness of the effects of sodium and potassium ions on the conformational state of the sodium-potassium pump. J Physiol (Lond) 1981 Mar;312:505-29

Karoum F, Chuang LW, Wyatt RJ: On the enzymatic hydrolysis of the sulfate conjugate of 3-methoxy-4-hydroxyphenylglycol (MHPG). Biochem Med 1980 Dec;24(3):314-20

Karplus M, Gelin BR, McCammon JA: Internal dynamics of proteins. Short time and long time motions of aromatic sidechains in PTI. Biophys J 1980;32(1):603-18

Karson C, Freed WJ, Kleinman JE, et al: Neuroleptics decrease blinking in schizophrenic subjects. Biol Psychiatry 1981 Jul;16(7):679-82

Kashparov IA, Semisotnov GV, Alakhov IuB: Svoĭstva i rol' ostatkov triptofana polipeptidnoĭ tsepi faktora élongatsii G E. coli. Biokhimiia 1981;46(8):1488-98 (Eng. Abstr.) (Rus)

Kassil' VG, Makukhina GV: Vozrastnye i polovye osobennosti vyrabotki i sokhraneniia uslovnoreflektornoĭ vkusovoĭ aversii u krys. Zh Vyssh Nerv Deiat 1981 May-Jun;31(3):630-2 (Rus)

Kateyama Y, Miyazaki S, Tsubokawa T: Electrophysiological evidence favoring intracaudate axon collaterals of GABAergic caudate output neurons in the cat. Brain Res 1981 Jul 6;216(1):180-6

Kather H, Simon B: Stimulatory and inhibitory effects of catecholamines and of prostaglandin E2 on human fat cell adenylate cyclase. Adv Cyclic Nucleotide Res 1981;14:555-62

Katharia SP, Sunta CM: Thermal quenching by phototransfer in LiF TLD-100. Phys Med Biol 1981 Jul;26(4):707-10

Kato Y, Kohketsu M: Relationship between polymorphism and bioavailability of amorbarbital in the rabbit. Chem Pharm Bull (Tokyo) 1981 Jan;29(1):268-72

Katon W, Williamson P, Ries R: A prospective study of 60 consecutive psychiatric consultations in a family medicine clinic. J Fam Pract 1981 Jul;13(1):47-56

Katz AM: Role of phosphorylation of the sarcoplasmic reticulum in the cardiac response to catecholamines. Eur Heart J 1980;Suppl A:29-33

AUTHOR SECTION

(23 ref.)

Katz B, Miledi R: Does the motor nerve impulse evoke 'non-quantal' transmitter release? Proc R Soc Lond [Biol] 1981 May 7;212(1186):131-7

Katz IR: Interaction between the oxygen and tryptophan dependence of synaptosomal tryptophan hydroxylase. J Neurochem 1981 Aug; 37(2):447-51

Katz RJ, Roth KA, Schmaltz K: Amphetamine and tranylcypromine in an animal model of depression: pharmacological specificity of the reversal effect. Neurosci Biobehav Rev 1981 Summer;5(2):259-64

Katz RJ, Hersh S: Amitriptyline and scopolamine in an animal model of depression. Neurosci Biobehav Rev 1981 Summer;5(2):265-71

Katz RJ: Animal models and human depressive disorders. Neurosci Biobehav Rev 1981 Summer;5(2):231-46 (243 ref.)

Katz RJ: The temporal structure of motivation IV: A reexamination of extinction effects in intracranial reward. Behav Neural Biol 1981 Jun; 32(2):191-200

Katz RJ: Animal model of depression: effects of electroconvulsive shock therapy. Neurosci Biobehav Rev 1981 Summer;5(2):273-7

Kaufman RA, Tietz NW: Ion effects in measurement of ionized calcium with a calcium-selective electrode. Clin Chem 1980 Apr;26(5):640-4

Kaulhausen H, Oney T, Feldmann R, et al: Decrease of vascular angiotensin sensitivity by L-dopa during human pregnancy. Am J Obstet Gynecol 1981 Jul 15;140(6):671-5

Keeler R: Effects of methysergide or phenoxybenzamine on the renal and cardiovascular responses to endotoxin in rats. Circ Shock 1981; 8(3):361-8

Kellar KJ, Cascio CS, Butler JA, et al: Differential effects of electroconvulsive shock and antidepressant drugs on serotonin-2 receptors in rat brain. Eur J Pharmacol 1981 Feb 19;69(4):515-8

Kelly MJ: An analysis of the effects of apomorphine and haloperidol on the release of [3H]-dopamine and [3H]-noradrenaline from rabbit brain slices. Arch Int Pharmacodyn Ther 1981 Mar;250(1):18-29

Kempf E, Mandel P: Reverse-phase high-performance liquid chromatographic separation and electrochemical detection of norepinephrine, dopamine, serotonin, and related major metabolites. Anal Biochem 1981 Apr;112(2):223-31

Kendler KS, Heninger GR, Roth RH: Brain contribution to the haloperidol-induced increase in plasma homovanillic acid. Eur J Pharmacol 1981 May 8;71(2-3):321-6

Kennedy JM, McNamara PE: High-performance liquid chromatographic analysis of pilocarpine hydrochloride, isopilocarpine, pilocarpic acid and isopilocarpic acid in eye-drop preparations. J Chromatogr 1981 Aug 7;212(3):331-8

Keri G, Parameswaran V, Trunkey DD, et al: Effects of septic shock plasma on adrenocortical cell function. Life Sci 1981 Apr 27;28(17):1917-23

Kern HL, Zulch GD: Dependence on Na+ of kinetics of the lenticular Na+, K+-activated ATPase. Exp Eye Res 1981 Jun;32(6):789-92

Kérouac R, Rioux F, St-Pierre S: Mechanism of neurotensin-induced pressor effect and tachycardia in guinea pigs. Life Sci 1981 Jun 1; 28(22):2477-87

Kerry RJ: Practical guide-lines of lithium prophylaxis. Bibl Psychiatr 1981;(161):197-205

Kersten L: Toxicity and renal elimination of lithium in rats of different ages. Arch Toxicol 1981 Apr;47(2):135-44

Keshavan HJ, Gurbani NK, Dandiya PC: Effects of fluoxetine on a specific serotonergic syndrome in rats. Indian J Med Res 1981 Apr;73:653-7

Keshavan HJ, Gurbani NK, Dandiya PC: Effects of fluoxetine on a specific serotonergic syndrome in rats. Indian J Med Res 1981 Apr;73:653-7

Kessler JA, Adler JE, Bohn MC, et al: Substance P in principal sympathetic neurons: regulation by impulse activity. Science 1981 Oct 16;214(4518):335-6

Kewley CF, Millar RP, Berman MC, et al: Depolarization- and ionophore-induced release of octacosa somatostatin from stalk median eminence synaptosomes. Science 1981 Aug 21;213(4510):913-5

Khamidullina AKh, Grebneva GV: Kholinergicheskie sdvigi i nibufinoterapiia pri pishchevoĭ allergii u deteĭ. Pediatriia 1981 Apr; (4):51-3 (Eng. Abstr.) **(Rus)**

Khan A, Hornblow AR, Walshe JW: Benzodiazepine dependence: a general practice survey. NZ Med J 1981 Jul 8;93(687):19-21

Khan MC: Lithium carbonate in the treatment of acute depressive illness. Bibl Psychiatr 1981;(161):244-8

Kida T, Ueha T, Nemoto A, et al: [Histochemical localization of Na+, K+-ATPase in rat submandibular gland. The effects of mineralocorticoid and sodium ion (author's transl)] Josai Shika Daigaku Kiyo 1980;(9):155-8 (Eng. Abstr.) **(Jpn)**

Kikta DC, Threatte RM, Barney CC, et al: Peripheral conversion of L-5-hydroxytryptophan to serotonin induces drinking in rats. Pharmacol Biochem Behav 1981 Jun;14(6):889-93

Kikuchi H, Suzuki Y, Hashimoto Y: Increase of beta-glucuronidase activity in the serum of rats administered organophosphate and carbamate insecticides. J Toxicol Sci 1981 Feb;6(1):27-35

Kilpatrick IC, Starr MS: Involvement of dopamine in circling responses to muscimol depends on intranigral site of injection. Eur J Pharmacol 1981 Feb 19;69(4):407-19

Kilts CD, Commissaris kL, Rech RH: Comparison of anti-conflict drug effects in three experimental animal models of anxiety. Psychopharmacology (Berlin) 1981;74(3):290-6

Kim DH, Akera T, Brody TM: Tissue binding sites involved in quinidine-cardiac glycoside interactions. J Pharmacol Exp Ther 1981 Aug;218(2):357-62

Kim JS, Kornhuber HH, Brand U, et al: Effects of chronic amphetamine treatment on the glutamate concentration in cerebrospinal fluid and brain: implications for a theory of schizophrenia. Neurosci Lett 1981 Jun 12;24(1):93-6

Kimura S, Koide Y, Tada R, et al: Inhibitory effect on calcium channel blockers on alpha -adrenergic activation of glycogenolysis and calcium efflux in perfused rat liver. Endocrinol Jpn 1981 Feb;28(1):69-78

Kimura S: [Chemical studies of enkephalin precursors in adrenal medulla (author's transl)] Tanpakushitsu Kakusan Koso 1981 Feb;26(2):125-37 (67 ref.) **(Jpn)**

Kinney EL, Moskowitz RM, Zelis R: The pharmacokinetics and pharmacology of oral diltiazem in normal volunteers. J Clin Pharmacol 1981 Aug-Sep;21(8-9):337-42

Kinniburgh DW, Boyd ND: Isolation of peptides from uremic plasma that inhibit phenytoin binding to normal plasma proteins. Clin Pharmacol Ther 1981 Aug;30(2):276-80

Kinsey RA, Kintanar A, Oldfield E: Dynamics of amino acid side chains in membrane proteins by high field solid state deuterium nuclear magnetic resonance spectroscopy. Phenylalanine, tyrosine, and tryptophan. J Biol Chem 1981 Sep 10;256(17):9028-36

Kirby AW, Schweitzer-Tong DE: GABA-antagonists and spatial summation in Y-type cat retinal ganglion cells. J Physiol (Lond) 1981 Mar;312:335-44

Kirch W, Köhler H, Spahn H, et al: Interaction of cimetidine with metoprolol, propranolol, or atenolol [letter] Lancet 1981 Sep 5; 2(8245):531-2

Kirkland SC, Ellison ML: Studies on the corticotrophin releasing activity of a posterior pituitary extract. J Endocrinol 1981 Jun;89(3):423-9

Kiselev VI, Ryzhkov AA, Panchenko AL: Rol' kallikrein-kininovoĭ sistemy v realizatsii gemodinamicheskikh éffektov katekholaminov. Fiziol Zh SSSR 1981 Apr;67(4):561-7 (Eng. Abstr.) **(Rus)**

Kiso Y, Yamaguchi M, Akita T, et al: Super-active enkephalin analogues. Simple tripeptide hydroxyalkylamides exhibit surprisingly high and long-lasting opioid activities. Naturwissenschaften 1981 Apr;68(4):210-2

Kitada Y, Miyauchi T, Satoh A, et al: Effects of antidepressants in the rat forced swimming test. Eur J Pharmacol 1981 Jun 19;72(2-3):145-52

Kitahama K, Valatx JL, Jouvet M: Paradoxical sleep deprivation and performance of an active avoidance task: impairment of c57BR mice and no effect in c57BL/6 mice. Physiol Behav 1981 Jul;27(1):41-50

Kitis G: Influence of cimetidine on pharmacokinetics of propranolol [letter] Br Med J [Clin Res] 1981 Jul 25;283(6286):309

Kitsikis A, Roberge AG: Changes in brain biogenic amines in cats performing a symmetrically reinforced go-nogo visual discrimination task. Behav Neural Biol 1981 Jun;32(2):133-47

Kleinrok AT, Zaczkiewicz A, Tomaszewski A, et al: The influence of taurine on acetylcholine content and synthesis in rat brain. Pol J Pharmacol Pharm 1980 May-Jun;32(3):313-7

Kleinrok Z, Kolasa K, Szurska G: Preliminary studies on the central action of new 1,5-benzodiazepine derivatives. Pol J Pharmacol Pharm 1980 May-Jun;32(3):247-60

Kleinrok Z, Turski L, Wawrzyniak M, et al: The locomotor and exploratory activities in rats after lesion of hippocampal pyramidal cells with kainic acid. Pol J Pharmacol Pharm 1980;32(5):625-37

Klemes Y, Etlinger JD, Goldberg AL: Properties of abnormal proteins degraded rapidly in reticulocytes. Intracellular aggregation of the globin molecules prior to hydrolysis. J Biol Chem 1981 Aug 25;256(16):8436-44

Klemparskaia NN, Tiurin EA, Ivanov AA, et al: Immunobiologicheskaia reaktsiia loshadeĭ na gemostimuliatsiiu. Zh Mikrobiol Epidemiol Immunobiol 1981 Apr;(4):104 **(Rus)**

Klerman GL: Depression in the medically ill. Psychiatr Clin North Am 1981 Aug;4(2):301-17

Kliachko S, Zor U: Increase in catecholamine-stimulated cyclic AMP and progesterone synthesis in rat granulosa cells during culture. Mol Cell Endocrinol 1981 Jul;23(1):23-32

Klinke R: Neurotransmitters in the cochlea and the cochlear nucleus. Acta Otolaryngol (Stockh) 1981 May-Jun;91(5-6):541-54 (88 ref.)

Kluwe WM, Hook JB: Comparative induction of xenobiotic metabolism in rodent kidney, testis and liver by commercial mixtures of polybrominated biphenyls and polychlorinated biphenyls, phenobarbital and 3-methylcholanthrene: absolute and temporal effects. Toxicology 1981;20(2-3):259-73

Knapp FW, Herald F: Face fly and horn fly reduction on cattle with fenvalerate ear tags. J Econ Entomol 1981 Jun;74(3):295-6

Knight PG, Gladwell RT, Cunningham FJ: Effect of gonadectomy on the concentrations of catecholamines in discrete areas of the diencephalon of the domestic fowl. J Endocrinol 1981 Jun;89(3):389-97

Knittel JJ, Makriyannis A: Studies on phenethylamine hallucinogens. 2. Conformations of arylmethoxyl groups using 13C NMR. J Med Chem 1981 Jul;24(7):906-9

Knobel M, Karniol IG, Strauss L: L-dopa and treatment of hyperactive children. Acta Paedopsychiatr (Basel) 1981 May;47(1):27-31

Knouse BF: Comment on phenytoin dosage [letter]

AUTHOR SECTION

Drug Intell Clin Pharm 1981 Mar;15(3):215

Knudtzon J: Thyrotropin-releasing hormone increases plasma levels of glucagon, insulin, glucose and free fatty acids in rabbits. Horm Metab Res 1981 Jul;13(7):371-5

Kobayashi S, Sekino J, Honda K, et al: Application of high-performance liquid chromatography with a chemiluminescence detection system to determine catecholamines in urine. Anal Biochem 1981 Mar 15; 112(1):99-104

Kochevar KE: Phototoxicity mechanisms: chlorpromazine photosensitized damage to DNA and cell membranes. J Invest Dermatol 1981 Jul; 77(1):59-64

Koella WP: GABA systems and behavior. Adv Biochem Psychopharmacol 1981;29:11-21 (32 ref.)

Koerner JF, Cotman CW: Micromolar L-2-amino-4-phosphonobutyric acid selectively inhibits perforant path synapses from lateral entorhinal cortex. Brain Res 1981 Jul 6;216(1):192-8

Kofler R, Tabarelli M, Berger P, et al: In vivo studies on prolactin function in the female rat: divergent effects of treatment with bromergocryptine and antisera to rat prolactin. J Reprod Immunol 1981 Sep;3(4):219-25

Koiter TR, Pols-Valkhof N, Schuiling GA: Effect of oestrogen on the responsiveness of the pituitary gland to LRH: the role of corpora lutea. Acta Endocrinol (Copenh) 1981 Sep;98(1):29-35

Koiwaya Y, Ashihara T, Nakamura M, et al: Plasma concentration of diltiazem after oral administration in normal volunteers. Clin Ther 1981; 3(6):436-40

Kölle EU: Zur Pharmokokinetik nach oraler Gabe von Prazepam. Fortschr Med 1981 Jun 11;99(22):874-9 (Eng. Abstr.) (Ger)

Kolta MG, Soliman KF: Tissue distribution of 3H-corticosterone in response to stress. Endokrinologie 1981 Apr;77(2):179-84

Kondo K, Suzuki H, Handa M, et al: Effects of intracerebroventricular administration of dopamine and metoclopramide on blood pressure in rats. Arch Int Pharmacodyn Ther 1981 Apr;250(2):273-8

König P, Schneider H: Stand der Lithiumbehandlung in Osterreich. Bibl Psychiatr 1981;(161):206-220 (Eng. Abstr.) (Ger)

Konno T, Kakita A, Taira T, et al: Maintenance of rat liver viability enhanced by cold flushing with oxygenated perfluorochemicals. Jpn J Surg 1981;11(3):209-13

Kono T, Ichinoe K, Nakajo S: Effects of ageing and gonadal steroid hormones on prolactin concentrations in the anterior pituitary of the chicken. Br Poult Sci 1980 Nov;21(6):431-6

Kononenko VS: Cholinesterase activity of nerve tissue as an indicator of asymmetry of brain centers. Hum Physiol 1980 May-Jun;6(3):194-8

Kontani H: [Effect of phenoxybenzamine on the adrenergic neurone blocking action of guanethidine in isolated guinea pig vas deferens (author's transl)] Yakugaku Zasshi 1980 Dec;100(12):1247-51 (Eng. Abstr.) (Jpn)

Kontro P: Comparison of the uptake processes of taurine, hypotaurine, and GABA. Adv Biochem Psychopharmacol 1981;29:161-7

Konturek SJ, Tasler J, Cieszkowski M, et al: Studies on the inhibition of pancreatic secretion by luminal somatostatin. Am J Physiol 1981 Aug;241(2):G109-15

Kopp U, Aurell M, Sjölander M, et al: The role of prostaglandins in the alpha- and beta-adrenoceptor mediated renin release response to graded renal nerve stimulation. Pflugers Arch 1981 Jul;391(1):1-8

Korczyn A: [Hypophyseal hormones--neurotransmitters? (editorial)] Harefuah 1980 Dec 15;99(12):441-2 (Heb)

Korkhov VV, Nikitina GV, Kamernitskiĭ AV, et al: Kontratseptivnaia aktivnost' i mekhanizm deĭstviia kompozitsiĭ 6-metilzameshchennykh D'6-pentaranov i mestranola. Farmakol Toksikol 1981 Jan-Feb; 44(1):95-8 (Eng. Abstr.) (Rus)

Korner PI, Head GA: Effects of noradrenergic and serotonergic neurons on blood pressure, heart rate and baroreceptor-heart rate reflex of the conscious rabbit. J Auton Nerv Syst 1981 Apr;3(2-4):511-23

Korpi ER, Oja SS: Distributive profiles of free and protein-incorporated tryptophan and valine in cerebral cortex slices from adult and 2-day-old rats. Brain Res 1981 Jul 6;216(1):219-23

Koskas JP, Sado PA, Devissaguet JP, et al: Application d'une microméthode de prélèvement et de dosage de la quinidine: I. Etude pharmacocinétique après administration par voie intraveineuse chez le rat. J Pharm Belg 1981 May-Jun;36(3):187-92 (Eng. Abstr.) (Fre)

Koskas JP, Sado PA, Devissaguet JP, et al: Etude de la biodisponibilité absolue d'une solution aqueuse de quinidine, administrée par voie orale au rat et du cycle entérohépatique de cet alcaloïde. J Pharm Belg 1981 May-Jun;36(3):193-9 (Eng. Abstr.) (Fre)

Köster G, Breuer H: Effect of oestradiol-17 beta on the metabolism of noradrenaline in brain slices of ovariectomized rats. Acta Endocrinol (Copenh) 1981 Sep;98(1):1-7

Kostiuk IF, Mikliaeva NN: Neĭrogumoral'naia reguliatsiia mikrotsirkuliatsii pri vibratsionnoĭ boleznia. Vrach Delo 1981;(6):100-2 (Rus)

Kothari PJ, Hathaway BA, Nichols DE, et al: Synthesis and serotonin-like activity of 2-amino-5,8-dimethoxy-6-methyl-1,2-dihydronaphthalene. J Med Chem 1981 Jul;24(7):882-4

Koup JR, Gibaldi M: Single point estimation of phenytoin dosing requirement. Res Commun Chem Pathol Pharmacol 1981 Jan;31(1):3-12

Kovalev GI, Raevskiĭ KS: Nipekotovaia kislota--konkurentnyĭ ingibitor netto-zakhvata 3H-GAMK sinaptosomami mozga krys. Biull Eksp Biol Med 1981 Jun;91(6):692-4 (Eng. Abstr.) (Rus)

Kovalev IE, Borisova LN: Vliianie induktorov mikrosomal'nykh oksidaz so smeshannoĭ funktsieĭ na immunnyĭ otvet myshei, vyzyvaemyi geterologichnymi éritrotsitami. Zh Mikrobiol Epidemiol Immunobiol 1981 Apr;(4):42-6 (Eng. Abstr.) (Rus)

Kozaki A, Watanabe J: Dose dependency of apparent volumes of distribution for methylene blue in rabbits. J Pharmacobiodyn 1981 Jan; 4(1):49-57

Kozhechkin SN: The influence of sodium gamma-hydroxybutyrate on GABA receptors and catecholamine effect potentiation. Arch Int Pharmacodyn Ther 1981 Apr;250(2):242-53

Kraft R, Otto A, Makower A, et al: Combined thin-layer chromatography/mass spectrometry without substance elution. Use of direct identification of phenols, steroids, nucleosides, biogenic amines, and amino acids. Anal Biochem 1981 May 1;113(1):193-6

Krantis A, Kerr DI: Autoradiographic localization of [3H]gamma-amino-butyric acid in the myenteric plexus of the guinea-pig small intestine. Neurosci Lett 1981 May 29;23(3):263-8

Krarup G, Mogensen AM: Karbamazepinforgiftning. Ugeskr Laeger 1981 Mar 2;143(10):603-6 (Eng. Abstr.) (Dan)

Kraus JF, Mull R, Kurtz P, et al: Monitoring of grape harvesters for evidence of cholinesterase inhibition. J Toxicol Environ Health 1981 Jan;7(1):19-31

Kreider MS, Winokur A, Krieger NR: The olfactory bulb is rich in TRH immunoreactivity. Brain Res 1981 Jul 27;217(1):69-77

Krisch B: Somatostatin-immunoreactive fiber projections into the brain stem and the spinal cord of the rat. Cell Tissue Res 1981;217(3):531-52

Krnjevic K: Action of GABA on hippocampal neurons. Adv Biochem Psychopharmacol 1981;29:231-7

Krogsgaard-Larsen P, Schultz B, Mikkelsen H, et al: THIP, isoguvacine, isoguvacine oxide, and related GABA agonists. Adv Biochem Psychopharmacol 1981;29:69-76 (31 ref.)

Krogsgaard-Larsen P, Snowman A, Lummis SC, et al: Characterization of the binding of the GABA agonist [3H]piperidine-4-sulphonic acid to bovine brain synaptic membranes. J Neurochem 1981 Aug; 37(2):401-9

Kromer W, Höllt V, Schmidt H, et al: Release of immunoreactive-dynorphin from the isolated guinea-pig small intestine is reduced during peristaltic activity. Neurosci Lett 1981 Aug 7; 25(1):53-6

Kropf D: Wirkungen von Lithium auf normale psychische Funktionen als Bedingungen für die Prophylaxe. Bibl Psychiatr 1981;(161):141-51 (Eng. Abstr.) (Ger)

Krstulovic AM, Bertani-Dziedzic L, Dziedzic SW, et al: Quantitative determination of 3-methoxy-4-hydroxyphenylethyleneglycol and its sulfate conjugate in human lumbar cerebrospinal fluid using liquid chromatography with amperometric detection. J Chromatogr 1981 May 8;223(2):305-14

Kruesi M, van Schiak J: Illicit haldol [letter] N Engl J Med 1981 Sep 24;305(13):769

Krzyżowski J, Lewicka-Wysocka H, Lukaszewska B, et al: Badania przemiany obwodowych amin katecholowych i indolowych u osób zdrowych. Korelacje kliniczno-biochemiczne. Pol Tyg Lek 1981 Mar 16;36(11):417-21 (Eng. Abstr.) (Pol)

Ksiezak HJ, Gibson GE: Oxygen dependence of glucose and acetylcholine metabolism in slices and synaptosomes from rat brain. J Neurochem 1981 Aug;37(2):305-14

Ksiezak HJ, Gibson GE: Acetylcholine synthesis and CO2 production from variously labeled glucose in rat brain slices and synaptosomes. J Neurochem 1981 Jul;37(1):88-94

Ku Y, Kishimoto A, Takai Y, et al: A new possible regulatory system for protein phosphorylation in human peripheral lymphocytes. II. Possible relation to phosphatidylinositol turnover induced by mitogens. J Immunol 1981 Oct;127(4):1375-9

Kubanis P, Zornetzer SF: Age-related behavioral and neurobiological changes: a review with an emphasis on memory. Behav Neural Biol 1981 Feb;31(2):115-72

Kuczenski R: Monovalent cations and striatal tyrosine hydroxylase. J Neurochem 1981 Sep;37(3):681-6

Kühne GE, Walther H, Köhler E, et al: Blutspiegelwirkungsprofil bei Thioridazin. Agressologie 1979;20(D):271-4 (Eng. Abstr.) (Ger)

Kulmala HK, Huang CC, Dinerstein RJ, et al: Specific in vivo binding of 77Br-p-bromospiroperidol in rat brain: a potential tool for gamma ray imaging. Life Sci 1981 Apr 27;28(17):1911-6

Kumar A, Chandra O, Saxena PN: Effect of haloperidol withdrawal on motor activity and circadian rhythm of rats. Arzneimittelforsch 1981; 31(7):1096-8

Kumar N, Flavin M: Preferential action of a brain detyrosinolating carboxypeptidase on polymerized tubulin. J Biol Chem 1981 Jul 25; 256(14):7678-86

Kunec-Vajic E: Effect of cholinesterase on the chemiluminescence of luminol. Experientia 1981 May 15;37(5):462-3

Kupfer DJ, Spiker DG: Refractory depression: prediction of non-response by clinical indicators. J Clin Psychiatry 1981 Aug;42(8):307-12

Kuratsuji T, Shimizu S, Iwasaki Y, et al: [Lithium therapy in congenital neutropenia (author's transl)] Rinsho Ketsueki 1981 Mar;22(3):317–24 (Eng. Abstr.) **(Jpn)**

Kurioka S, Kimura Y, Matsuda M: Effects of sodium and bicarbonate ions on gamma-aminobutyric acid receptor binding in synaptic membranes of rat brain. J Neurochem 1981 Aug;37(2):418–21

Kurioka S, Hayata H, Matsuda M: Characterization of gamma-aminobutyric acid binding sites on crude synaptic membranes. J Neurochem 1981 Aug;37(2):283–8

Kurz C: Les psychotropes, un outil thérapeutique dont il faut savoir se servir. Soins Psychiatr 1981 Jan;(7):4 **(Fre)**

Kusek JC: The effects of phenytoin on in vitro protein synthesis in oral and non-oral tissues of the rat. Arch Oral Biol 1980;25(11–12):745–7

Kutsenko SA, Savateev NV: Liuminestsentno-gistokhimicheskoe izuchenie vliianiia atropina i dimetoksidikhlorvinilfosfata na soderzhanie katekholaminov v nekotorykh strukturakh golovnog mozga krys. Biull Eksp Biol Med 1981 Jun;91(6):702–3 (Eng. Abstr.) **(Rus)**

Kvetnanskiĭ R, Belova TI, Oprshalova Z, et al: Katekholaminy plazmy krovi u krys liniĭ Avgust i Vistar pri émotsional'nom stressa. Fiziol Zh SSSR 1981 Apr;67(4):516–23 (Eng. Abstr.) **(Rus)**

Kvetnanskiĭ R, Belova TI, Iindra A, et al: Izmeneniia reninovoĭ aktivnosti plazmy krovi u krys linii Avgust i Vistar pri émotsional'nom stresse. Fiziol Zh SSSR 1981 Jun;67(6):911–5 **(Rus)**

Kwietnanski R, Torda T, Tigranian RA, et al: Sostoianie katekholaminov i fermentov ikh sinteza v mozgovom sloe nadpochechnikov krys posle poleta na biosputnike 'Kosmos-936'. Kosm Biol Aviakosm Med 1981 Jun–Jul;15(4):64–5 (Eng. Abstr.) **(Rus)**

L

Labeyrie S, Neuzil E: Addition de tyrosine ou de phénylalanine aux cultures de Pseudomonas aeruginosa: influence sur la croissance microbienne et la pigmentation. Ann Microbiol (Paris) 1981 Jan–Feb;132A(1):31–40 (Eng. Abstr.) **(Fre)**

Laborit H: Physiopathologie de l'inhibition et propositions d'une réponse thérapeutique originale. Agressologie 1981;22(2):45–53 (90 ref.) (Eng. Abstr.) **(Fre)**

Laborit H, Baron C, Ferran C, et al: Effets du chlorhydrate de minaprine sur les variations de poids, de pression artérielle et de concentration des amines cérébrales provoquées par les électrochocs plantaires inévitables. Agressologie 1981;22(2):59–62 (Eng. Abstr.) **(Fre)**

Labowitz RJ, Newman JH: Appropriate treatment of fibromyositis [letter] Del Med J 1981 Aug;53(8):389

Lader M: Benzodiazepines--panacea or poison? Aust NZ J Psychiatry 1981 Mar;15(1):1–9

Ladisich W: Effects of althesin in psychotherapy of schizophrenics. Preliminary report. Acta Psychiatr Belg 1980 Jul–Aug;80(4):445–51

Laekeman GM, Bult H, Herman AG: Differential interaction of 5-HT with chicken and rat aorta. Arch Int Pharmacodyn Ther 1981 Apr;250(2):318–20

Laguzzi R: Effets de l'injection intraventriculaire de la méthiothépine et de la métergoline sur le sommeil du rat. C R Soc Biol (Paris) 1981;175(2):160–3 (Eng. Abstr.) **(Fre)**

Lai H, Carino MA, Sperry R, et al: Effects of microinjection of 2-chloro-11 (2-dimethylaminoethoxy)-dibenzo[b,f]-thiepine (zotepine), thioridazine and haloperidol into the striatum and nucleus accumbens on stereotypic behaviour and motor activity. J Pharm Pharmacol 1981 Apr;33(4):252–4

Lai HC, Carino MA, Horita A: Effects of chronic haloperidol, thioridazine and zotepine treatment on apomorphine elicited stereotypic behavior and 3H-spiroperidol binding sites in the striatum of the rat. Proc West Pharmacol Soc 1981;24:5–6

Lai ML, Hsieh YY, Chen RC, et al: A new modified method of measurement of diphenylhydantoin and phenobarbital in serum by high pressure liquid chromatography. Taiwan I Hsueh Hui Tsa Chih 1980 Nov;79(11):1002–10

Lakowicz JR, Freshwater G, Weber G: Nanosecond segmental mobilities of tryptophan residues in proteins observed by lifetime-resolved fluorescence anisotropies. Biophys J 1980;32(1):591–601

Lam G, Chiou WL: Arterial and venous blood sampling in pharmacokinetic studies: propranolol in rabbits and dogs. Res Commun Chem Pathol Pharmacol 1981 Jul;33(1):33–48

LaManna JC, Harik SI, Light AI, et al: Norepinephrine depletion alters cerebral oxidative metabolism in the 'active' state. Brain Res 1981 Jan 5;204(1):87–101

Lambert JD, Flatman JA: The interaction between barbiturate anaesthetics and excitatory amino acid responses on cat spinal neurones. Neuropharmacology 1981 Mar;20(3):227–40

Lamberts R, Wuttke W: Puberty of female rats may in part be explained by decreased hypothalamic dopamine receptor sensitivity. Brain Res 1981 Jun 29;215(1–2):375–81

Lamberts SW, Visser TJ: The effects of histidyl-proline-diketopiperazine, a metabolite of TRH, on prolactin release by the rat pituitary gland in vitro. Eur J Pharmacol 1981 May 8;71(2–3):337–41

Lamers JM, Stinis HT, de Jonge HR: On the role of cyclic AMP and Ca2+-calmodulin-dependent phosphorylation in the control of (Ca2+ + Mg2+)-ATPase of cardiac sarcolemma. FEBS Lett 1981 May 5;127(1):139–43

Lamour Y, Dutar P, Jobert A: Distribution laminaire des réponses excitatrices à l'acétylcholine dans le cortex somesthésique du rat: étude microiontophorétique. C R Seances Acad Sci [III] 1981 Jun 1;292(20):1121–4 (Eng. Abstr.) **(Fre)**

Landauer AA: Diazepam and driving ability. Med J Aust 1981 Jun 13;1(12):624–6

Lange E, Riedel C, König L, et al: Klinische Vergleichsprüfung Trazodone-Clomipramin. Psychiatr Neurol Med Psychol (Leipz) 1980 Dec;32(12):748–50 **(Ger)**

Lange F: ACTH-Bestimmung in den Hypophysenvorderlappen nach Adrenalektomie und Nebennierenrinden-Hormonbehandlung mit der mikrophotometrischen und der Radioimmunoassay-Methode. Microsc Acta 1981 Jul;84(4):329–37 (Eng. Abstr.) **(Ger)**

Langel IuL, Speek MA, Iarv IaL: Vliianie pH na gidroliz kholinesterazoĭ razlichnykh substratov. Biokhimiia 1980 Dec;45(12):2130–8 (Eng. Abstr.) **(Rus)**

Langer G, Karobath M, Sieghart W, et al: Effects of antidepressant treatment with clomipramine on hormonal responses to thyrotropin-releasing hormone and insulin-induced hypoglycemia: implications for the 'monoamine-hypothesis'. Pharmacopsychiatria 1981 May;14(3):100–6

Langer SZ, Javoy-Agid F, Raisman R, et al: Distribution of specific high-affinity binding sites for [3H]imipramine in human brain. J Neurochem 1981 Aug;37(2):267–71

Langer SZ: Presynaptic regulation of the release of catecholamines. Pharmacol Rev 1980 Dec;32(4):337–62

Langer SZ, Raisman R, Briley M: High-affinity [3H] DMI binding is associated with neuronal noradrenaline uptake in the periphery and the central nervous system. Eur J Pharmacol 1981 Jul 10;72(4):423–4

Lapierre YD, Rastogi RB, Singhal RL: Neurochemical changes produced by acute treatment with clobazam, a new 1,5-benzodiazepine. Gen Pharmacol 1981;12(4):261–6

Lara R, Tapia R, Cervantes F, et al: Mathematical model of synaptic plasticity: II. Habituation. Neurol Res 1980;2(1):1–18

Lardennois B, El Khansa A, Amory JP, et al: La phénoxybenzamine en pathologie prostatique. A propos de 300 observations. J Urol (Paris) 1981;87(4):243–8 (Eng. Abstr.) **(Fre)**

Larney E: Soins infirmiers et chimiothérapie. Soins Psychiatr 1981 Jan;(7):47–51 **(Fre)**

Larrea GA, Calvo JC, Foglia VG, et al: Effect of testosterone on the hypothalamic-pituitary-testicular axis of the old male rat. Horm Metab Res 1981 Jul;13(7):396–9

Larsen JK: Monoaminooksydase-haemmere. Ugeskr Laeger 1981 Jun 8;143(24):1549–52 **(Dan)**

Larsson OM, Schousboe A: Comparison between (RS)-nipecotic acid and GABA transport in cultured astrocytes: coupling with two sodium ions. Neurochem Res 1981 Mar;6(3):257–66

Lathrop DA, Valle R, Gaum WE, et al: The effect of diltiazem and nisoldipine on spontaneously active human atrial tissue. J Mol Cell Cardiol 1981 Jan;13(1):111–5

Laties AM, Stone RA, Brecha NC: Substance P-like immunoreactive nerve fibers in the trabecular meshwork. Invest Ophthalmol Vis Sci 1981 Sep;21(3):484–6

Lauder JM, Sze PY, Krebs H: Maternal influences on tryptophan hydroxylase activity in embryonic rat brain. Dev Neurosci 1981;4(4):291–5

Lauven PM, Stoeckel H, Schwilden H, et al: Klinische Pharmakokinetik von Midazolam, Flunitrazepam und Diazepam. Anaesth Intensivther Notfallmed 1981 Jun;16(3):135–42 (Eng. Abstr.) **(Ger)**

Lawlor JF, Blaustein M: Evaluation of free thyroxin measurements in patients with non-thyroidal illnesses. Clin Chem 1981 Aug;27(8):1457–9

Lawson LA, Blouin RA, Smith RB, et al: Phenytoin-dexamethasone interaction: a previously unreported observation. Surg Neurol 1981 Jul;16(1):23–4

Leander JD: Drug effects on multiple and alternating mixed-schedule performance. J Pharmacol Exp Ther 1981 Sep;218(3):728–33

Leckman JF, Maas JW, Heninger GR: Covariance of plasma free 3-methoxy-4-hydroxyphenethyleneglycol and diastolic blood pressure. Eur J Pharmacol 1981 Mar 12;70(2):111–20

Lecomte-Yerna MJ, Hazee-Hagelstein MT, Charlet-Renard C, et al: Un mécanisme intracellulaire de l'action de l'inhibine sur la sécrétion de l'hormone folliculo-stimulante et de l'hormone lutéinisante induite par le LH-RH in vitro. C R Trav Lab Carlsberg 1981;175(3):385–8 (Eng. Abstr.) **(Fre)**

Leconte P, Hennevin E: Post-learning paradoxical sleep, reticular activation and noradrenergic activity. Physiol Behav 1981 Apr;26(4):587–94

Lee CM, Iversen LL: Release of somatostatin from extra-hypothalamic rat brain slices: inhibition by dopamine and morphine. Brain Res 1981 Aug 31;219(2):355–61

Lee CM, Emson PC, Iversen LL: Chromatographic behaviour and post-mortem stability of somatostatin in the rat and mouse brain. Brain Res 1981 Sep 7;220(1):159–66

AUTHOR SECTION

Lee HS, Oh SH: Effect of dexamethasone and epinephrine on metallothionein level in the perfused rat liver. Yonsei Med J 1980; 21(1):18–23

Lee TP: The inhibition of PMN beta-glucuronidase release by Aroclor 1254. Environ Res 1981 Aug;25(2):386–90

Lee WB, Lumbers ER: Angiotensin and the cardiac baroreflex response to phenylephrine. Clin Exp Pharmacol Physiol 1981 Mar–Apr; 8(2):109–17

Leff AR, Munoz NM: Selective autonomic stimulation of canine trachealis with dimethylphenylpiperazinium. J Appl Physiol 1981 Aug; 51(2):428–37

Leff AR, Munoz NM: Cholinergic and alpha adrenergic augmentation of histamine-induced contraction of canine airway smooth muscle. J Pharmacol Exp Ther 1981 Sep;218(3):582–7

LeGatt DF, Baker GB, Coutts RT: Concomitant analysis of normetanephrine and 3-methoxytyramine in brain: a new gas-liquid chromatography procedure. Res Commun Chem Pathol Pharmacol 1981 Jul;33(1):61–8

Lehmann CR, Ereshefsky L, Saklad SR, et al: Very high dose loxapine in refractory schizophrenic patients. Am J Psychiatry 1981 Sep; 138(9):1212–4

Lehmann J, Arbilla S, Langer SZ: Dopamine receptor mediated inhibition by pergolide of electrically-evoked 3H-dopamine release from striatal slices of cat and rat: slight effect of ascorbate. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):31–5

Lehmann M, Keul J, Wybitul K: Einfluss einer stufenweisen Laufband- und Fahrradergometrie auf die Plasmacatecholamine, energiereichen Substrate, aerobe und anaerobe Kapazität. Klin Wochenschr 1981 Jun 1;59(11):553–9 (Eng. Abstr.) **(Ger)**

Lehmann M, Keul J, Berg A, et al: Plasmacatecholamine und metabolische Veränderungen bei Frauen während Laufbandergometrie. Eur J Applied Physiol 1981;46(3):305–15 **(Ger)**

Lehrman SN, Bauman ML: Carbamazepine overdose. Am J Dis Child 1981 Aug;135(8):768–9

Lehtovirta P, Ranta T: Effect of short-term bromocriptine treatment on amniotic fluid prolactin concentration in the first half of pregnancy. Acta Endocrinol (Copenh) 1981 Aug;97(4):559–61

Leibow D: The psychiatrist's perspective: two images of the patient. Ann NY Acad Sci 1981;368:123–7

Leith NJ, Barrett RJ: Self-stimulation and amphetamine: tolerance to d and l isomers and cross tolerance to cocaine and methylphenidate. Psychopharmacology (Berlin) 1981;74(1):23–8

Lembeck F, Donnerer J: Time course of capsaicin-induced functional impairments in comparison with changes in neuronal substance P content. Naunyn Schmiedebergs Arch Pharmacol 1981 Jun;316(3):240–3

Lemmer B: Abhängigkeit bei Benzodiazepinen und Appetitzüglern. Ein Interview nit Prof. Dr. B Lemmer, Frankfurt. Med Monatsschr Pharm 1981 Aug;4(8):234–7 **(Ger)**

Lemoine JM, Lépine JP: Le lithium. Soins Psychiatr 1981 Jan;(7):37–42 **(Fre)**

Lenehan T, Omer LM, Kenny M, et al: The effect of multiple rising doses of Ro 11-2465 (serotonin uptake inhibitor) on serotonin content of human platelets. Psychopharmacology (Berlin) 1981;74(1):1–3

Lentzen H, Philippu A: Physico-chemical properties of phenethylamines and their uptake into synaptic vesicles of the caudate nucleus. Biochem Pharmacol 1981 Jul 1;30(13):1759–64

Lenz G, Küfferle B, Wolf R: Lithiumprophylaxe schizoaffektiver Psychosen. Bibl Psychiatr 1981;(161):45–57 (54 ref.) **(Ger)**

Lépine JP, Lemoine JM: Associations et interactions en psychopharmacologie. Soins Psychiatr 1981 Jan;(7):43–6 **(Fre)**

Leroux P, Tonon MC, Jégou S, et al: Stimulatory effect of prostaglandin E1 on thyroliberin-induced alpha-melanotropin release from perifused neuro-intermediate lobes of frog pituitary gland. Prostaglandins 1981 Apr;21(4):599–608

Lesne M, Devos DM, Reynaert M: Enterogastric cycle and intoxication with hydroquinidine: a case report. Clin Toxicol 1981 Jun;18(6):659–62

Leung PC, Arendash GW, Whitmoyer DI, et al: Electrical stimulation of mesencephalic noradrenergic pathway: effects on luteinizing hormone levels in blood of ovariectomized and ovariectomized, steroid-primed rats. Endocrinology 1981 Sep;109(3):720–8

Levalle O, Tropea L, Aparicio N, et al: D-tryptophan-6-LH-RH-at los doses in the treatment of male subfertility. Andrologia 1981 May–Jun; 13(3):207–11

Levenson AJ: Psychotropic drug use in the elderly: an overview. Am Fam Physician 1981 Aug;24(2):194–9

Levi G, Gallo V: Glutamate as a putative transmitter in the cerebellum: stimulation by GABA of glutamic acid release from specific pools. J Neurochem 1981 Jul;37(1):22–31

Levi G, Banay-Schwartz M, Raiteri M: Studies on the release of exogenous and endogenous GABA and glutamate from rat brain synaptosomes. Neurochem Res 1981 Mar;6(3):275–85

Levin BE, Natelson BH: The relation of plasma norepinephrine and epinephrine levels over time in humans. J Auton Nerv Syst 1980 Dec; 2(4):315–25

Levine MS, Clausen ML, Butcher SH: Behavioral effects of phencyclidine in the developing cat. Neuropharmacology 1981 Aug;20(8):743–5

Levine RL, McIntosh TK, Lothrop DA, et al: Circadian periodicity of plasma corticosterone levels in rats subjected to hemorrhagic shock and surgical trauma. Horm Res 1980;13(6):385–95

Levitan IB, Adams WB: Cyclic AMP modulation of a specific ion channel in an identified nerve cell: possible role for protein phosphorylation. Adv Cyclic Nucleotide Res 1981;14:647–53

Levy JA, Heppner GH: Alterations of immune reactivity by haloperidol and delta-9-tetrahydrocannabinol. J Immunopharmacol 1981; 3(1):93–109

Leyne P: Le traitement du syndrome anxio-dépressif chex la femme jeune. A propos d'une observation. Sem Hop Paris 1981 Jun 18–25; 57(25–28):1226–7 (Eng. Abstr.) **(Fre)**

Liewendahl K, Helenius T, Majuri H, et al: Effect of anticonvulsant and antidepressant drugs on iodothyronines in serum. Scand J Clin Lab Invest 1980;40(8):767–74

Lightman SL, James VH, Linsell C, et al: Studies of diurnal changes in plasma renin activity, and plasma noradrenaline, aldosterone and cortisol concentrations in man. Clin Endocrinol (Oxf) 1981 Mar;14(3):213–23

Liljequist R, Mattila MJ, Linnoila M: Alterations in human memory following acute maprotiline, diazepam and codeine administration. Acta Pharmacol Toxicol (Copenh) 1981 Feb;48(2):190–2

Lim M, Linton RA, Wolff CB, et al: Propranolol, exercise, and arterial plasma potassium [letter] Lancet 1981 Sep 12;2(8246):591

Lin CW, Maayani S, Wilk S: [3H]dihydroergocryptine binding to bovine striatal membranes defined by a low d-butaclamol concentration: antagonism by substituted benzamides. Biochem Pharmacol 1981 Jun 1;30(11):1305–14

Lindamood C 3d, Colasanti BK: Involvement of brain monoamines in the delta-9-tetrahydrocannabinol-induced reduction of hippocampal choline uptake. J Neurochem 1981 Sep;37(3):788–91

Linde R, Doelle GC, Alexander N, et al: Reversible inhibition of testicular steroidogenesis and spermatogenesis by a potent gonadotropin-releasing hormone agonist in normal men: an approach toward the development of a male contraceptive. N Engl J Med 1981 Sep 17;305(12):663–7

Linden M, Chaskel R: Information and consent in schizophrenic patients in long-term treatment. Schizophr Bull 1981;7(3):372–8

Linden RJ, Mary DA: Role of dopamine in the diuresis caused by stimulation of atrial receptors. Q J Exp Physiol 1981 Apr;66(2):155–61

Lindner G, Grosse G: Uber die Wirkung von Substanz P auf das Wachstum von Nervenfasern unter In-vitro-Bedingungen. Z Mikrosk Anat Forsch 1981;95(3):390–4 (Eng. Abstr.) **(Ger)**

Lingjaerde O: The art of measuring serotonin uptake in platelets [letter] Br J Psychiatry 1981 1 Feb;138:181

Lingjaerde O, Kildemo O: Dopamine uptake in platelets: two different low-affinity, saturable mechanisms. Agents Actions 1981 Jul;11(4):410–6

Linnoila M, Gold P, Potter WZ, et al: Tricyclic antidepressants do not alter thyroid hormone levels in patients suffering from a major affective disorder. Psychiatry Res 1981 Jun;4(3):357–60

Linton EA, White N, Lira de Tineo O, et al: 2-hydroxyoestradiol inhibits prolactin release from the superfused rat pituitary gland. J Endocrinol 1981 Sep;90(3):315–22

Lippa AS, Pelham RW, Beer B, et al: Brain cholinergic dysfunction and memory in aged rats. Neurobiol Aging 1980 Summer;1(1):13–9

Lippa AS, Critchett DJ, Ehlert F, et al: Age-related alterations in neurotransmitter receptors: an electrophysiological and biochemical analysis. Neurobiol Aging 1981 Spring;2(1):3–8

Lippton HL, Meyer RL, Parey SE, et al: Analysis of responses to dopamine in the mesenteric vascular bed of the cat. Arch Int Pharmacodyn Ther 1981 May;251(1):136–49

Lipton JS, Petterborg LJ, Reiter RJ: Influence of propranolol, phenoxybenzamine of phentolamine in the in vivo nocturnal rise of pineal melatonin levels in the Syrian hamster. Life Sci 1981 May 21; 28(21):2377–82

Lisoprawski A, Blanc G, Glowinski J: Activation by stress of the habenulo-interpeduncular substance P neurons in the rat. Neurosci Lett 1981 Aug 7;25(1):47–51

Litvinov SA: Vliianie atsetilkholina i gistamina na soderzhanie élektrolitov i katekholaminov v stenke sosudov v usloviiakh rentgenoobluchenia i deĭstviia tsistamina. Farmakol Toksikol 1981 Jan–Feb;44(1):55–9 (Eng. Abstr.) **(Rus)**

Liu PS, Marquez VE, Driscoll JS, et al: Cyclic urea nucleosides. Cytidine deaminase activity as a function of aglycon ring size. J Med Chem 1981 Jun;24(6):662–6

Liubimov BI, Boĭko SS, Smol'nikova NM, et al: Dinamika soderzhaniia fenazepama v krovi mini-svineĭ pri beremennosti. Farmakol Toksikol 1981 Jan–Feb;44(1):43–6 (Eng. Abstr.) **(Rus)**

Livertoux MH, Bessiere J: Comportement électrochimique de la phénothiazine en milieu diméthylsulfoxyde application analytique. Ann Pharm Fr 1980;38(6):513–20 (Eng. Abstr.) **(Fre)**

Livio M, Palmier C, Villa S, et al: Differential effects of itanoxone--a new hypolipidemic and hypouricemic drug--on platelet and vascular prostaglandin generation in rats. Atherosclerosis 1981 Jul;39(4):469–77

Lo LY, Land G, Bye A: Sensitive assay for pseudoephedrine and its metabolite, norpseudoephedrine in plasma and urine using gas--liquid chromatography with electron-capture detection. J Chromatogr 1981 Feb 13;222(2):297–302

AUTHOR SECTION

Lobacheva II, Popova NK: Mezhlineinye razlichiia v urovne serotonina i 5-gidorksiindoluksusnoi kisloty v postnatal'nom ontogeneze myshei linii C57BL/6J i BALB/cLac. Ontogenez 1981;12(3):306-10 (Eng. Abstr.) **(Rus)**

Lockey SD: A new method of administering aqueous epinephrine: the EpiPen, an automatic syringe. J Asthma Res 1980 Jul;17(4):153-5

Lodge D: Uptake inhibitors, amino acids, and spinal neurones. Adv Biochem Psychopharmacol 1981;29:327-32 (32 ref.)

Loertzer HJ, Wagner G: Untersuchungen über den Einfluss von Lärm auf die Biotransformation von Hexobarbital bei der Ratte. Z Gesamte Hyg 1981;27(6):438-40 (Eng. Abstr.) **(Ger)**

Loewit K, Kofler R, Tabarelli M, et al: Effect of bromocryptine on 20 alpha-hydroxysteroiddehydrogenase regulation in the corpus luteum of the pregnant rat. Acta Endocrinol (Copenh) 1981 Sep;98(1):133-6

Login IS, MacLeod RM: The direct effect of reserpine in vitro on prolactin release from rat anterior pituitary glands. Brain Res 1981 Jan 5; 204(1):79-85

Loh B: The effect of phenoxybenzamine on the gastrin response to glycine stimulation. Gastroenterol Jpn 1981;16(3):205-12

Loh YP: Processing, turnover and release of corticotropins, endorphins and melanotropin in the toad pituitary intermediate lobe. Ciba Found Symp 1981;(81):55-78

Lokiec F, Cohen Y, Jacquot C: Cageing density and dopamine striatal elimination after amphetamine in the rat. Psychopharmacology (Berlin) 1981;73(4):402-3

Lombardo A, Goi GC, Marchesini S, et al: Influence of age and sex on five human plasma lysosomal enzymes assayed by automated procedures. Clin Chim Acta 1981 Jun 18;113(2):141-52

Longworth JW: A new component in protein fluorescence. Ann NY Acad Sci 1981;366:237-45

Loosemore MJ, Wogan GN, Walsh C: Determination of partition ratios for allylisopropylacetamide during suicidal processing by a phenobarbital-induced cytochrome P-450 isozyme from rat liver. J Biol Chem 1981 Aug 25;256(16):8705-12

Löscher W: Effect of inhibitors of GABA aminotransferase on the metabolism of GABA in brain tissue and synaptosomal fractions. J Neurochem 1981 Apr;36(4):1521-7

Löscher W: Valproate induced changes in GABA metabolism at the subcellular level. Biochem Pharmacol 1981 Jun 1;30(11):1364-6

Lotti VJ, Chang RS, Kling P: Pre- and postsynaptic adrenergic activation by norepinephrine reuptake inhibitors in the field-stimulated rat vas deferens. Life Sci 1981 Aug 10;29(6):633-9

Love BL, Moore RG, Thomas J, et al: Pharmacokinetics of zimelidine in humans--plasma levels and urinary excretion of zimelidine and norzimelidine after intravenous and oral administration of zimelidine. Eur J Clin Pharmacol 1981;20(2):135-9

Lovell KL: Changes in brain norepinephrine content in mice following neonatal 6-hydroxydopamine. Brain Res Bull 1981 Jul;7(1):41-4

Lucchi L, Memo M, Airaghi ML, et al: Chronic lead treatment induces in rat a specific and differential effect on dopamine receptors in different brain areas. Brain Res 1981 Jun 1;213(2):397-404

Lukhtai VA: Sostoianie obmena katekholaminov na rannikh étapakh razvitiia khronicheskoi serouglerodnoi intoksikatsii (obzor literatury). Vrach Delo 1981 May;(5):110-4 (33 ref.) (Eng. Abstr.) **(Rus)**

Lundberg JM, Fried G, Fahrenkrug J, et al: Subcellular fractionation of cat submandibular gland: comparative studies on the distribution of acetylcholine and vasoactive intestinal polypeptide (VIP). Neuroscience 1981;6(6):1001-10

Lundberg U, de Château P, Winberg J, et al: Catecholamine and cortisol excretion patterns in three-year-old children and their parents. J Human Stress 1981 Sep;7(3):3-11

Lundborg P, Aström H, Bengtsson C, et al: Effect of beta-adrenoceptor blockade on exercise performance and metabolism. Clin Sci 1981 Sep; 61(3):299-305

Luzhnikov EA, Novikovskaia TV, Il'nitskaia TI, et al: Narusheniia funktsii pecheni pri ékzotoksicheskom shoke i ikh lechenie. Ter Arkh 1981; 53(4):86-91 (Eng. Abstr.) **(Rus)**

Lyness WH, Mycek MJ: In vitro cellular adaptation of serotonergic processes after chronic central phenobarbital administration. Brain Res 1981 Jan 5;204(1):248-52

Lyon K, Wilson J, Golden CJ, et al: Effects of long-term neuroleptic use on brain density. Psychiatry Res 1981 Aug;5(1):33-7

M

Maayan ML, Volpert EM, From A: Norepinephrine and thyrotropin effects on the thyroid in vitro: simultaneous stimulation of iodide organification and antagonism of thyroxine release. Endocrinology 1981 Sep;109(3):930-4

Mabuchi H, Nakahashi H: Systematic separation of medium-sized biologically active peptides by high-performance liquid chromatography. J Chromatogr 1981 Aug 28;213(2):275-86

McAinsh J, Holmes BF, Baber NS, et al: Bioavailability of propranolol and bendrofluazide formulations. Biopharm Drug Dispos 1981 Apr-Jun; 2(2):167-75

McCallum NK, Shaw SM: Chromatographic analysis for delta1-tetrahydrocannabinol in blood and brain. J Anal Toxicol 1981 May-Jun;5(3):148-9

McCammon RL, Hilgenberg JC, Stoelting RK: Effect of propranolol on circulatory responses to induction of diazepam-nitrous oxide anesthesia and to endotracheal intubation. Anesth Analg (Cleve) 1981 Aug; 60(8):579-83

McCann SM, Negro-Vilar A, Ojeda SR, et al: Steroid effects on hypothalamic-gonadotropin interactions. Exp Brain Res 1981;Suppl 3:142-50

McCarthy BW, Gomes UR, Neethling AC, et al: gamma-Aminobutyric acid concentration in cerebrospinal fluid in schizophrenia. J Neurochem 1981 Apr;36(4):1406-8

McCarty R, Gold PE: Plasma catecholamines: effects of footshock level and hormonal modulators of memory storage. Horm Behav 1981 Jun; 15(2):168-82

McComb DJ, Ryan N, Ryder D, et al: Response to thyrotropin-releasing hormone (TRH) of rat lactotrophs and somatotrophs deprived of hypothalamic control. Endokrinologie 1981 Mar;77(3):303-16

McCord EF, Bucks RR, Boxer SG: Laser chemically induced dynamic nuclear polarization study of the reaction between photoexcited flavins and tryptophan derivatives at 360 MHz. Biochemistry 1981 May; 20(10):2880-8

McDermott JR, Smith AI, Biggins JA, et al: Degradation of luteinizing hormone-releasing hormone by serum and plasma in vitro. Regul Pept 1981 May;2(2):69-79

McDevitt JT, Setler PE: Differential effects of dopamine agonists in mature and immature rats. Eur J Pharmacol 1981 Jun 10;72(1):69-75

McDonald DM, Mitchell RA: The neural pathway involved in 'efferent inhibition' of chemoreceptors in the cat carotid body. J Comp Neurol 1981 Sep 20;201(3):457-76

McEachron DL, Kripke DF, Wyborney VG: Lithium promotes entrainment of rats to long circadian light-dark cycles. Psychiatry Res 1981 Aug; 5(1):1-9

McGee R, Golus P, Russell-Jones C: Long-term effect of pentobarbital anesthesia on neophobia in the rat. Behav Neural Biol 1981 Jul; 32(3):376-9

MacGorman LR, Rizza RA, Gerich JE: Physiological concentrations of growth hormone exert insulin-like and insulin antagonistic effects on both hepatic and extrahepatic tissues in man. J Clin Endocrinol Metab 1981 Sep;53(3):556-9

McGrath CJ, Rempel WE, Addis PB, et al: Acepromazine and droperidol inhibition of halothane-induced malignant hyperthermia (porcine stress syndrome) in swine. Am J Vet Res 1981 Feb;42(2):195-8

McGraw NP, Castagnoli N Jr: Studies on chiral interactions of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane and the corresponding N-hydroxy metabolites with cytochrome P-450. J Med Chem 1981 Mar;24(3):299-304

McGuirk SM, Muir WW, Sams RA: Pharmacokinetic analysis of intravenously and orally administered quinidine in horses. Am J Vet Res 1981 Jun;42(6):938-42

Mack RB: Are your patients speeding? NC Med J 1981 Jul;42(7):489

Mackes K, Itoh M, Greene K, et al: Radioimmunoassay of human plasma somatostatin. Diabetes 1981 Sep;30(9):728-34

McLachlan EM, Oldfield BJ: Some observations on the catecholaminergic innervation of the intermediate zone of the thoracolumbar spinal cord of the cat. J Comp Neurol 1981 Aug 20;200(4):529-44

McMillan M, Frelinger JA, Jones PP, et al: Structure of murine Ia antigens. Two dimensional electrophoretic analyses and high pressure liquid chromatography tryptic peptide maps of products of the I-A and I-E subregions and of an associated invariant polypeptide. J Exp Med 1981 Apr 1;153(4):936-50

McMillen BA: Comparative effects of classical and atypical antipsychotic drugs in combination with a non-amphetamine stimulant on rat brain dopamine metabolism. J Pharm Pharmacol 1981 Aug;33(8):544-6

McNatty KP, Gibb M, Dobson C, et al: Evidence that changes in luteinizing hormone secretion regulate the growth of the preovulatory follicle in the ewe. J Endocrinol 1981 Sep;90(3):375-89

McNeilly AS, Hunter M, Land RB, et al: Inadequate corpus luteum function after the induction of ovulation in anoestrous ewes by LH-RH or an LH-RH agonist. J Reprod Fertil 1981 Sep;63(1):137-44

McPherson GA, Malta E, Raper C: Effects of some catecholamines on the cat cardiovascular system: interactions with adrenoceptor antagonists. J Cardiovasc Pharmacol 1981 Jul-Aug;3(4):739-52

Maffla AG: Double-blind assessment of the activity of minaprine (30038-CB) in child psychiatry. Pharmatherapeutica 1981;2(9):601-6

Mager PP: Overall-response parameter analysis applied to butyrophenones. Act Nerv Super (Praha) 1981 Jun;23(2):130-5

Magoffin DA, Reynolds DS, Erickson GF: Direct inhibitory effect of GnRH on androgen secretion by ovarian interstitial cells. Endocrinology 1981 Aug;109(2):661-3

Mains RE, Eipper BA: Comparison of rat anterior and intermediate pituitary in tissue culture: corticotropin (ACTH) and beta-endorphin. Ciba Found Symp 1981;(81):32-54

Maixner W, Long JP, Wright CB, et al: Peripheral vascular effects of a new dopamine analog: 5-6-dihydroxy-2-methylaminotetralin (M-8).

J Cardiovasc Pharmacol 1981 Mar-Apr;3(2):381-9

Maj J, Sypniewska M: Central action of mepiprazole. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):475-84

Maj J: Studies on the action of antidepressant drugs of second generation. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):437-49

Majewski H, Rand MJ: An interaction between prejunctional alpha-adrenoceptors and prejunctional beta-adrenoceptors. Eur J Pharmacol 1981 Feb 19;69(4):493-8

Makarski JS: Stimulation of cyclic AMP production by vasoactive agents in cultured bovine aortic and pulmonary artery endothelial cells. In Vitro 1981 May;17(5):450-8

Maksay G, Tegyey Z, Simon-Trompler E, et al: Structural parameters in the microsomal hydrolysis of 3-acyloxy-1, 4-benzodiazepines and the multiplicity of the esterases involved. Eur J Drug Metab Pharmacokinet 1980;5(4):193-200

Maksay G, Kardos J, Simonyi M, et al: Specific binding of racemic oxazepam esters to rat brain synaptosomes and the influence of bioactivation by esterases. Arzneimittelforsch 1981;31(6):979-81

Malas KL, de Fraites EG, van Kammen DP: Neuroendocrine effects of D,L-propranolol [letter] Lancet 1981 Aug 22;2(8243):424

Malendowicz LK, Nikicicz H, Majchrzak M, et al: Effect or partial hepatectomy on secretion and metabolism of corticosterone in the rat. Endokrinologie 1981 Mar;77(3):291-6

Malik KU, Nasjletti A: Inhibitory action of bradykinin on release of the adrenergic transmitter in the isolated lapine kidney. Experientia 1981 May 15;37(5):496-7

Malikova LA, Arefolov VA: Vliianie nekotorykh GAMK-ergicheskikh veshchestv na metabolizm dofamina v mozge krysy. Farmakol Toksikol 1981 Jan-Feb;44(1):37-40 (Eng. Abstr.) **(Rus)**

Małolepszy J, Jankowska R, Panaszek B: Effect of isoproterenol and propranolol on the mast cell degranulation and on the passive cutaneous anaphylaxis in mice. Arch Immunol Ther Exp (Warsz) 1980;28(6):873-8

Manchanda R, Hirsch SR: (Des-Tyr)-gamma-endorphin in the treatment of schizophrenia. Psychol Med 1981 May;11(2):401-4

Mandell AJ, Russo PV: Striatal tyrosine hydroxylase activity: multiple conformational kinetic oscillators and product concentration frequencies. J Neurosci 1981 Apr;1(4):380-9

Mándi Y, Molnár J: Effect of chlorpromazine on conjugal plasmid transfer and sex pili. Acta Microbiol Acad Sci Hung 1981;28(2):205-10

Mann JJ, Friedman E, Georgotas A, et al: The antidepressant effects of trazodone and inhibition of platelet serotonin reuptake. Commun Psychopharmacol 1980;4(4):293-301

Manukhin BN, Volina EV, Markova LN, et al: Biogenic monoamines in early embryos of sea urchins. Dev Neurosci 1981;4(4):322-8

Marakhova II, Pospelova TV, Vereninov AA, et al: izmenenie transport shchelochnykh kationov cherez plazmaticheskuiu membranu kletok linii CHO-K1, ustolchivykh k bromistomu étidiiu. Tsitologiia 1981 Apr;23(4):410-8 (Eng. Abstr.) **(Rus)**

Marasco WA, Showell HJ, Becker EL: Substance P binds to the formylpeptide chemotaxis receptor on the rabbit neutrophil. Biochem Biophys Res Commun 1981 Apr 30;99(4):1065-72

Marcucci F, Airoldi L, Zavattini G, et al: Metabolism of pinazepam by rat liver microsomes. Eur J Drug Metab Pharmacokinet 1981;6(2):109-14

Margel S, Hirsh J: Hemoperfusion for detoxification of mercury. A model:treatment of severe mercury poisoning by encapsulated chelating spheres, Part I. Biomater Med Devices Artif Organs 1981;9(2):107-25

Mariani E, Schenone P, Bondavalli F, et al: Synthesis and pharmacological activity of (bicyclo [2.2.1] hept-2-ylidene)acetic acid amides and 2-(bicyclo [2.2.1] hept-2-ylidene)ethanamines. Farmaco [Sci] 1981 Apr;36(4):283-91

Marie C: Ontogenesis of the adrenal glucocorticoids and of the target function of the enzymatic tyrosine transaminase activity in the chick embryo. J Endocrinol 1981 Aug;90(2):193-200

Marín J, Rico ML, Salaices M: Interference of pentobarbitone with the contraction of vascular smooth muscle in goat middle cerebral artery. J Pharm Pharmacol 1981 Jun;33(6):357-61

Markey KA, Sze PY: Influence of adrenal epinephrine on postnatal development of tyrosine hydroxylase activity in the superior cervical ganglion. Dev Neurosci 1981;4(4):267-72

Märki F, Schenkel L, Petrack B, et al: Rapid conversion of somatostatin to active metabolite in human plasma. FEBS Lett 1981 May 5;127(1):22-4

Markstein R: Neurochemical effects of some ergot derivatives: a basis for their antiparkinson actions. J Neural Transm 1981;51(1-2):39-59

Marotte LR, Mark RF, Wye-Dvorak J: Retinotectal reorganization in goldfish-III. Effect of thyroxine. Neuroscience 1981;6(8):1591-600

Marple DN, Nachreiner RF, Pritchett JF, et al: The relationship of thyroxine secretion rate to growth of swine. J Anim Sci 1981 Mar;52(3):500-4

Marquis JK, Lippa AS, Pelham RW: Dopamine receptor alterations with aging in mouse and rat corpus striatum. Biochem Pharmacol 1981 Jul 1;30(13):1876-8

Marsden CD: Dopamine hypothesis in acute psychosis [letter] Br J Psychiatry 1981 Mar;138:269-70

Marshall SM, Kesson CM: Severe lithium poisoning. Drug Intell Clin Pharm 1981 Jul-Aug;15(7-8):598-9

Martin B, Rotten D, Jolivet A, et al: Binding of steroids by proteins in follicular fluid of the human ovary. J Clin Endocrinol Metab 1981 Aug;53(2):443-7

Martin BR, Balster RL, Razdan RK, et al: Behavioral comparisons of the stereoisomers of tetrahydrocannabinols. Life Sci 1981 Aug 10;29(6):565-74

Martin RH, Glass MR, Chapman C, et al: Suppression by bromocriptine of the serum lactalbumin peak associated with human lactogenesis. Clin Endocrinol (Oxf) 1981 Apr;14(4):363-6

Martín del Rio R: Gamma-aminobutyric acid system in rat oviduct. J Biol Chem 1981 Oct 10;256(19):9816-9

Martin-Du Pan R, Vallotton MB: Implications cliniques des données actuelles sur le contrôle neuropharmacologique des hormones antéhypophysaires. Schweiz Med Wochenschr 1980 Nov 29;110(48):1784-1814 (346 ref.) (Eng. Abstr.) **(Fre)**

Martineau J, Garreau B, Barthelemy C, et al: Effects of vitamin B6 on averaged evoked potentials in infantile autism. Biol Psychiatry 1981 Jul;16(7):627-41

Martínez AB, Gómez-Brenes RA, Bressani R: Relación del contenido de lisina y triptofaro con el de zeina, durante la germinación del grano de maiz, y su posible vinculación con el ciclo vegetativo de la planta. Arch Latinoam Nutr 1980 Dec;30(4):607-33 (Eng. Abstr.) **(Spa)**

Martini A, Bonollo L, Nicolis FB, et al: Effects of caroxazone, a reversible monoamine oxidase inhibitor, on the pressor response to oral tyramine in man. Br J Clin Pharmacol 1981 Jun;11(6):611-5

Martini A, Bonollo L, Nicolis FB, et al: Effects of caroxazone, a reversible monoamine oxidase inhibitor, on the pressor response to intravenous tyramine in man. Br J Clin Pharmacol 1981 Jun;11(6):605-10

Marwaha J, Hoffer B, Freedman R: Electrophysiological actions of neurotensin in rat cerebellum. Regul Pept 1980 Oct;1(2):115-25

Mashkovskii MD, Gorkin VZ, Asnina VV, et al: Vliianie pirazidola i depranila na monoaminoksidazu kishechnika krysy. Biull Eksp Biol Med 1981 Mar;91(3):309-11 (Eng. Abstr.) **(Rus)**

Mason WD, Amick EN: High-pressure liquid chromatographic analysis of phenylpropanolamine in human plasma following derivatization with O-phthalaldehyde. J Pharm Sci 1981 Jun;70(6):707-9

Massé G: Psychopathie ou déséquilibre psychique. Infirm Fr 1981 Jun;(226):3-5 **(Fre)**

Massenti MF, Scarlata G, Nastasi A: Beta-glucuronidase activity in Enterobacteriaceae. Boll Ist Sieroter Milan 1981;60(1):26-30

Massotti M, Guidotti A, Costa E: Characterization of benzodiazepine and gamma-aminobutyric recognition sites and their endogenous modulators. J Neurosci 1981 Apr;1(4):409-18

Massotti M, Mazzari S, Schmid R, et al: Endogenous inhibitors of Na+-independent [3H]GABA binding to crude synaptic membranes. Neurochem Res 1981 May;6(5):551-65

Materia A, Modlin IM, Albert D, et al: The effect of somatostatin and 16,16-dimethyl-prostaglandin E2 on bombesin-stimulated canine gastric acid, plasma gastrin and pancreatic polypeptide secretion. Regul Pept 1981 Jan;1(4):297-305

Mathers DA, Barker JL: GABA and muscimol open ion channels of different lifetimes on cultured mouse spinal cord cells. Brain Res 1981 Jan 5;204(1):242-7

Mathison RD, Dreifuss JJ: The neurohypophysial GABA system. Adv Biochem Psychopharmacol 1981;29:343-50 (23 ref.)

Mathur S, Hall JN: Phenothiazine withdrawal in schizophrenics in a hostel [letter] Br J Psychiatry 1981 Mar;138:271-2

Matiushin AI, Naumov IuI: O vozmozhnoi roli nukleaz v mekhanizme indutsiruiushchego éffekta fenobarbitala. Farmakol Toksikol 1981 Mar-Apr;44(2):208-10 (Eng. Abstr.) **(Rus)**

Matsui H: Adrenal medullary secretory response to pontine and mesencephalic stimulation in the rat. Neuroendocrinology 1981 Aug;33(2):84-7

Matsukawa S, Mihara S, Hosoya T: Thyrotropin-dependence of the distribution of peroxidase in rat thyroid gland. Tohoku J Exp Med 1981 Apr;133(4):431-43

Matsuki A, Wakayama S, Tsubo T, et al: [Effects of GSH on endocrine function and lysosomal enzyme levels during cardiopulmonary bypass in man (author's transl)] Masui 1981 Feb;30(2):150-7 (Eng. Abstr.) **(Jpn)**

Matsuki A, Oyama T: Effects of extracorporeal circulation on plasma cholinesterase activity in man. Agressologie 1981;22(2):79-81

Matsumoto M, Kimura K, Fujisawa A, et al: Diurnal variations in monoamine contents in discrete brain regions of the mongolian gerbil (Meriones unguiculatus). J Neurochem 1981 Sep;37(3):792-4

Matsuo H, Kangawa K, Mizuno K, et al: [New endogenous 'big' enkephalins (author's transl)] Tanpakushitsu Kakusan Koso 1981 Feb;26(2):102-14 (44 ref.) **(Jpn)**

Matsuoka H, Mulrow PJ, Franco-Saenz R, et al: Effects of beta-lipotropin and beta-lipotropin-derived peptides on aldosterone production in the rat adrenal gland. J Clin Invest 1981 Sep;68(3):752-9

Mattice WL, Robinson RM: Conformational properties of central nervous system myelin basic protein, beta-endorphin, and beta-lipotropin in water and in the presence of anionic lipids. Biopolymers 1981 Jul;20(7):1421-34

AUTHOR SECTION

Mattila J, Männistö PT: Studies on the role of the pineal gland in the regulation of TSH secretion in postpuberal male rats. Horm Res 1981; 14(1):24-35

Mattsson JL, Young RW, Curran CR, et al: Acute and chronic propylene glycol dinitrate exposure in the monkey. Aviat Space Environ Med 1981 Jun;52(6):340-5

Matzke GR, Sawchuk RJ: Elevated serum phenytoin concentrations in a uremic patient when measured by enzyme-multiplied immunoassay. Drug Intell Clin Pharm 1981 May;15(5):386-8

Maugh TH 2d: Biochemical markers identify mental states [news] Science 1981 Oct 2;214(4516):39-41

May SW, Phillips RS, Mueller PW, et al: Dopamine beta-hydroxylase. Comparative specificities and mechanisms of the oxygenation reactions. J Biol Chem 1981 Aug 25;256(16):8470-5

Mayer ML: Inhibitory actions of amino acids in the preoptic-anterior hypothalamus of the rat. Exp Brain Res 1981;43(2):154-8

Mayorga LS, Bertini F: Acid hydrolases in the epididymis of normal, castrated, vasectomized, cryptorchid and cryptepididymal rats. Int J Androl 1981 APr;4(2):208-19

Meden-Vrtovec H: Posredni uticaj sintetskog LHRH na karakteristike cervikalog sekreta. Jugosl Ginekol Opstet 1980 May-Aug; 20(3-4):236-42 (Eng. Abstr.) (Ser)

Medrano E, Iujvidin S, Mordoh J: Synthesis of phosphatidyl-dCMP in human lymphocytes and its enhancement by chlorpromazine. Eur J Biochem 1981 May 15;116(2):249-53

Medvecký J, Medvecká E: Noveril bei Depressionen. Agressologie 1979; 20(D):311-2 (Eng. Abstr.) (Ger)

Medvedev OS, Val'dman AV, Titov MI: Vliianie enkefalinov na protsessy tsentral'noi reguliatsii gemodinamiki. Biull Eksp Biol Med 1981 May; 91(5):574-6 (Eng. Abstr.) (Rus)

Megens AA, Cools AR: Presence of a particular subpopulation of dopamine receptors within the septal nuclei: a behavioural study on cats. Eur J Pharmacol 1981 May 8;71(2-3):247-58

Meidan R, Koch Y: Binding of luteinizing hormone-releasing hormone analogues to dispersed rat pituitary cells. Life Sci 1981 Apr 27; 28(17):1961-7

Meites J, Huang HH, Steger RW: Differences in negative and positive feedback of gonadal steroids on release of gonadotropins and prolactin in young and old rats. Exp Brain Res 1981;Suppl 3:151-7

Mejsnar J, Jirák E: Thermogenic response as the function of extravascular influx of infused noradrenaline. Experientia 1981 May 15;37(5):482-3

Mellanby J, Gray JA, Quintero S, et al: Septal driving of hippocampal theta rhythm: a role for gamma-aminobutyrate in the effects of minor tranquillizers? Neuroscience 1981;6(7):1412-21

Melloni GF, Melloni R, Minoja GM, et al: Clinical tolerability of ibopamine hydrochloride (SB 7505). Eur J Clin Pharmacol 1981; 19(6):409-11

Mellström B, Bertilsson L, Säwe J, et al: E- and Z-10-hydroxylation of nortriptyline: relationship to polymorphic debrisoquine hydroxylation. Clin Pharmacol Ther 1981 Aug;[illegible]:189-93

Mel'nichenko GA, Bukhteeva NF, Kapeliovich MR, et al: Parlodel v lechenii gigantomastii. Sov Med 1981;(5):114-5 (Rus)

Meltzer HY, Simonovic M: Effect of 3-PPP, a putative dopamine autoreceptor agonist, on rat serum prolactin levels. Life Sci 1981 Jul 6;29(1):99-105

Meltzer HY: Prolactin and psychiatry. Am J Psychiatry 1981 Sep; 138(9):1203-6

Meltzer HY, Busch DA, Creese IR, et al: Effect of intramuscular chlorpromazine on serum prolactin levels in schizophrenic patients and normal controls. Psychiatry Res 1981 Aug;5(1):95-105

Melzacka M, Rurak A, Vetulani J: Preliminary study of the biotransformation of two new drugs, trazodone and etoperidone. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):551-6

Mendlewicz J: Responders and non-responders to lithium therapy. Some potential biological indicators. Bibl Psychiatr 1981;(161):63-8 (39 ref.)

Menniti FS, Baum MJ: Differential effects of estrogen and androgen on locomotor activity induced in castrated male rats by amphetamine, a novel environment, or apomorphine. Brain Res 1981 Jul 6;216(1):89-107

Menniti FS, Erskine MS, Baum MJ: Persistence of dihydrotestosterone inhibition of lordosis in estrogen-primed rats fed a tryptophan-deficient diet. Brain Res Bull 1981 Jul;7(1):1-4

Menon GN, Norris BJ: Simultaneous determination of hydroxyzine hydrochloride and benzyl alcohol in injection solutions by high-performance liquid chromatography. J Pharm Sci 1981 Jun; 70(6):697-8

Menuck M, Voineskos G: Rapid parenteral treatment of acute psychosis. Compr Psychiatry 1981 Jul-Aug;22(4):351-61 (69 ref.)

Mertvetsov NP: Mnozhestvennye formy tirozinaminotransferazy v kletkakh krys i ikh rol' v gomeostaze kletki. Vopr Med Khim 1981 Mar-Apr;27(2):154-66 (Eng. Abstr.) (Rus)

Messalli E, Quirino R, Ricciardi I, et al: La bromocriptina nel trattamento della anovulazione normoprolattinemica. Riv Ital Ginecol 1980; 59(2-3):111-8 (Ita)

Mesulam MM, Dichter M: Concurrent acetylcholinesterase staining and gamma-aminobutyric acid uptake of cortical neurons in culture. J Histochem Cytochem 1981 Feb;29(2):306-8

Meyer FP, Walther H, Kühne GE: Uber den Einfluss von Thioridazin auf kognitive, psychomotorische und Reaktionsleistungen bei Patienten mit dysthym-depressivem Syndrom. Pharmacopsychiatria 1981 May; 14(3):94-9 (Ger)

Meyerson BJ: Comparison of the effects of beta-endorphin and morphine on exploratory and socio-sexual behaviour in the male rat. Eur J Pharmacol 1981 Feb 19;69(4):453-63

Mezhiborskaia NA: Reaktivnye izmeneniia kapilliarov sosudistykh tel mozga starykh zhivotnykh. Arkh Anat Gistol Embriol 1981 Apr; 80(4):24-31 (Eng. Abstr.) (Rus)

Michel K, Kolakowska T: A survey of prescribing psychotropic drugs in two psychiatric hospitals. Br J Psychiatry 1981 Mar;138:217-21

Michel T, Hoffman BB, Lefkowitz RJ, et al: Different sedimentation properties of agonist- and antagonist-labelled platelet alpha 2 adrenergic receptors. Biochem Biophys Res Commun 1981 Jun 16;100(3):1131-6

Michels RC, Ober KP, Hennessy JF: Measurement of active ion transport in man. Utilizing intact human erythrocytes. Ann Clin Lab Sci 1981 Mar-Apr;11(2):158-64

Midha KK, Charette C, McGilveray IJ, et al: Application of GLC-AFID and GLC-MS procedures to analysis of plasma in suspected cases of psychotropic drug overdose. Clin Toxicol 1981 Jun;18(6):713-29

Midtgård U, Bech C: Responses to catecholamines and nerve stimulation of the perfused rete tibiotarsale and associated blood vessels in the hind limb of the Mallard (Anas platyrhynchos). Acta Physiol Scand 1981 May;112(1):77-81

Migliaccio GP, Byrn SR: Comparisons of rotamer populations of nialamide, azaperone, and chloroquine in solid state and in solution. J Pharm Sci 1981 Mar;70(3):284-7

Migulla H, Mack H: Eine modifizierte fluorimetrische Methode zur Bestimmung von Propranolol in Humanplasma] Pharmazie 1981 Jun; 36(6):443-4 (Ger)

Millan MJ, Tsang YF, Prezewlocki R, et al: The influence of foot-shock stress upon brain, pituitary and spinal cord pools of immunoreactive dynorphin in rats. Neurosci Lett 1981 Jun 12;24(1):75-9

Millar TJ, Unsicker K: Catecholamine-storing cells in the adrenal medulla of the pre- and postnatal rat. Acetylcholinesterase as a means for early discrimination of cell types. Cell Tissue Res 1981;217(1):155-70

Miller A, Costa M, Furness JB, et al: Substance P immunoreactive sensory nerves supply the rat iris and cornea. Neurosci Lett 1981 May 29; 23(3):243-9

Miller ME, Garland WA, Min BH, et al: Clonazepam acetylation in fast and slow acetylators. Clin Pharmacol Ther 1981 Sep;30(3):343-7

Miller RJ: Peptides as neurotransmitters: focus on the enkephalins and endorphins. Pharmacol Ther [B] 1981;12(1):73-108 (214 ref.)

Milutinovic S: Psihofarmaci i bubreg. Lijec Vjesn 1980;102(11):647-51 (Eng. Abstr.) (Scr)

Minaire Y, Forichon J, Dallevet G, et al: Combined effects of cold and somatostatin on glucose kinetics in dogs. Eur J Applied Physiol 1981; 46(3):249-59

Minami M, Mori K, Nagatsu T: The effect of light exercise on the plasma superoxide dismutase activity and on the plasma noradrenaline concentration. Ind Health 1981;19(2):133-8

Minchin RF, Ilett KF: Comparative uptake of quinine and quinidine in rat lung. J Pharm Pharmacol 1981 Jul;33(7):464-6

Mineeva MF, Tümmler D, Kuznetsova EA, et al: Povyshenie srodstva tirozingidroksilazy gipotalamusa k tirozinu kak rezul'tat vozdeistviia dofamina na sinaptosomal'nuiu membranu. Dokl Akad Nauk SSSR 1981; 258(2):501-4 (Rus)

Minegishi A, Fukumori R, Satoh T, et al: Interaction of lithium and disulfiram in hexobarbital hypnosis: possible role of the 5-HT system. J Pharmacol Exp Ther 1981 Aug;218(2):481-7

Minenko AN, Kiselev GV, Bergman IU: Obmen fosfolipidov pri desensitizatsii Gladkomyshechnogo sloia ileuma morskikh svinok atsetilkholinom i veshchestvom p. Ukr Biokhim Zh 1980 Sep-Oct; 52(5):577-81 (Eng. Abstr.) (Rus)

Minnear FL, Barrie PS, Malik AB: Effects of epinephrine and norepinephrine infusion on lung fluid balance in sheep. J Appl Physiol 1981 Jun;50(6):1353-7

Minota S, Dun NJ, Karczmar AG: Substance P-induced depolarization in sympathetic neurons: not simple K-inactivation. Brain Res 1981 Jul 6;216(1):224-8

Mioduszewski R, Critchlow V: Marked and selective suppression of prolactin secretion after interruption of neural connections of the medial basal hypothalamus of the rat. Brain Res 1981 Jul 6;216(1):35-44

Mirmiran M, van de Poll NE, Corner MA, et al: Suppression of active sleep by chronic treatment with chlorimipramine during early postnatal development: effects upon adult sleep and behavior in the rat. Brain Res 1981 Jan 5;204(1):129-46

Mirro MJ: Effects of quinidine, procainamide and disopyramide on automaticity and cyclic AMP content of guinea-pig atria. J Mol Cell Cardiol 1981 Jul;13(7):641-53

Mishra KP, [illegible] LD, Singh BB: Effect of dielectric discharge on drug treated mammalian cells. Indian J Exp Biol 1981 Jun;19(6):520-3

Mishra R, Leith NJ, Steranka L, et al: The noradrenaline receptor coupled adenylate cyclase system in brain. Lack of modification by changes in the availability of serotonin.

AUTHOR SECTION

Naunyn Schmiedebergs Arch Pharmacol 1981 Jun;316(3):218–24

Misionzhnik EIu, Vertogradova OP, Krasnov VN, et al: Nekotorye osobennosti izmeneniia urovnia adrenergicheskikh i serotoninergicheskikh pokazatelei u bol'nykh s depressivnymi sostoianiiami. Zh Nevropatol Psikhiatr 1981;81(4):543–51 (Eng. Abstr.) (Rus)

Misler S, Hurlbut WP: Tests of an electrostatic screening hypothesis of the inhibition of neurotransmitter release by cations at the frog neuromuscular junction. Biophys J 1980 Jul;31(1):9–30

Mitchell DB, Acosta D: Evaluation of the cytotoxicity of tricyclic antidepressants in primary cultures of rat hepatocytes. J Toxicol Environ Health 1981 Jan;7(1):83–92

Mitchell SC, Waring RH: A comparison of the in vivo metebolism of phenothiazine and promazine in the neonatal guinea pig. Biol Neonate 1981;39(5–6):285–9

Mitsuma T, Nogimori T: [Measurement of free thyroxine in serum with radioimmunoassay (author's transl)] Horumon To Rinsho 1981 Jan; 29(1):127–31 (Jpn)

Miyabo S, Ooya E, Hayashi S: Effect of intrahypothalamic implantation of cortisone acetate on the onset of circadian corticosterone rhythm in neonatal female rats. Neuroendocrinology 1981 Jul;33(1):47–51

Miyauchi T, Kikuchi K, Satoh S: Further studies on the potentiating effect of lithium chloride on methamphetamine-induced stereotypy in mice. Jpn J Pharmacol 1981 Feb;31(1):61–8

Miyazaki K, Arita T, Oka I, et al: High-performance liquid chromatographic determination of haloperidol in plasma. J Chromatogr 1981 May 8;223(2):449–53

Mizuno A, Asakura T: Effect of aminooxyacetic acid on endogenous GABA release from rat retina. Exp Eye Res 1981 Aug;33(2):197–202

Mizuochi T, Nishimura Y, Kato K, et al: Comparative studies of asparagine-linked oligosaccharide structures of rat liver microsomal and lysosomal beta-glucuronidases. Arch Biochem Biophys 1981 Jun; 209(1):298–303

Mizutani T, Wagi K, Terai Y: Estimation of diazepam adsorbed on glass surfaces and silicone-coated surfaces as models of surfaces of containers. Chem Pharm Bull (Tokyo) 1981 Apr;29(4):1182–3

Modak AT, Stavinoha WB, Deam AP: Effect of short electromagnetic pulses on brain acetylcholine content and spontaneous motor activity of mice. Bioelectromagnetics 1981;2(1):89–92

Modlin IM, Lamers CB, Walsh JH: Stimulation of canine pancreatic polypeptide, gastrin, and gastric acid secretion by ranatensin, litorin, bombesin nonapeptide and substance P. Regul Pept 1981 Jan;1(4):279–88

Moggi G, Giampietro O, Coluccia A, et al: Preliminari risultati sull'induzione di gravidanza con l'associazione farmacologia ciclofenile-bromocriptina. Minerva Ginecol 1981 Jun;33(6):532–3 (Ita)

Moglia A, Tartara A, Arrigo A, et al: Chronic treatment with phenytoin in rats: effects of peripheral nervous system. Farmaco [Sci] 1981 Jun; 36(6):419–24

Möhler H, Burkard WP, Keller HH, et al: Benzodiazepine antagonist Ro 15–1788: binding characteristics and interaction with drug-induced changes in dopamine turnover and cerebellar cGMP levels. J Neurochem 1981 Sep;37(3):714–22

Moiseeva NI: Sovremennye predstavleniia o mekhanizmakh reguliatsii i tselevoi funktsii sna. Usp Fiziol Nauk 1981 Jun–Sep;12(3):86–105 (197 ref.) (Rus)

Molcan J, Guensberger E: Verhältniss der pharmakotherapie und psychotherapie bei psychosen. Agressologie 1979;20(D):283–5 (Eng. Abstr.) (Ger)

Molcan J, Caplová T, Koníková M, et al: Dibenzepin (Noveril) in Hohen dosen bei der Behandlung der Depressionen. Agressologie 1979; 20(D):307–9 (Eng. Abstr.) (Ger)

Molina VA, Orsingher OA: Effects of Mg-pemoline on the central catecholaminergic system. Arch Int Pharmacodyn Ther 1981 May; 251(1):66–79

Møller SE, Kirk L: Decreased tryptophan availability in endogenous depression caused by disturbed plasma leucine clearance. Prog Neuropsychopharmacol 1981;5(3):277–9

Møller SE, Reisby N, Ortmann J, et al: Relevance of tryptophan and tyrosine availability in endogenous and 'non-endogenous' depressives treated with imipramine or clomipramine. J Affective Disord 1981 Sep; 3(3):231–44

Momose K, Gomi Y: [Studies on isolated smooth muscle cells. VI. Dispersion procedures for acetylcholine-sensitive smooth muscle cells of guinea pig (author's transl)] Nippon Heikatsukin Gakkai Zasshi 1980 Mar;16(1):29–36 (Eng. Abstr.) (Jpn)

Monnet F, Lichtensteiger W: Endogenous alpha-melanotropin and central dopamine systems in physical and psychological stress. Exp Brain Res 1981;42(2):203–11

Montgomery SA, McAuley R, Montgomery DB, et al: Pharmacokinetics and efficacy of maprotiline and amitriptyline in endogenous depression: a double-blind controlled trial. Clin Ther 1980;3(4):292–310

Moodbidri SB, Vijayalakshmi S, Bandivdekar AH, et al: Inhibition of hypothalamic GnRH synthesis by inhibin. Experientia 1981 May 15; 37(5):525–6

Morel-Maroger A: Tiapride et stéréotypies verbales ou motrices. Sem Hop Paris 1981 Apr 18–25;57(15–16):825–9 (Eng. Abstr.) (Fre)

Morelli M, Imperato A, Porceddu ML, et al: Role of dorsal mesencephalic reticular formation and deep layers of superior colliculus in turning behaviour elicited from the striatum. Brain Res 1981 Jun 29; 215(1–2):337–41

Moretti A, Caccia C, Martini A, et al: Effect of caroxazone, a new antidepressant drug, on monoamine oxidases in healthy volunteers. Br J Clin Pharmacol 1981 May;11(5):511–5

Morfei A, Burducea O, Neuman R, et al: Investigations concerning the action of serveral chemical and biological agents on HBsAg. Virologie 1980 Oct–Dec;31(4):273–8

Morgan AA: Cholinesterase problems arising in a plant manufacturing tri-aryl phosphates. J Soc Occup Med 1981 Jul;31(3):119–22

Morgan HG: Management of suicidal behaviour. Br J Psychiatry 1981 Mar;138:259–60

Morgenstern R: Kainic acid induced lesion of ventral tegmental area: locomotor effect of apomorphine. Acta Biol Med Ger 1980; 39(8–9):911–5

Mori K, Seino Y, Itoh Z, et al: Motilin release by intravenous infusion of nutrients and somatostatin in conscious dogs. Regul Pept 1981 Jan; 1(4):265–70

Mori T: Effects of various membrane phospholipid-interacting drugs on three species of multifunctional protein kinases. Kobe J Med Sci 1981 Apr;27(2):77–89

Möricke R, Schuster E, Caruso M: Metabolische Auswirkungen der i.v. Noradrenalingabe bei Stoffwechselgesunden. Z Gesamte Inn Med 1981 Jul 1;36(13):433–43 (Eng. Abstr.) (Ger)

Morier E, Fermandjian S, Lhoste JM, et al: Conformational analysis of pGlu-His-Amph and pGlu-His-Pro-Amph related to their central nervous system activity. Biochimie 1981 Jun;63(6):495–505

Morin AM, Tanaka IA, Wasterlain CG: Norharman inhibition of [3H]diazepam binding in mouse brain. Life Sci 1981 May 18; 28(20):2257–63

Morley JE, Tuck ML, Mayes DM, et al: Thyrotropin-releasing hormone increases plasma norepinephrine in man. Horm Res 1981;14(1):18–23

Moroder L, Gemeiner M, Göhring W, et al: Totalsynthese von Somatostatin-28. Hoppe Seylers Z Physiol Chem 1981 Jun; 362(6):697–716 (Eng. Abstr.) (Ger)

Morot-Gaudry Y, Bourgoin S, Hamon M: Kinetic characteristics of newly synthesized 3H-5-HT in the brain of control and reserpinized mice. Evidence for the heterogeneous distribution of 5-HT in serotoninergic neurons. Naunyn Schmiedebergs Arch Pharmacol 1981 Jul;316(4):311–6

Morris LA, Kanouse DE: Consumer reactions to the tone of written drug information. Am J Hosp Pharm 1981 May;38(5):667–71

Morris MD, Gebhart GF: Antianxiety agents and emotional behavior, an information processing analysis. Prog Neuropsychopharmacol 1981; 5(3):219–40

Moss J, Manganiello VC, Hom BE, et al: Effects of d- and l-propranolol on the responsiveness of human fibroblasts to choleragen and prostaglandin E1. Biochem Pharmacol 1981 Jun 1;30(11):1263–9

Mougeot G, Hugues FC, Julien D, et al: Influence of propranolol and acebutolol on isoprenaline-induced changes in heart rate and peripheral blood flow in man. Arch Int Pharmacodyn Ther 1981 May; 251(1):116–25

Moult PJ, Dacie JE, Rees LH, et al: Prolactin pulsatility in patients with gonadal dysfunction. Clin Endocrinol (Oxf) 1981 Apr;14(4):387–94

Mount ME, Oehme FW: Diagnostic criteria for carbaryl poisoning in sheep. Arch Environ Contam Toxicol 1981 Jul;10(4):483–95

Mourre C, Calas A, Gonella J: Radioautographic study of uptake and storage of indoleamines in the rabbit enterochromaffin cells. Neurosci Lett 1981 May 29;23(3):251–6

Mousa S, Mullet D, Couri D: Sensitive and specific high performance liquid chromatographic method for methionine and leucine enkephalins. Life Sci 1981 Jul 6;29(1):61–8

Mudge AW: Effect of chemical environment on levels of substance P and somatostatin in cultured sensory neurones. Nature 1981 Aug 20; 292(5825):764–7

Mueller RA, Lundberg DB, Breese GR: Alteration of aminophylline-induced respiratory stimulation by perturbation of biogenic amine systems. J Pharmacol Exp Ther 1981 Sep;218(3):593–9

Muir WW: Drugs used to produce standing chemical restraint in horses. Vet Clin North Am [Large Anim Pract] 1981 May;3(1):17–44 (128 ref.)

Muller E, Dowling RH: Prolactin and the small intestine. Effect of hyperprolactinaemia on mucosal structure in the rat. Gut 1981 Jul; 22(7):558–65

Müller H: Psychopharmaka: Wohltat, Gefahr, Missbrauch. Med Klin 1981 Jan 2;76(1):1 (Ger)

Müller TH, Unsicker K: High-performance liquid chromatography with electrochemical detection as a highly efficient tool for studying catecholaminergic systems. I. Quantification of noradrenaline, adrenaline and dopamine in cultured adrenal medullary cells. J Neurosci Methods 1981 Jun;4(1):39–52

Müller-Lissner SA, Will N, Müller-Duysing W, et al: Schwimmkapseln mit langsamer Wirkstoffabgabe. Eine neue orale Darreichungsform von Medikamenten. Dtsch Med Wochenschr 1981 Sep 4;106(36):1143–7 (Eng. Abstr.) (Ger)

Münz H, Stumpf WE, Jennes L: LHRH systems in brain of platyfish.

AUTHOR SECTION

Brain Res 1981 Sep 21;221(1):1-13

Muratov VD, Bulaev VM: Prostaglandiny i nervnaia sistema (obzor literatury). Farmakol Toksikol 1981 Jan-Feb;44(1):121-8 (117 ref.) (Rus)

Murphy WA, Meyers CA, Coy DH: Potent, highly selective inhibition of growth hormone secretion by position 4 somatostatin analogs. Endocrinology 1981 Aug;109(2):491-5

Murray J, Dunn G, Williams P, et al: Factors affecting the consumption of psychotropic drugs. Psychol Med 1981 Aug;11(3):551-60

Murrin LC: Neurotransmitter receptors: neuroanatomical localization through autoradiography. Int Rev Neurobiol 1981;22:111-71 (379 ref.)

Muscettola G, Potter WZ, Gordon EK, et al: Methodological issues in the measurement of urinary MHPG. Psychiatry Res 1981 Jun; 4(3):267-76

Myers R, Rogers MA, Hume SP: Histochemical evidence for radiation enhancement of lysosomal response following hyperthermia of tail cartilage in baby rat. Radiat Res 1981 Aug;87(2):329-40

Myrzakhanov NM: Izmeneniia limfotoka pri refleksakh s limfaticheskikh sosudov. Fiziol Zh SSSR 1981 Mar;67(3):410-3 (Rus)

N

Nabeshima T, Fujimori K, Ho IK: Effect of acute or chronic pentobarbital administration on the steady state levels and the turnover rates of catecholamines in discrete brain areas of mice. Prog Neuropsychopharmacol 1981;5(2):121-8

Nabeshima T, Fontenot J, Ho IK: Effects of chronic administration of pentobarbital or morphine on the brain microsomal cytochrome P-450 system. Biochem Pharmacol 1981 May 15;30(10):1142-5

Nadi NS, Head R, Grillo M, et al: Chemical deafferentation of the olfactory bulb: plasticity of the levels of tyrosine hydroxylase, dopamine and norepinephrine. Brain Res 1981 Jun 1;213(2):365-77

Naftchi NE, Abrahams SJ, St. Paul HM, et al: Substance P and leucine-enkephalin changes after chordotomy and morphine treatment. Peptides (Fayetteville) 1981;2 Suppl 1:61-70

Naftchi NE, Abrahams SJ, Crain SM, et al: Presence of leucine-enkephalin in organotypic explants of fetal mouse spinal cord. Peptides (Fayetteville) 1981;2 Suppl 1:57-60

Nagao M, Takahashi Y, Yahagi T, et al: Mutagenicities of gamma-carboline derivatives related to potent mutagens found in tryptophan pyrolysates. Carcinogenesis 1980 May;1(5):451-4

Nagasawa T, Utagawa T, Goto J, et al: Syntheses of L-tyrosine-related amino acids by tyrosine phenol-lyase of Citrobacter intermedius. Eur J Biochem 1981 Jun;117(1):33-40

[illegible]gel-Hiemke M, Schümann HJ: A radioenzymatic method for determination of normetanephrine in blood plasma. J Biochem Biophys Methods 1981 Jun;4(5-6):255-9

Nag[illegible]iemke M, Schümann HJ: A sensitive radioenzymatic assay for dihydroxymandelic acid, dihydroxypenylglycol and dihydroxyphenylacetic acid . J Biochem Biophys Methods 1981 Jun; 4(5-6):261-70

Nagele RG, Piet[illegible]o JF, Lee H, et al: Diazepam-induced neural tube closure defects i[illegible]planted early chick embryos. Teratology 1981 Jun; 23(3):343-9

Nagy SU, Csaba G: Lo[illegible]lasting amplification and deformation of thyroid receptors after thyro[illegible]pin (TSH) and gonadotropin (GTH) treatment of chickens in the fo[illegible]l period. Acta Physiol Acad Sci Hung 1980; 56(3):303-7

Nagy SU, Csaba G: Dose-dependence of the thyrotropin (TSH) receptor damaging effect of gonadotropin in the newborn rats. Acta Physiol Acad Sci Hung 1980;56(4):417-20

Náhunek K, Svestka J, C[illegible]ková E: Further clinical experiences with optical isomers of the L and D clorothepin. Agressologie 1979; 20(D):275-8

Náhunek K, Svestka J, Ceskovà E: K otázce rozdilnosti terapeutických odpovédi po jednotlivých neurolepticich ve srovnáni s perphenazinem u schizofrennich nemocných. Cesk Psychiatr 1981 Feb;77(1):25-30 (Eng. Abstr.) (Cze)

Naik DR, Sar M, Stumpf WE: Immunohistochemical localization of enkephalin in the central nervous system and pituitary of the lizard, Anolis carolinensis. J Comp Neurol 1981 Jun 1;198(4):583-601

Nakagawa T, Sh'noda N, Matsumura K, et al: [Studies on free thyroxine measurement with radioimmunoassay kit -evaluation of GammaCoat free T4 kit (author's transl)] Kaku Igaku 1981 Apr;18(3):385-400 (Jpn)

Nakahara T: [Emotional stress and biochemical responses of completely recovered manic depressive patients (author's transl)] Seishin Shinkeigaku Zasshi 1981;83(5):263-74 (Jpn)

Nakai T, Yamada R: [Studies on new radioenzymatic assay kit for catecholamine determination and plasma levels of catecholamines (author's transl)] Rinsho Byori 1980 Sep;28(9):915-9 (Jpn)

Nakamura K, Nakamura K: Influence of sino-aortic baroreceptor denervation on catecholamines, catecholamine-synthesizing enzymes and choline acetyltransferase activity in the brainstem nuclei of the rat. Jpn J Pharmacol 1981 Feb;31(1):95-105

Nakamura K: Recent advances in psychotropic drugs in the Japanese pharmaceutical industry. Rev Pure Appl Pharmacol Sci 1980 Oct-Dec; 1(4):357-80 (84 ref.)

Nakamura S, Tsai CT, Iwama K: Antagonizing effects of haloperidol and bicuculline on inhibition of neurons of the substantia nigra, pars compacta. Exp Neurol 1981 Jul;73(1):304-9

Nakao K, Yoshimasa T, Oki S, et al: Presence of dynorphin-like immunoreactivity in rat pituitary gland and hypothalamus. Regul Pept 1981 Jun;2(3):201-8

Nakata K, Kurahashi K: Effects of C-terminal octapeptide of cholecystokinin and prostaglandins on adrenergic functions in the guinea-pig gallbladder and sphincter of Oddi. Jpn J Pharmacol 1981 Feb;31(1):77-83

Nakaya H, Kanno M, Kenda K, et al: [Electrophysiologic effects of calcium channel blocking agents on the sinus node function in anesthetized dogs (author's transl)] Nippon Yakurigaku Zasshi 1980 Nov;76(8):697-707 (Eng. Abstr.) (Jpn)

Nanopoulos D, Maitre M, Belin MF, et al: Autoradiographic and immunocytochemical evidence for the existence of GABAergic neurons in the nucleus raphe dorsalis—possible existence of neurons containing 5HT and glutamate decarboxylase. Adv Biochem Psychopharmacol 1981;29:519-25

Narita H, Ikezawa K, Sato M, et al: [Effects of diltiazem on cardiac function in the dog (author's transl)] Nippon Yakurigaku Zasshi 1981 Jan;77(1):51-9 (Eng. Abstr.) (Jpn)

Nash HL, Wallis DI: Effects of divalent cations on responses of a sympathetic ganglion to 5-hydroxytryptamine and 1,1-dimethyl-4-phenyl piperazinium. Br J Pharmacol 1981 Jul; 73(3):759-72

Nasjletti A, Malik KU: Renal kinin-prostaglandin relationship: implications for renal function. Kidney Int 1981 Jun;19(6):860-8 (73 ref.)

Nasjletti A, Malik KU: Interrelationships among prostaglandins and vasoactive substances. Med Clin North Am 1981 Jul;65(4):881-9 (60 ref.)

Nasr S, Daiguji M, Tong C, et al: Comparison of midday serum dopamine-beta-hydroxylase activity in depressed patients and normal controls. Commun Psychopharmacol 1980;4(4):263-7

Natelson BH, Tapp WN, Adamus JE, et al: Humoral indices of stress in rats. Physiol Behav 1981 Jun;26(6):1049-54

Nazar K: Zależność między wielkością zasobów węglowodanowych organizmu a reakcją neurohormonalną na wysilek fizyczny u człowieka. Pol Tyg Lek 1981 May 18;36(20):735-7 (Pol)

Neamtu M, Leucuta S: Étude physico-chemique de l'interaction du diazépam avec des excipients hydrophiles. Ann Pharm Fr 1980; 38(6):507-11 (Eng. Abstr.) (Fre)

Neatherlin JS, Kamp CW, Guthrie MD: Synaptic transmission within the central nervous system. J Neurosurg Nurs 1981 Jun;13(3):146-9

Nechiporuk TS, Vasil'ev AN, Parkhomets TI: Vliianie gidrazin-syl'fata na sostav lipidov v gomogenate i plazmaticheskikh membranakh pecheni krys. Ukr Biokhim Zh 1980 Sep-Oct;52(5):636-42 (Eng. Abstr.)(Rus)

Negishi K: Density of retinal catecholamine-accumulating cells in different-sized goldfish. Exp Eye Res 1981 Aug;33(2):223-32

Negro-Vilar A, Ojeda SR: Hypophysiotropic hormones of the hypothalamus. Int Rev Physiol 1981;24:97-156 (378 ref.)

Nehlig A, Lehr PR: Glucose and 3-hydroxybutyrate utilization by chick telencephalon during postnatal development. Experientia 1981 Jun; 37(6):553-5

Neild TO: The action of 5-hydroxytryptamine and possible 5-hydroxytryptamine antagonists on neurones of the guinea-pig submucous plexus. Gen Pharmacol 1981;12(4):281-4

Nester TJ: Propranolol and thyroxine metabolism [letter] Drug Intell Clin Pharm 1981 Feb;15(2):131-2

Nett TM, Crowder ME, Moss GE, et al: GnRH-receptor interaction. V. Down-regulation of pituitary receptors for GnRH in ovariectomized ewes by infusion of homologous hormone. Biol Reprod 1981 Jun; 24(5):1145-55

Neufeld RW, Broga MI: Evaluation of information sequential aspects of schizophrenic performance. II. Research strategies and methodological issues. J Nerv Ment Dis 1981 Sep;169(9):569-79 (77 ref.)

Neuvonen PJ, Tokola R, Kaste M: Cimetidine interaction with phenytoin [letter] Br Med J [Clin Res] 1981 Aug 15;283(6289):501

Newton DW, Fung EY, Williams DA: Stability of five catecholamines and terbutaline sulfate in 5% dextrose injection in the absence and presence of aminophylline. Am J Hosp Pharm 1981 Sep;38(9):1314-9

Nezhentsev MV: Vliianie gidrokortizona i kholinolitikov na ustoĭchivost' éritrotsitov krys k gipoosmoticheskomu gemolizu. Farmakol Toksikol 1981 Mar-Apr;44(2):188-91 (Eng. Abstr.) (Rus)

Nguyen-Legros J, Berger B, Alvarez C: High resolution radioautography of central dopaminergic fibers labelled in vitro with [3H]dopamine or [3H]norepinephrine. Brain Res 1981 Jun 1;213(2):265-76

Nichols BP, van Cleemput M, Yanofsky C: Nucleotide sequence of Escherichia coli trpE. Anthranilate synthetase component I contains no tryptophan residues. J Mol Biol 1981 Feb 15;146(1):45-54

Nichols DJ, Chevins PF: Effects of housing on corticosterone rhythm and stress responses in female mice. Physiol Behav 1981 Jul;27(1):1-5

AUTHOR SECTION

Nickolson VJ: Potentiation by Des–Tyr–gamma–endorphin on apomorphine–induced changes in rat open field behavior. Eur J Pharmacol 1981 Jun 10;72(1):77–81

Nickolson VJ: Detailed analysis of the effects of apomorphine and d–amphetamine on spontaneous locomotor behaviour of rats as measured in a TV–based, automated open–field system. Eur J Pharmacol 1981 Jun 10;72(1):45–56

Nieber K, Milenov K, Bergmann J, et al: Contractile response of longitudinal and circular smooth muscles of guinea pig stomach and ileum to substance P. Acta Biol Med Ger 1981;40(2):209–16

Nigro D, Enero MA: Cocaine facilitates the effects of alpha–agonists and antagonists on adrenergic neurotransmission. Gen Pharmacol 1981; 12(4):255–9

Nininger JE, Ingber P, Bryant SG: Hazards of mistaking haloperidol for diazepam [letter] Am J Psychiatry 1981 Aug;138(8):1130

Nirmala J, Sastry KS: Photodynamic breakdown of purine bases & nucleosides sensitized by methylene blue. Indian J Biochem Biophys 1980 Dec;17(6):488–9

Nishikawa T, Tanaka M, Kohno Y, et al: Involvement of noradrenergic and dopaminergic neurons in shock–induced jumping in rats. Eur J Pharmacol 1981 May 22;71(4):429–36

Nishikawa T, Saito M: Competitive nephelometric immunoassay of carbamazepine and its epoxide metabolite in patient blood plasma. J Pharmacobiodyn 1981 Jan;4(1):77–83

Nishimura C, Ida S, Kuriyama K: Alteration of GABA system in frog retina following short light and dark adaptations – a quantitative comparison with retinal taurine. Brain Res 1981 Aug 31;219(2):433–8

Nishino T, Lahiri S: Effects of dopamine on chemoreflexes in breathing. J Appl Physiol 1981 Apr;50(4):892–7

Niso R, Villani L, Contestabile A, et al: Biogenic amine terminals in the goldfish cerebellum and optic tectum: a fluorescence and autoradiographic study. Basic Appl Histochem 1981;25(2):113–9

Nistri A: New insights into the mechanism of action of inhibitory amino acids on frog spinal neurones. Adv Biochem Psychopharmacol 1981; 29:263–9

Nitsch C: Glutamate as a transmitter of the hippocampal commissural system. Adv Biochem Psychopharmacol 1981;29:97–104

Noe HN: Voiding dysfunction in the child with problem 'wetting'. JDBP 1980 Mar;1(1):29–33

Nomura S, Yamazaki K, Sawa Y, et al: Palmar skin potential reflex and serum dopamine–beta–hydroxylase activity of the aged. Folia Psychiatr Neurol Jpn 1981;35(1):3–9

Nomura Y, Okuma Y, Segawa T, et al: Comparison of synaptosomal and glial uptake of pipecolic acid and GABA in rat brain. Neurochem Res 1981 Apr;6(4):391–400

Nomura Y, Yotsumoto I, Oki K: Age–related changes in the central catecholaminergic function and its interaction with methamphetamine during postnatal life in the rat. J Pharm Pharmacol 1981 Apr;33(4):264–6

Nordström O, Bartfai T: 8–Br–cyclic GMP mimics activation of muscarinic autoreceptor and inhibits acetylcholine release from rat hippocampal slices. Brain Res 1981 Jun 1;213(2):467–71

Norman TR, Burrows GD, Bianchi GN, et al: Doxepin plasma levels and anxiolytic response. Int Pharmacopsychiatry 1980;15(4):247–52

Norton TR, Ohizumi Y, Shibata S: Excitatory effect of a new polypeptide (anthopleurin–B) from sea anemone on the guinea–pig vas deferens. Br J Pharmacol 1981 Sep;74(1):23–8

Nousaine DA: Hyperventilation versus bicarbonate therapy for alkalinization in tricyclic antidepressant overdose [letter] West J Med 1981 Aug;135(2):160–1

Nowak JZ, Bielkiewicz B: Effect of histamine H1– and H2–receptor agonists on gamma–aminobutyric acid (GABA) content in hypothalamus and striatum of the rat brain. Arch Immunol Ther Exp (Warsz) 1980;28(6):917–20

Nowik–Jurek M, Łańcucki J: Histamina i serotonina we krwi i skórze po oparzeniu drugiego stopnia u szczurów. Pol Tyg Lek 1981 May 4;36(18):631–5 (Eng. Abstr.) **(Pol)**

Nozaki M, Martin WR, Driver MB, et al: Use of gastric fistula rats for the study of sedative, hypnotic and antianxiety drugs. Drug Alcohol Depend 1981 Jun;7(3):221–31

Nutt RF, Holly FW, Homnick C, et al: Synthesis of thyrotropin–releasing hormone analogues with selective central nervous system effects. J Med Chem 1981 Jun;24(6):692–8

Nyakas C, Lévay G, Viltsek J, et al: Effects of neonatal ACTH4–10 administration on adult adaptive behavior and brain tyrosine hydroxylase activity. Dev Neurosci 1981;4(3):225–32

Nyfeler F, Fasel P, Walter P: Short–term stimulation of net glycogen production by insulin in rat hepatocytes. Biochim Biophys Acta 1981 Jun 11;675(1):17–23

O

Oberlander C, Hunt PF, Dumont C, et al: Dopamine independent rotational response to unilateral intranigral injection of serotonin. Life Sci 1981 Jun 8;28(23):2595–601

O'Brien RA, Schlosser W, Spirt NM, et al: Antagonism of benzodiazepine receptors by beta carbolines. Life Sci 1981 Jul 6;29(1):75–82

Ochs HR: Plasmaspiegelverhalten von Diazepam nach hohen Dosen in der Intensivmedizin. Anaesth Intensivther Notfallmed 1981 Jun; 16(3):143–4 (Eng. Abstr.) **(Ger)**

Ochs HR, Greenblatt DJ, Otten H: Disposition of oxazepam in relation to age, sex, and cigarette smoking. Klin Wochenschr 1981 Aug 17; 59([illegible]):899–903

O'Connor JE, Rejent TA: EMIT cannabinoid assay: confirmation by RIA and GC/MS. J Anal Toxicol 1981 Jul–Aug;5(4):168–73

O'Connor M: Pindolol in schizophrenia [letter] Med J Aust 1981 Apr 18;1(8):429

O'Connor PC, Slater P: Effect of cocaine on contractile responses to noradrenaline of canine isolated mesenteric vein. J Pharm Pharmacol 1981 Jan;33(1):55–8

O'Connor PC, Slater P: Effect of cocaine on noradrenaline contractions of mesenteric vein: pre or postjunctional mechanism? J Pharm Pharmacol 1981 Jan;33(1):58–60

Odintsova TI, Ermokhina TM, Krasheninnikov IA: Lokalizatsiia ostatkov tirozina v gistone H1 zarodyshei pshenitsy. Biokhimiia 1981 Jan; 46(1):162–71 (Eng. Abstr.) **(Rus)**

Oertel H, Kaliner M: The biologic activity of mast cell granules in rat skin: effects of adrenocorticosteroids on late–phase inflammatory responses induced by mast cell granules. J Allergy Clin Immunol 1981 Sep;68(3):238–45

Ogata N, Abe H: Further support for the postsynaptic action of substance P and its blockade with baclofen in neurons of the guinea–pig hypothalamus in vitro. Experientia 1981 Jul 15;37(7):759–61

Ogawa N, Yamawaki Y, Kuroda H, et al: Effects of bromocriptine on receptor binding of methionine–enkephalin. Neurosci Lett 1981 May 6;23(2):215–8

Ogborne WL: Interesting uses of beta blockers (3): Beta blockers in anxiety. Aust Fam Physician 1981 Jun;10(6):472–5

Oguchi K, Kobayashi S, Uesato T, et al: Studies on beta–phenylethylamine deamination by human placental monoamine oxidase. Jpn J Pharmacol 1981 Feb;31(1):7–14

O'Hara DS, Curfman GD, Trumbull CG, et al: The relation between reduced protein degradation and elevated adenosine 3',5'–monophosphate in isolated rat atria. Circ Res 1981 Sep; 49(3):609–17

Ohmi N, Bhargava MM, Arias IM: The effect of phenobarbital and 3'–methyl–N,N–dimethyl–4–aminoazobenzene administration on catalytic, binding and immunological properties of ligandin subunits in rat liver. Biochim Biophys Acta 1981 Jul;675(2):276–80

Ohta M: [On the National Institute of Hygienic Sciences standard (the Japanese Pharmacopoeia standard) 'Reserpine Reference Standard (control 761)' (author's transl)] Eisei Shikenjo Hokoku 1980;98:132–3 (Eng. Abstr.) **(Jpn)**

Ohta T, Isa M, Suzuki Y, et al: Formation of mutagens from tryptophan by the reaction with nitrite. Biochem Biophys Res Commun 1981 May 15;100(1):52–7

Oja SS, Korpi ER, Kontro P: Potassium–stimulated release of taurine, hypotaurine, and GABA from brain tissue in vitro. Adv Biochem Psychopharmacol 1981;29:175–81

Ojeda C, Rougier O, Tourneur Y: Effects of Cs on acetylcholine induced current. Is ik1 increased by acetylcholine in frog atrium? Pflugers Arch 1981 Jul;391(1):57–9

Okuma T: Differential sensitivity to the effects of psychotropic drugs: psychotics vs normals; Asian vs Western populations. Folia Psychiatr Neurol Jpn 1981;35(1):79–87

Okuno S, Fujisawa H: Inactivation of tyrosine 3–monooxygenase by acetone precipitation and its restoration by incubation with a sulfhydryl agent and iron. Biochim Biophys Acta 1981 Apr 14;658(2):327–33

Olarte SW, Masnik R: Enhancing medication compliance in coffee groups. Hosp Community Psychiatry 1981 Jun;32(6):417–9

Oliva I, Levy B, Martineaud JP: Effects du Praxinor sur l'hémodynamique d'un circulation périphérique. Sem Hop Paris 1981 May 18–25; 57(19–20):1034–8 (Eng. Abstr.) **(Fre)**

Oliver C, Conte–Devolx B, Giraud P, et al: Contrôle hypothalamique de la sécrétion d'ACTH. Horm Res 1980;13(4–5):230–41 (Eng. Abstr.) **(Fre)**

Olpe HR: The cortical projection of the dorsal raphe nucleus: some electrophysiological and pharmacological properties. Brain Res 1981 Jul 6;216(1):61–71

Olpe HR, Schellenberg A, Steinmann MW: Differential actions of mianserin and iprindole on the sensitivity of cortical neurons to noradrenaline: effect of chronic treatment. Eur J Pharmacol 1981 Jul 10;72(4):381–5

Olschowka JA, Molliver ME, Grzanna R, et al: Ultrastructural demonstration of noradrenergic synapses in the rat central nervous system by dopamine–beta–hydroxylase immunocytochemistry. J Histochem Cytochem 1981 Feb;29(2):271–80

Olsen RW: GABA–benzodiazepine–barbiturate receptor interactions. J Neurochem 1981 Jul;37(1):1–13 (146 ref.)

Olsen UB: Changes of urinary kallikrein and kinin excretions induced by adrenalin infusion in conscious dogs. Scand J Clin Lab Invest 1980 Apr;40(2):173–8

AUTHOR SECTION

Olson JS: Mental patients, treatment, and the right to refuse. Ann NY Acad Sci 1981;368:119-21

Ong GL, Bruning HA: Dilated fixed pupils due to administration of high doses of dopamine hydrochloride. Crit Care Med 1981 Sep;9(9):658-9

Ono JK, Salvaterra PM: Snake alpha-toxin effects on cholinergic and noncholinergic responses of Aplysia californica neurons. J Neurosci 1981 Mar;1(3):259-70

Ooka-Souda S: Changes in certain diurnal hormonal rhythms in developing male rats exposed to adiurnal environmental cues. Mech Ageing Dev 1981 Mar;15(3):227-33 **(eng)**

Oppenoorth E, Erblich-Baumhackl E, Lenz G, et al: Reaktionsfähigkeit bei Lithiumprophylaxe. Bibl Psychiatr 1981;(161):152-69 (Eng. Abstr.) **(Ger)**

Orlova NV: Vliianie skopolamina na protsessy formirovaniia i fiksatsii vremennykh sviazei u krys s izmenennym soderzhaniem noradrenalina v golovnom mozge. Zh Vyssh Nerv Deiat 1981 May-Jun;31(3):571-6 (Eng. Abstr.) **(Rus)**

Ortmann R, Martin S, Waldmeier PC: Supersensitivity to L-5-hydroxytryptophan after 5,7-dihydroxytryptamine injections in desmethylimipramine- and nomifensine-pretreated rats: behavioral evidence for postsynaptic supersensitivity. Psychopharmacology (Berlin) 1981;74(2):109-14

Ossowska K, Wolfarth S: The effect of imipramine and mianserin on the behavior and EEG afterdischarges induced by single electric stimulation of the rabbit amygdala. Pol J Pharmacol Pharm 1980 Jul-Aug; 32(4):513-22

Oswald R, Changeux JP: Ultraviolet light-induced labeling by noncompetitive blockers of the acetylcholine receptor from Torpedo marmorata. Proc Natl Acad Sci USA 1981 Jun;78(6):3925-9

Oswald WD: Wirkungsprüfungen von Arzneimitteln mit Hilfe psychometrischer Methoden. Möglichkeiten und Probleme. Med Welt 1981 Aug 21;32(34):1225-31 **(Ger)**

Otten U, Goedert M, Baumann JB, et al: Stimulation of the pituitary-adrenocortical axis and induction of tyrosine hydroxylase by nerve growth factor are not dependent on mouse submaxillary gland isorenin. Brain Res 1981 Jul 27;217(1):207-11

Ouimet CC, Patrick RL, Ebner FF: An ultrastructural and biochemical analysis of norepinephrine-containing varicosities in the cerebral cortex of the turtle Pseudemys. J Comp Neurol 1981 Jan 10;195(2):289-304

Ovcharov R, Danchev N: Vzaimootnoshenie na trankvilizatorite diazepam i lonetil s dopaminova mediatsiia v tesntralnata nervna sistema. Eksp Med Morfol 1981;20(2):88-96 (Eng. Abstr.) **(Bul)**

Owasoyo JO, Egbunike GN, Iramain CA: The influence of thyroid gland and thyroxine on the acetylcholinesterase activity of rat brain and adenohypophysis. Endokrinologie 1981 Apr;77(2):242-6

Owen F, Baker HF, Ridley RM, et al: Effect of chronic amphetamine administration on central dopaminergic mechanisms in the vervet. Psychopharmacology (Berlin) 1981;74(3):213-6

P

Pace CS, Tarvin JT: Somatostatin: mechanism of action in pancreatic islet beta-cells. Diabetes 1981 Oct;30(10):836-42

Paelowski L: Different action of 5-hydroxytryptamine (5-HT) uptake inhibitors on fenfluramine- but not p-chloramphetamine-induced hyperthermia in rats. J Pharm Pharmacol 1981 Aug;33(8):538-40

Pala F, De Cosmo G, Sabato AF, et al: A simple rapid identification of psychotropic drugs by infrared spectrophotometry in emergency--preliminary description. Resuscitation 1981 Jun; 9(2):125-31

Palacios JM, Kuhar MJ, Rapoport SI, et al: Increases and decreases in local cerebral glucose utilization in response to GABA agonists. Eur J Pharmacol 1981 May 8;71(2-3):333-6

Palacios JM, Niehoff DL, Kuhar MJ: [3H]Spiperone binding sites in brain: autoradiographic localization of multiple receptors. Brain Res 1981 Jun 1;213(2):277-89

Palacios JM, Niehoff DL, Kuhar MJ: Receptor autoradiography with tritium-sensitive film: potential for computerized densitometry. Neurosci Lett 1981 Sep 1;25(2):101-5

Palkovits M, Epelbaum J, Gros C: Met-enkephalin concentrations in individual brain nuclei of ansa lenticularis and stria terminalis transected rats. Brain Res 1981 Jul 6;216(1):203-9

Palkovits M: Catecholamines in the hypothalamus: an anatomical review. Neuroendocrinology 1981 Aug;33(2):123-8

Palma JA, Enders J, de Oliva PP: Effects of epinephrine on plasma fibrinogen levels in rats submitted to tissue injury. Experientia 1981 Jul 15;37(7):780-2

Pan XG, Chen DY, Zhao ZH, et al: Studies on mechanism of action of luteinizing releasing hormone (LH-RH) in ovulation of fish--intracellular distribution of LH-RH-A in pituitary gonadotrophs as revealed by electron-microscopic autoradiography. Sci Sin 1981 Jul; 24(7):982-8

Panteleeva GP, Mikhailova NM, Beliaev BS: Sravnitel'naia kharakteristika profilakticheskikh svoistv karbonata litiia kratkovremennogo i retardirovannogo deistviia pri éndogennykh affektivnykh psikhozakh. Zh Nevropatol Psikhiatr 1981;81(3):406-12 (Eng. Abstr.) **(Rus)**

Panula P, Wu JY, Emson P: Ultrastructure of GABA-neurons in cultures of rat neostriatum. Brain Res 1981 Aug 24;219(1):202-7

Pape BE: Isolation and identification of a metabolite of haloperidol. J Anal Toxicol 1981 May-Jun;5(3):113-7

Papir-Krichell D, Feldman S: Response of medial septal neurons to the iontophoretic application of glucocorticoids. Exp Neurol 1981 Sep; 73(3):801-11

Paramonova GI: Vozrastnye osobennosti izmeneniia fermentov mikrosomal'nogo okisleniia pecheni krys pod vliianiem barbituratov. Farmakol Toksikol 1981 Jan-Feb;44(1):98-101 (Eng. Abstr.) **(Rus)**

Pardal JF, Granata AR, Gimeno AL, et al: Similar regulatory mechanism underlying 3H-noradrenaline release from isolated hypothalamus and perfused tail artery or the rat by Latrodectus antheratus (black widow spider) venom gland extract and by potassium. Toxicon 1981; 19(2):249-54

Pardal JF, Pardal MF: Dextro-phenylalanine as inhibitor of the noradrenaline release from the isolated rat hypothalamus. Acta Neurol Latinoam 1979;25(3-4):235-48

Park MK, Sheridan PH: Comparison of reserpine-induced supersensitivity of newborn and adult rabbit ventricular muscles to cardiotonic agents. Dev Pharmacol Ther 1981;2(4):240-9

Parker DM, Holbrook JJ, Birdsall B, et al: H NMR studies of Tyr-237 of lactate dehydrogenase. FEBS Lett 1981 Jun 29;129(1):33-5

Parsons CM, Potter LM: Utilization of amino acid analogues in diets of young turkeys. Br J Nutr 1981 Jul;46(1):77-86

Pasch T: Die Anwendung von Flunitrazepam in der Intensivmedizin. Anaesth Intensivther Notfallmed 1981 Jun;16(3):145-9 (Eng. Abstr.) **(Ger)**

Passo SS, Thornborough JR, Ferris CF: A functional analysis of dopaminergic innervation of the neurohypophysis. Am J Physiol 1981 Sep;241(3):E186-90

Patel J, Marangos PJ, Goodwin FK: [3H] Ethyl beta-carboline-3-carboxylate binding to the benzodiazepine receptor is not affected by GABA. Eur J Pharmacol 1981 Jul 10;72(4):419-20

Patel P, Bose D, Greenway C: Effects of prazosin and phenoxybenzamine on alpha- and beta-receptor-mediated responses in intestinal resistance and capacitance vessels. J Cardiovasc Pharmacol 1981 Sep-Oct; 3(5):1050-9

Patsalos PN, Lascelles PT: Inhibition of in vitro diphenylhydantoin hydroxylation by different anticonvulsant drug combinations: a kinetic analysis. Gen Pharmacol 1981;12(1):51-5

Patwardhan RV, Johnson RF, Sinclair AP, et al: Lack of tolerance and rapid recovery of cimetidine-inhibited chlordiazepoxide (Librium) elimination. Gastroenterology 1981 Sep;81(3):547-51

Paul SM, Rehavi M, Rice KC, et al: Does high affinity [3H] imipramine binding label serotonin reuptake sites in brain and platelet? Life Sci 1981 Jun 15;28(24):2753-60

Paull WK, Turkelson CM, Thomas CR, et al: Immunohistochemical demonstration of a testicular substance related to luteinizing hormone-releasing hormone. Science 1981 Sep 11;213(4513):1263-4

Paupardin-Tritsch D, Deterre P, Gerschenfeld HM: Relationship between two voltage-dependent serotonin responses of molluscan neurones. Brain Res 1981 Jul 27;217(1):201-6

Pawlowski L, Ruczyńska J, Górka Z: Citalopram: a new potent inhibitor of serotonin (5-HT) uptake with central 5-HT-mimetic properties. Psychopharmacology (Berlin) 1981;74(2):161-5

Payer AF, Battle CL, Peake RL: Ultrastructural and cytochemical effects of trypan blue on TSH stimulation of thyroid follicular cells. Cell Tissue Res 1981;218(3):547-56

Payk TR: Ambulante Behandlung mit Psychopharmaka. Med Klin 1981 Jan 2;76(1):2-10 **(Ger)**

Paykel ES: Psychopharmacological and social aspects of schizophrenia: recent developments. Aust NZ J Psychiatry 1980 Dec;14(4):241-7

Pearce JB: Drug treatment of depression in children. Acta Paedopsychiatr (Basel) 1981 Feb;46(5-6):317-28

Pearlson GD, Robinson RG: Suction lesions of the frontal cerebral cortex in the rat induce asymmetrical behavioral and catecholaminergic responses. Brain Res 1981 Aug 10;218(1-2):233-42

Peces R, Horcajada C, López-Novoa JM, et al: Hyperprolactinemia in chronic renal failure: impaired responsiveness to stimulation and suppression. Normalization after transplantation. Nephron 1981; 28(1):11-6

Péczely P, Pethes G: Effect of ovariectomy, thyroidectomy and of thyroxine treatment on the plasma level of corticosterone of the female Japanese quail. Acta Biol Acad Sci Hung 1981;32(1):1-6

Péczely P, Pethes G: Plasma corticosterone, thyroxine and triiodothyronine level in the collared dove (Streptopelia decaocto) during the reproductive cycle. Acta Physiol Acad Sci Hung 1980; 56(4):421-30

Pedersen KE: Clinical aspects of the digoxin-quinidine interaction. Dan Med Bull 1981 Aug;28(3):128-31

Peel HW, Perrigo BJ: Detection of cannabinoids in blood using EMIT. J Anal Toxicol 1981 Jul-Aug;5(4):165-7

Pelletier G, Steinbusch HW, Verhofstad AA: Immunoreactive substance P and serotonin present in the same dense-core vesicles. Nature 1981

AUTHOR SECTION

Sep 3;293(5827):71-2

Pellmer TC: Transmitter control of voltage-dependent currents. Life Sci 1981 May 18;28(20):2199-205 (36 ref.)

Perassi NI, Loyber I: Circulating thyroxine levels in institutionalized children. Arch Int Physicl Biochim 1980 Dec;88(5):491-5

Perez G, Ungaro B, Morrone G, et al: La risposta glicoregolatrice alla infusione di glucagone e di epinefrina nella uremia cronica. Minerva Nefrol 1979 Jul-Sep;26(3):349-52 (Eng. Abstr.) **(Ita)**

Péronnet F, Nadeau RA, de Champlain J, et al: Exercise plasma catecholamines in dogs: role of adrenals and cardiac nerve endings. Am J Physiol 1981 Aug;241(2):H243-7

Perry TL, Kish SJ, Hansen S, et al: Elevation of brain GABA content by chronic low-dosage administration of hydrazine, a metabolite of isoniazid. J Neurochem 1981 Jul;37(1):32-9

Persson M, Wiklund L: Scattered catecholaminergic cells in the dorsolateral tegmentum caudal to locus coeruleus in cat. Neurosci Lett 1981 May 29;23(3):275-80

Perucca E, Ruprah M, Richens A: Altered drug binding to serum proteins in pregnant women: therapeutic relevance. J R Soc Med 1981 Jun; 74(6):422-6

Peselow E, Lautin A, Gershon S: Prophylactic and therapeutic profile of lithium. Bibl Psychiatr 1981;(161):1-31 (158 ref.)

Peters LL, Hoefer MT, Ben-Jonathan N: The posterior pituitary: regulation of anterior pituitary prolactin secretion. Science 1981 Aug 7;213(4508):659-61

Petersen EN: Pre- and postsynaptic alpha-adrenoceptor antagonism by neuroleptics in vivo. Eur J Pharmacol 1981 Feb 19;69(4):399-405

Peterson DF, Bishop VS: Influences of selective sympathetic denervation on coronary reactive hyperemia in conscious dogs. J Auton Nerv Syst 1980 May;2(1):47-59

Peterson LG: On being a necessary evil at a mental health center. Hosp Community Psychiatry 1981 Sep;32(9):644

Peterson SL, Albertson TE, Lakin ML, et al: Anticonvulsant properties of melatonin on seizures in mice. Proc West Pharmacol Soc 1981;24:7-10

Pethes G, Seprödi A, Péczely P, et al: Effect of a synthetic LH-RH agonist on the endocrine function of the testis, adrenocortex and thyroid gland in cocks. Acta Physiol Acad Sci Hung 1980;56(3):281-7

Pettersen JE, Teien G, Ulsaker GA: Identification of 2-chlorothioxanthen-9-one in gastric aspirate in a case of chlorprothixene poisoning. J Pharm Sci 1981 Jul;70(7):812-3

Pettibone DJ, Mueller GP: Alpha-adrenergic stimulation by clonidine increases plasma concentrations of immunoreactive beta-endorphin in rats. Endocrinology 1981 Sep;109(3):798-802

Petursson H, Lader MH: Withdrawal from long-term benzodiazepine treatment. Br Med J [Clin Res] 1981 Sep 5;283(6292):643-5

Petursson H, Lader MH: Benzodiazepine dependence. Br J Addict 1981; 76(2):133-45 (107 ref.)

Petursson H, Shur E, Checkley S, et al: A neuroendocrine approach to benzodiazepine tolerance and dependence. Br J Clin Pharmacol 1981 May;11(5):526-8

Peyer M, Pletscher A: Liberation of catecholamines and 5-hydroxytryptamine from human blood-platelets. Naunyn Schmiedebergs Arch Pharmacol 1981 Feb;316(1):81-6

Pfeffer JM: Management of the acutely disturbed patient on the general ward. Br J Hosp Med 1981 Jul;26(1):73-8

Pfister C, Wolny HJ: Gamma-Aminobuttersüre- (GABA-) Fluorescenz bei der Ninhydrin-Reaktion im octanolischen Mileiu. Fluorescenzhistochemische Untersuchung. 3. Mitteilung. Acta Histochem (Jena) 1981;68(2):231-7 (Eng. Abstr.) **(Ger)**

Pfister C, Hölzel B, Danner H: GABA-haltige Neurone im Nucleus raphes dorsalis der Ratte. Acta Histochem (Jena) 1981;68(1):117-24 (Eng. Abstr.) **(Ger)**

Phillis JW, Wu PH, Bender AS: Inhibition of adenosine uptake into rat brain synaptosomes by the benzodiazepines. Gen Pharmacol 1981; 12(1):67-70

Pickar D, Cohen RM, Jimerson DC, et al: Tyramine infusions and selective monoamine oxidase inhibitor treatment. I. Changes in pressor sensitivity. Psychopharmacology (Berlin) 1981;74(1):4-7

Pickar D, Cohen RM, Jimerson DC, et al: Tyramine infusions and selective monoamine oxidase inhibitor treatment. II. Interrelationships among pressor sensitivity changes, platelet MAO inhibition, and plasma MHPG reduction. Psychopharmacology (Berlin) 1981;74(1):8-12

Pickett EE, Hawkins JL: Determination of lithium in small-animal tissues at physiological levels by flame emission photometry. Anal Biochem 1981 Apr;112(2):213-8

Piekut DT, Knigge KM: Immunocytochemical analysis of the rat pineal gland using antisera generated against luteinizing hormone-releasing hormone (LHRH). J Histochem Cytochem 1981 May;29(5):616-22

Pierce JR Jr, Trostle DC, Warner JJ: Propranolol and retroperitoneal fibrosis [letter] Ann Intern Med 1981 Aug;95(2):244

Pillai NP, Ramaswamy S, Gopalakrishnan V, et al: Contractile effect of prolactin on guinea pig isolated ileum. Eur J Pharmacol 1981 Jun 10; 72(1):11-6

Pincus JH, Hsiao K: Calcium uptake mechanisms affected by some convulsant and anticonvulsant drugs. Brain Res 1981 Jul 27; 217(1):119-27

Pinder RM, Blum A, Stulemeijer SM, et al: A double-blind multicentre trial comparing the efficacy and side-effects of mianserin and chlorimipramine in depressed in- and outpatients. Int Pharmacopsychiatry 1980;15(4):218-27

Pinelli A, Colombo R, Manitto P, et al: Drugs affecting porphyrin and lipid metabolism in rats: effects exerted by allylisopropylacetamide and related molecules. Pharmacology 1981;22(6):337-42

Pisarev AA: Vliianie fiziologicheski aktivnykh veshchestv i farmakologicheskikh preparatov na mikrotsirkuliatornoe ruslo (obzor literatury). Farmakol Toksikol 1981 Mar-Apr;44(2):247-52 (109 ref.) **(Rus)**

Platou ES, Refsum H, Amlie JP, et al: Influence of beta-adrenergic and cholinergic blockade on the electrophysiological effects of melperone in the dog heart in situ. Cardiovasc Res 1981 Mar;15(3):137-43

Platz T, Hinterhuber H: Die hochdosierte Neuroleptikatherapie. Pharmacopsychiatria 1981 Jul;14(4):141-7 (82 ref.) (Eng. Abstr.)**(Ger)**

Plech A: The influence of microinjections of cholinomimetics into nypothalamus on the locomotor activity of rats. Agressologie 1979; 20(D):279-82

Plech A, Szkilnik R, Zieliński M, et al: Effects of intrahypothalamic injections of kainic acid on the behaviour of rats. Acta Physiol Pol 1981 Mar-Apr;32(2):145-54

Pogády J, Vencovský E, Zižka V: Klinické zkušenosti s léčbou depresi nomifensinem. Cesk Psychiatr 1981 Feb;77(1):11-6 (Eng. Abstr.)**(Slo)**

Pogliani E, Corvi G, Mandelli V, et al: Preliminary human pharmacology studies on the inhibition of platelet aggregation by indobufen (K 3920). Haematologica (Pavia) 1981 Apr;66(2):160-70

Poklis A: An evaluation of EMIT-dau Benzodiazepine Metabolite Assay for urine drug screening. J Anal Toxicol 1981 Jul-Aug;5(4):174-6

Polc P, Ropert N, Wright DM: Ethyl beta-carboline-3-carboxylate antagonizes the action of GABA and benzodiazepines in the hippocampus. Brain Res 1981 Jul 27;217(1):216-20

Pöldinger W: Die Dauermedikation mit Antidepressiva als Prophylaxe. Bibl Psychiatr 1981;(161):237-43 **(Ger)**

Polezhaeva AI, Mashkovskii MD: Sravnitel'noe midriaticheskoe deistvie antidepressantov raznykh grupp. Farmakol Toksikol 1981 Jan-Feb; 44(1):15-7 (Eng. Abstr.) **(Rus)**

Pollitt E, Leibel RL, Greenfield D: Brief fasting, stress, and cognition in children. Am J Clin Nutr 1981 Aug;34(8):1526-33

Polonsky K, Jaspan J, Pugh W, et al: Insulin and glucagon breakthrough of somatostatin suppression: importance of portal vein hormone measurements. Diabetes 1981 Aug;30(8):664-9

Pomara N, Gershon S: Psychopharmacotherapy: from the 1950s to the 1980s. Psychosomatics 1981 Jun;22(6):526-30

Pong SS, Dehaven R, Wang CC: Stimulation of benzodiazepine binding to rat brain membranes and solubilized receptor complex by avermectin B1a and gamma-aminobutyric acid. Biochim Biophys Acta 1981 Aug 6;646(1):143-50

Ponzio F, Achilli G, Algeri S: A rapid and simple method for the determination of picogram levels of 3-methoxytyramine in brain tissue using liquid chromatography with electrochemical detection. J Neurochem 1981 Apr;36(4):1361-7

Ponzio F, Consolazione A, Calderini G, et al: Biochemical effects of quipazine on rat striatal dopaminergic system. Life Sci 1981 Jul 6; 29(1):83-91

Popova NK, Voitenko NN: Brain serotonin metabolism in hibernation. Pharmacol Biochem Behav 1981 Jun;14(6):773-7

Popova NK, Lobacheva II: Uchastie serotoninergicheskoi sistemy mozga v formirovanii stressornoi reaktivnosti gipofizarno-nadpochechnikovogo kompleksa. Ontogenez 1981; 12(4):382-9 (Eng. Abstr.) **(Rus)**

Populin M, De Vanna M, Poldrugo F: La flufenazina decxanoato (F.D.) nel trattamento ambulatoriale di pazienti schizofrenici. Minerva Psichiatr 1981 Apr-Jun;22(2):85-92 (73 ref.) (Eng. Abstr.) **(Ita)**

Porto CS, Abreu LC, Picarelli ZP: Influence of castration upon the seminal vesicle response to parasympathomimetic drugs. Arch Int Pharmacodyn Ther 1981 Apr;250(2):204-11

Poshivalov VP: GAMK-ergicheskie korreliaty agressivnosti i vnutrividovoi obshchitel'nosti myshei, podvergnutykh izoliatsii. Biull Eksp Biol Med 1981 May;91(5):584-7 (Eng. Abstr.) **(Rus)**

Poskonova MA, Akopian AR, Chemeris NK: Diffuziia atsetilkholina cherez membranu neirona. Dokl Akad Nauk SSSR 1981;257(6):1496-9 **(Rus)**

Post RM, Pickar D, Naber D, et al: Effect of carbamazepine on CSF opioid activity: relationship to antidepressant response. Psychiatry Res 1981 Aug;5(1):59-66

Potter DE, Rowland JM: Adrenergic drugs and intraocular pressure. Gen Pharmacol 1981;12(1):1-13

Pouchelet M, Shore GC: Chloramphenicol inhibits hormone-dependent induction of cytoplasmic mRNA coding for the mitochondrial enzyme, carbamyl phosphate synthetase, in Rana catesbeiana tadpoles. Biochim Biophys Acta 1981 Jun 26;654(1):67-76

Poupon RE, Le Quernec L, Maurice M, et al: Le phénobarbital ne modifie ni le débit biliaire ni l'activité de la Na+, K+-ATPase des membranes plasmiques hépatocytaires chez le hamster. Gastroenterol Clin Biol 1981 Jun-Jul;5(6-7):604-10 (Eng. Abstr.) **(Fre)**

AUTHOR SECTION

Pourcho RG: Autoradiographic localization of [3H]muscimol in the cat retina. Brain Res 1981 Jun 29;215(1-2):187-99

Powell ML, Wagoner RR, Chen CH, et al: Aromatic hydroxylation of propranolol. Stereochemical aspects of the formation of 4'-hydroxypropranolol in the rat. Res Commun Chem Pathol Pharmacol 1980 Dec;30(3):387-400

Powell R, White MC, Daniels M, et al: Domperidone directly stimulates TSH secretion in vitro. FEBS Lett 1981 Jun 29;129(1):97-9

Pradhan S, Hanson G, Lovenberg W: Inverse relation of substance P-like immunoreactivity in dorsal raphe nucleus to serotonin levels in pons-medulla following administration of cocaine and 5-hydroxytryptophan. Biochem Pharmacol 1981 May 15;30(10):1071-6

Prado de Carvalho L, Zornetzer SF: The involvement of the locus coeruleus in memory. Behav Neural Biol 1981 Feb;31(2):173-86

Prange AJ Jr, Utiger RD: What does brain thyrotropin-releasing hormone do? [editorial] N Engl J Med 1981 Oct 29;305(18):1089-90

Predy PA, Kokkinidis L: Post-amphetamine depression of self-stimulation behavior in rats: prophylactic effects of lithium. Neurosci Lett 1981 May 29;23(3):343-7

Preradovic M: Najčešće komplikacije kod neuroleptične terapije. Prikaz bolesnika. Vojnosanit Pregl 1981 May-Jun;38(3):211-2 (Ser)

Presl J: Regulace endokrinní funkce placenty. Cesk Gynekol 1981 Jul; 46(6):466-7 (Cze)

Presslich O, Mairhofer ML, Oppenoorth E, et al: Maximale motorische Nervenleitgeschwindigkeit unter Lithium. Bibl Psychiatr 1981; (161):121-8 (Eng. Abstr.) (Ger)

Prior M: 'Problem children' and stimulant drug treatment. Aust NZ J Psychiatry 1981 Jun;15(2):117-21

Proctor RC: Prescription medication in the workplace. Occupational absenteeism, accidents, and performance when using non-psychoactive and psychoactive medication. NC Med J 1981 Aug;42(8):545-7

Przegalinski E, Baran L, Kędrek G: The central action of salbutamol, a beta-agonist with a potential antidepressant activity. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):485-93

Przegaliński E, Kordecka-Magiera A, Mogilnicka E, et al: Chronic treatment with some atypical antidepressants increases the brain level of 3-methoxy-4-hydroxyphenylglycol (MHPG) in rats. Psychopharmacology (Berlin) 1981;74(2):187-90

Publicover SJ, Duncan CJ: Diamide, temperature and spontaneous transmitter release at the neuromuscular junction: stimulation of exocytosis by a direct effect on membrane fusion? Eur J Pharmacol 1981 Mar 12;70(2):203-11

Puller M: Inaccurate creatinine clearance tests [letter] Am J Psychiatry 1981 Sep;138(9):1258-9

Purushotham KR, Raghupathi M, Ramamurthi R: Neuroendocrine involvement in regulation of isocitrate & glucose-6-phosphate dehydrogenase activities in the fresh water field crab Oziotelphusa senex senex. Indian J Exp Biol 1981 Apr;19(4):399-400

Puzynski S, Bidzinski A, Hauptmann M, et al: Peripheral metabolism of indoleamines and catecholamines in endogenous depressive syndrome. Agressologie 1979;20(D):245-51

Pycock CJ, Kerwin RW: The status of glycine as a supraspinal neurotransmitter. Life Sci 1981 Jun 15;28(24):2679-86 (81 ref.)

Pycock CJ, Dawbarn D, Kerwin RW: Roles of GABA and glycine in the substantia nigra. Adv Biochem Psychopharmacol 1981;29:77-87 (52 ref.)

Q

Quast U: Zum molekularen Wirkungsmechanismus der Benzodiazepine. Fortschr Med 1981 May 28;99(20):788-94 (Eng. Abstr.) (Ger)

Quilligan EJ, Clewlow F, Johnston BM, et al: Effect of 5-hydroxytryptophan on electrocortical activity and breathing movements of fetal sheep. Am J Obstet Gynecol 1981 Oct 1;141(3):271-5

Quinn MR, Cagan RH: GABA binding to dendrodendritic synaptosomal membranes from rat olfactory bulbs. Adv Biochem Psychopharmacol 1981;29:421-8

Quirce CM, Odio M, Solano JM: The effects of predictable and unpredictable schedules of physical restraint upon rats. Life Sci 1981 Apr 27;28(17):1897-902

Quitkin FM, Kane J, Rifkin A, et al: Prophylactic lithium carbonate with and without imipramine for bipolar 1 patients. A double-blind study. Arch Gen Psychiatry 1981 Aug;38(8):902-7

R

Rabii J, Buonomo F, Scanes CG: Role of serotonin in the regulation of growth hormone and prolactin secretion in the domestic fowl. J Endocrinol 1981 Sep;90(3):355-8

Rácz I, Plachy J, Szabónét T, et al: Benzil-izokinolin vázas alkaloidok kölcsönhatása barbiturátokkal. A sósavas papaverin és a fenobarbitálnátrium kölcsönhatása. I. A kölcsönhatás jellegének tanulmányozása fizikai, kémiai és biológiai módszerekkel. Acta Pharm Hung 1980 Nov;50(6):248-56 (Eng. Abstr.) (Hun)

Rácz I, Plachy J, Szabóné Tábori M, et al: Benzil-izokinolin vázas alkaloidok kölcsönhatása barbiturátokkal. A sósavas papaverin és a fenobarbitálnátrium kölcsönhatása. II. Az inkompatibilitás kivédésének gyógyszertechnológiai lehetőségei. Acta Pharm Hung 1980 Nov; 50(6):257-62 (Eng. Abstr.) (Hun)

Raevskiĭ VV: O roli iader shva v formirovanii aktivnosti neironov somatosensornoĭ kory kotenka. Zh Vyssh Nerv Deiat 1981;31(2):349-57 (Eng. Abstr.) (Rus)

Ragheb M, Wilson WH, Ban TA, et al: Amoxapine: once versus divided daily doses in neurotic and endogenous depression. J Clin Psychiatry 1981 Aug;42(8):318-21

Rahman MK, Nagatsu T, Kato T: Aromatic L-amino acid decarboxylase activity in central and peripheral tissues and serum of rats with L-DOPA and L-5-hydroxytryptophan as substrates. Biochem Pharmacol 1981 Mar 15;30(6):645-9

Raju K, Vijayan E: Neurotensin and substance P: differential effects on plasma cholesterol levels in conscious ovariectomized rats. Regul Pept 1981 Aug;2(4):265-74

Rakowicz-Szulczyńska EM, Horst A: Incorporation of various amino acids into non-histone chromatin protein fractions of spleen cells of mice immunized with IgG. Mol Cell Biochem 1981 Jun 9;37(1):13-9

Ramade F, Bouillé C, Baylé JD: Hypothalamic multiunit activity correlates of the adrenocortical response to stress. Neurosci Lett 1981 May 29; 23(3):297-302

Ramirez-Gonzalez D, Widy-Tyszkiewicz E, Almazan G, et al: Effect of cold, restraint, reserpine, and splanchnicotomy on the ornithine decarboxylase activity of rat adrenal medulla and cortex. Exp Neurol 1981 Sep;73(3):632-41

Ramseier F, Gastpar M, Girard J: TSH, HGH, HPr, and cortisol response to TRH in depressed patients. Acta Psychiatr Belg 1980 Jul-Aug; 80(4):399-409

Rang HP: The characteristics of synaptic currents and responses to acetylcholine of rat submandibular ganglion cells. J Physiol (Lond) 1981 Feb;311:23-55

Rao GH, Reddy RK, White JG: Low dose aspirin, platelet function and prostaglandin synthesis: influence of epinephrine and alpha adrenergic blockade. Prostaglandins Med 1981 May;6(5):485-94

Rao KP, Rao MS: Effects of fluphenazine hydrochloride on the bone-marrow cells of Swiss mice. Mutat Res 1981 Jul;89(3):237-40

Rapoport RM, Takimoto GS, Cho AK: Compartmental analysis of tyramine-induced norepinephrine depletion. Pharmacology 1981; 22(4):235-42

Rassin DK, Sturman JA, Gaull GE: Sulfur amino acid metabolism in the developing rhesus monkey brain: subcellular studies of taurine, cysteinesulfinic acid decarboxylase, gamma-aminobutyric acid, and glutamic acid decarboxylase. J Neurochem 1981 Sep;37(3):740-8

Rastogi RB, Singhal RL: MK-771 enhances the turnover of norepinephrine in brain. Res Commun Chem Pathol Pharmacol 1981 Jul;33(1):187-90

Rastogi RB, Singhal RL, Lapierre YD: Effects of short- and long-term neuroleptic treatment on brain serotonin synthesis and turnover: focus on the serotonin hypothesis of schizophrenia. Life Sci 1981 Aug 17; 29(7):735-41

Rasul M: Acutely ill schizophrenic patients treated with loxapine. A clinical study in a community mental health center. Clin Ther 1980; 3(4):242-9

Ratner A, Woo W, Yelvington D, et al: Effect of lergotrile mesylate and methysergide on morphine induced increase in prolactin release. Proc West Pharmacol Soc 1981;24:335-9

Ratner RA: Mania, crime and the insanity defense: a case report. Bull Am Acad Psychiatry Law 1981;9(1):23-32

Rauste-von Wright M, von Wright J, Frankenhaeuser M: Relationships between sex-related psychological characteristics during adolescence and catecholamine excretion during achievement stress. Psychophysiology 1981 Jul;18(4):362-70

Raymond V, Lépine J, Giguère V, et al: Parallel stimulation of ACTH, beta-LPH + beta-endorphin and alpha-MSH release by alpha-adrenergic agents in rat anterior pituitary cells in culture. Mol Cell Endocrinol 1981 Jun;22(3):295-303

Redburn DA, Massey SC: GABA and its interaction with ACh in the rabbit retina. Adv Biochem Psychopharmacol 1981;29:169-74

Reddrop CJ, Riess W, Slater TF: Interactions of carbon tetrachloride and promethazine in the rat--I. Effects of promethazine on the concentrations of carbon tetrachloride in blood and liver, and on the production of chloroform. Biochem Pharmacol 1981 Jun 15; 30(12):1443-7

Reddrop CJ, Riess W, Slater TF: Interactions of carbon tetrachloride and promethazine in the rat--II. Elimination of carbon tetrachloride and chloroform in expired air as indications of their metabolism in the intact animal. Biochem Pharmacol 1981 Jun 15;30(12):1449-55

Reed DJ, Yen MH: The effect of lithium on electrolyte transport by the in situ choroid plexus of the cat. J Physiol (Lond) 1980 Dec;309:329-39

Refsum H, Amlie JP, Platou ES, et al: Electrophysiological effects of melperone in the dog heart in situ - a new antiarrhythmic drug. Cardiovasc Res 1981 Mar;15(3):131-6

Regan JW, Roeske WR, Ruth WH, et al: Reductions in retinal gamma-aminobutyric acid (GABA) content and in [3H]flunitrazepam binding after postnatal monosodium glutamate injections in rats. J Pharmacol Exp Ther 1981 Sep;218(3):791-6

Reichelt KL: Peptider som informasjonsoverfører ved psykiatriske sykdommer. Nord Med 1980 Nov;95(11):283-6 **(Nor)**

Reigle TG, Isaac WL, Isaac W: Behavioral and neurochemical interactions of dextroamphetamine and methylphenidate in rats. J Pharm Sci 1981 Jul;70(7):816-8

Reimann IW, Frölich JC: Effects of diclofenac on lithium kinetics. Clin Pharmacol Ther 1981 Sep;30(3):348-52

Reimann W, Steinhauer HB, Hedler L, et al: Effect of prostaglandins D2, E2 and F2alpha on catecholamine release from slices of rat and rabbit brain. Eur J Pharmacol 1981 Feb 19;69(4):421-7

Reinecke M: Immunohistochemical localization of polypeptide hormones in endocrine cells of the digestive tract of Branchiostoma lanceolatum. Cell Tissue Res 1981;219(3):445-56

Reisine T: Adaptive changes in catecholamine receptors in the central nervous system. Neuroscience 1981;6(8):1471-502

Rémy C, Dubois MP: Immunohistochemical evidence of methionine enkephalin-like material in the brain of the migratory locust. Cell Tissue Res 1981;218(2):271-8

Reubi JC, Perrin MH, Rivier JE, et al: High affinity binding sites for a somatostatin-28 analog in rat brain. Life Sci 1981 May 11; 28(19):2191-8

Revusky S, Coombes S, Pohl RW: Failure of albino guinea pigs to exhibit Lavin's poisoned partner effect. Behav Neural Biol 1981 May; 32(1):111-3

Rey AC, Buchsbaum MS, Post RM: Apomorphine, haloperidol and the average evoked potentials in normal human volunteers. Commun Psychopharmacol 1980;4(4):327-34

Reyl F, Lewis MJ: Somatostatin is a potent activator of phosphoprotein phosphatases in the digestive tract. Biochim Biophys Acta 1981 Jul; 675(2):297-300

Reymond M, Lemarchand-Béraud T: Differential effects of testosterone and its metabolites on gonadotrophin secretion in the intact adult male rat. Horm Res 1981;14(2):114-29

Reymond MJ, Porter JC: Secretion of hypothalamic dopamine into pituitary stalk blood of aged female rats. Brain Res Bull 1981 Jul; 7(1):69-73

Reynolds FH Jr, Todaro GJ, Fryling C, et al: Human transforming growth factors induce tyrosine phosphorylation of EGF receptors. Nature 1981 Jul 16;292(5820):259-62

Reynolds GP, Riederer P: The effects of lisuride and some other dopaminergic agonists on receptor binding in human brain. J Neural Transm 1981;51(1-2):107-11

Reynolds V, Jenner DA, Palmer CD, et al: Catecholamine excretion rates in relation to life-styles in the male population of Otmoor, Oxfordshire. Ann Hum Biol 1981 May-Jun;8(3):197-209

Rhoads ML: Cholinesterase in the parasitic nematode, Stephanurus dentatus. Characterization and sex dependence of a secretory cholinesterase. J Biol Chem 1981 Sep 10;256(17):9316-23

Richardson PJ: Quantitation of cholinergic synaptosomes from guinea pig brain. J Neurochem 1981 Jul;37(1):258-60

Richardson SB, Hollander CS, Prasad JA, et al: Somatostatin release from rat hypothalamus in vitro: effects of melatonin and serotonin. Endocrinology 1981 Aug;109(2):602-6

Rick JT, Whittle KL, Cross SH: Disruption and facilitation of cue discrimination in the rat by cholinergic agents. Neuropharmacology 1981 Aug;20(8):747-52

Rickaby DA, Linehan JH, Bronikowski TA, et al: Kinetics of serotonin uptake in the dog lung. J Appl Physiol 1981 Aug;51(2):405-14

Ridley RM, Haystead TA, Baker HF, et al: A new approach to the role of noradrenaline in learning: problem-solving in the marmoset after alpha-noradrenergic receptor blockade. Pharmacol Biochem Behav 1981 Jun;14(6):849-55

Rieger H, Schardt W, Schmid-Schönbein H: Belastungsinduzierte Plättchenaggregation. In-vitro- und Ex-vivo-Aggregation menschlicher Blutplättchen nach Zufuhr kristallinen Adrenalins und nach ergometrischer Belastung. Dtsch Med Wochenschr 1981 Jul 17; 106(29-30):942-5 (Eng. Abstr.) **(Ger)**

Rimón R: Endorfiinit psykiatriassa. Duodecim 1980;96(21):1387-9 **(Fin)**

Ring J, Sovak M: Release of serotonin from human platelets in vitro by radiographic contrast media. Invest Radiol 1981 May-Jun;16(3):245-8

Risch SC, Kalin NH, Cohen RM, et al: Muscarinic cholinergic influences on ACTH and beta-endorphin release mechanisms in human subjects. Peptides (Fayetteville) 1981;2 Suppl 1:95-7

Ritchie T, Glusman S, Haber B: The filum terminale of the frog spinal cord, a nontransformed glial preparation: II. Uptake of serotonin. Neurochem Res 1981 Apr;6(4):441-52

Rittmannsberger H, Schöny W, Hofmann G, et al: Stoffwechseluntersuchungen unter Lithium. Bibl Psychiatr 1981; (161):129-33 **(Ger)**

Rivier C, Vale W: Temporal relationship between the abortifacient effects of GnRH antagonists and hormonal secretion. Biol Reprod 1981 Jun; 24(5):1061-7

Roberts E, Krause DN, Wong E, et al: Different efficacies of d- and l-gamma-amino-beta-hydroxybutyric acids in GABA receptor and transport test systems. J Neurosci 1981 Feb;1(2):132-40

Roberts F: The in vitro iontophoretic release of radiolabelled histamine, N'-methylhistamine and GABA from 7-barrelled glass micropipettes. Neuropharmacology 1981 Jul;20(7):711-4

Roberts GW, Crow TJ, Polak JM: Neurotensin: first report of a cortical pathway. Peptides (Fayetteville) 1981;2 Suppl 1:37-43

Roberts MH, Wright DM: The effects of chronic section of dorsal roots on the responsiveness of motoneurones to 5-hydroxytryptamine and a substance P analogue. Br J Pharmacol 1981 Jul;73(3):589-94

Robertson A, Laferrière A, Franklin KB: Amphetamine and increases in current intensity modulate reward in the hypothalamus and substantia nigra but not in the prefrontal cortex. Physiol Behav 1981 May; 26(5):809-13

Roccatagliata G, Albano C, Abbruzzese G: CSF-MHPG in depressive syndromes: basal values and imipramine-induced modifications. Neuropsychobiology 1981;7(4):169-71

Roccatagliata G, Maini A, Bino G: Escrezione urinaria di MHPG nelle depressioni endogene. Un indice clinico-terapeutico. Minerva Psichiatr 1981 Apr-Jun;22(2):75-8 (Eng. Abstr.) **(Ita)**

Rodgers RL, McNeill JH: Agonist selectivity of reserpine induced inotropic supersensitivity. Proc West Pharmacol Soc 1981;24:233-6

Rodriguez L, Chiarini A, Zecchi V: Studio in vitro della partizione di farmaci in sistemi trifasici. Nota III - Partizione di alcune benzodiazepine in sistemi trifasici A/O/A. Farmaco [Prat] 1981 Jun; 36(6):304-11 (Eng. Abstr.) **(Ita)**

Roffman M, Cordasco F, Kling A: Apomorphine-induced stereotypy in mature and senescent rats following cessation of chronic haloperidol treatment. Commun Psychopharmacol 1980;4(4):283-6

Rokyta R, Mares P, Sobotka P: Electrocorticographic activity induced by gamma hydroxybutyrate in the rat during ontogenesis. Experientia 1981 Jul 15;37(7):750-2

Roliński Z, Kozak W: Beta-adrenoreceptor antagonists enhance the benzodiazepine-induced suppression of footshock induced fighting in mice. Pol J Pharmacol Pharm 1980;32(5):731-8

Romantsev EF, Nikandrova TI, Zhulanova ZI, et al: Stimuliatsiia biosinteza prostaglandinov E2 i F2 v golovnom mozgu myshei linii F1 (CBA X C57BL) trankvilizatorom fenazepamom. Dokl Akad Nauk SSSR 1981; 258(1):239-42 **(Rus)**

Rondeau DB, Jolicoeur FB, Merkel AD, et al: Drugs and taste aversion. Neurosci Biobehav Rev 1981 Summer;5(2):279-94 (135 ref.)

Rönn O, Johnsson G, Lundborg P: Interaction in healthy volunteers between prenalterol, a selective beta 1-adrenoceptor agonist, and metoprolol or propranolol. J Cardiovasc Pharmacol 1981 May-Jun; 3(3):477-84

Roomi MW, Goldberg DM: Comparison of gamma-glutamyl transferase induction by phenobarbital in the rat, guinea pig and rabbit. Biochem Pharmacol 1981 Jun 15;30(12):1563-71

Roos BE: The polysymptomatic melancholic as patient in the internist's office. Acta Med Scand 1981;209(6):433-6

Rorie DK, Rusch NJ, Shepherd JT, et al: Prejunctional inhibition of norepinephrine release caused by acetylcholine in the human saphenous vein. Circ Res 1981 Aug;49(2):337-41

Rosenberg HC, Chiu TH: Regional specificity of benzodiazepine receptor down-regulation during chronic treatment of rats with flurazepam. Neurosci Lett 1981 Jun 12;24(1):49-52

Roskos SR, Takahashi T: Psychodynamic aspects in the use of monoamine oxidase inhibitor antidepressants. Bull Menninger Clin 1981 Mar; 45(2):143-8

Ross SR, Rodgers SR: Physostigmine in amoxapine overdose [letter] Am J Hosp Pharm 1981 Aug;38(8):1121-2

Rosseel MT, Bogaert MG: High-performance liquid chromatographic determination of propranolol and 4-hydroxypropranolol in plasma. J Pharm Sci 1981 Jun;70(6):688-9

Rossen B, Steiness I: The pathophysiology of acute renal failure after chlorprothixene overdosage. Acta Med Scand 1961;209(6):525-7

Rostock A, Poppe H, Nowak R, et al: Untersuchungen zur Kreislaufnebenwirkung von 3-[3'-Diethylaminopropyl-(1')-carbamoyl]-6,7-dimethoxy-1-thiaisochxid ('16-252'). Pharmazie 1981 Apr;36(4):287-90 **(Ger)**

Roth KA, Katz RJ, Sibel M, et al: Central epinergic inhibition of corticosterone release in rat. Life Sci 1981 May 21;28(21):2389-94

Roth KA, Katz RJ: Further studies on a novel animal model of depression: therapeutic effects of a tricyclic antidepressant. Neurosci Biobehav Rev 1981 Summer;5(2):253-8

Rothwell NJ, Stock MJ, Wyllie MG: Na+, K+-ATPase activity and noradrenaline turnover in brown adipose tissue of rats exhibiting diet-induced thermogenesis. Biochem Pharmacol 1981 Jun 15; 30(12):1709-12

Roubein IF, Embree LJ, Jackson DW, et al: The effect of hypoxia on monoamine levels in discrete regions of aged rat brain. Neurobiol Aging 1981 Spring;2(1):37-40

Roufogalis BD: The role of calmodulin in synaptic transmission. Proc West Pharmacol Soc 1981;24:197-201

Rougeul A: Modifications électrographiques et comportementales provoquées par l'administration de benzodiazépines au babouin en contention. Actual Pharmacol (Paris) 1981;33:77-90 **(Fre)**

AUTHOR SECTION

Rouillon F, Wahl G: Médicaments antidépresseurs. Soins Psychiatr 1981 Jan;(7):27-32 **(Fre)**

Rouillon F: Les psychodysleptiques. Soins Psychiatr 1981 Mar;(8):41-4 **(Fre)**

Rouleau D, Barden N: Inhibition of anterior pituitary prostaglandin-stimulated adenylyl cyclase activity by somatostatin. Can J Biochem 1981 Apr;59(4):307-10

Rousset B, Mornex R: Identification of an intracellular pathway of thyroxine synthesis by dispersed thyroid cells. Biochim Biophys Acta 1981 Aug 5;676(1):8-18

Rovida S, Ravera GB: Impiego della trasformazione in ridits per la valutazione dell'attività di psicofarmaci. Arch E Maragliano Patol Clin 1979;35:41-6 **(Ita)**

Rowell FJ, Hui SM, Fairbairn AF, et al: Total and free serum haloperidol levels in schizophrenic patients and the effect of age thioridazine and fatty acid on haloperidol-serum protein binding in vitro. Br J Clin Pharmacol 1981 Apr;11(4):377-82

Ruberg M, Enjalbert A, Arancibia S, et al: Regulation of prolactin secretion at the pituitary level. Exp Brain Res 1981;Suppl 3:182-99 (62 ref.)

Rubinow DR, Post RM, Pickar D, et al: Relationship between urinary free cortisol and CSF opioid binding activity in depressed patients and normal volunteers. Psychiatry Res 1981 Aug;5(1):87-93

Rudnick HL: The halcion affair [letter] S Afr Med J 1981 Sep 5;60(10):378

Rudorfer MV, Robins E: Fatal nortriptyline overdose, plasma levels, and in vivo methylation of tricyclic antidepressants. Am J Psychiatry 1981 Jul;138(7):982-3

Ruffalo RL, Thompson JF, Segal JL: Diazepam-cimetidine drug interaction: a clinically significant effect. South Med J 1981 Sep; 74(9):1075-8 (20 ref.)

Ruffalo RL, Thompson JF, Segal J: Cimetidine-benzodiazepine drug interaction. Am J Hosp Pharm 1981 Sep;38(9):1365-6

Rumigny JF, Maitre M, Cash C, et al: Regional and subcellular localization in rat brain of the enzymes that can synthesize gamma-hydroxybutyric acid. J Neurochem 1981 Apr;36(4):1433-8

Rumiński W, Markiewicz M, Książek A, et al: Stężenie adrenaliny i noradrenaliny we krwi chorych przed cewnikowaniem serca i po jego wykonaniu. Pol Tyg Lek 1981 Mar 30;36(13):461-3 (Eng. Abstr.) **(Pol)**

Ruprecht J, Baggen MG, Valkenburg M: Twee patiënten vergiftigd met een centraal aangrijpend anticholinergicum. Ned Tijdschr Geneeskd 1981 Jun 27;125(26):1041-2 (Eng. Abstr.) **(Dut)**

Rush AJ, Kovacs M, Beck AT, et al: Differential effects of cognitive therapy and pharmacotherapy on depressive symptoms. J Affective Disord 1981 Sep;3(3):221-9

Russell JA, Bartlett S: Adrenergic neurotransmission in airways: inhibition by acetylcholine. J Appl Physiol 1981 Aug;51(2):376-83

Russell SM: Differential effects of somatostatin on the release of bioactive and immunoactive rat growth hormone in vitro. Neuroendocrinology 1981 Aug;33(2):67-72

Russell WJ, Morris RG, Frewin DB, et al: Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981 Aug;53(8):837-9

Russo S, Cardinali S: Valutazione clinica comparativa dell'efficacia della metergolina e della bromocriptina sulla inibizione della lattazione puerperale. Riv Ital Ginecol 1980;59(2-3):301-9 (Eng. Abstr.) **(Ita)**

Rybakowski J, Potok E, Strzyzewski W: The activity of the lithium--sodium countertransport system in erythrocytes in depression and mania. J Affective Disord 1981 Mar;3(1):59-64

Rylance GW, Moreland TA: Saliva carbamazepine and phenytoin level monitoring. Arch Dis Child 1981 Aug;56(8):637-40

Rzempoluch J: Badania nad wpływem hormonu uwalniającego gonadotropiny, klomidu i L-dopa na wydzielanie gonadotropiny kosmówkowej, hormonu pobudzającego pęcherzyki i prolaktyny w pierwszym trymestrze niepowikłanej ciąży u kobiet. Ginekol Pol 1981 Jan;52(2):211-4 **(Pol)**

S

Saarma IuM, Saarma MM: Rol' psikhofarmakoterapii v lechenii bol'nykh pozhilogo vozrasta s organicheskimi psikhicheskimi sindromami. Vestn Akad Med Nauk SSSR 1980;(12):50-3 (Eng. Abstr.) **(Rus)**

Sabbah HN, Stein PD: Effect of inotropic interventions on rate of change of ventricular diastolic dimensions. Am J Physiol 1981 Sep; 241(3):H376-80

Sachse G, Svedberg J, Laube H: Effect of glucose and arginine on L-enkephalin secretion of the isolated perfused rat pancreas. Horm Metab Res 1981 Jun;13(6):360

Sagalovich BM, Melkumova GG: Izuchenie mekhanizma slukhovoi adaptatsii s pomoshch'iu odnovremennoi registratsii slukhovykh vyzvannykh potentsialov kory golovnogo mozga i mikrofonnykh potentsialov ulitki. Biull Eksp Biol Med 1981 May;91(5):520-2 (Eng. Abstr.) **(Rus)**

Saito A: [Changes of hypothalamic LH-RH content induced by estradiol injection into female rats (author's transl)] Nippon Sanka Fujinka Gakkai Zasshi 1981 Aug;33(8):1227-34 (Eng. Abstr.) **(Jpn)**

Saito M, Kato H, Suda M, et al: Parenteral feeding abolishes the circadian adrenocortical rhythm in rats. Experientia 1981 Jul 15;37(7):754-5

Sajgó M, Gesztesi A, Sidó T: Determination of tofisopam in serum by high-performance liquid chromatography. J Chromatogr 1981 Feb 13; 222(2):303-7

Sakai K: Vasoconstriction produced by intracoronary cholinomimetic drugs in isolated donor-perfused hearts of rhesus monkeys: comparison with pig, dog, and rabbit hearts. J Cardiovasc Pharmacol 1981 May-Jun; 3(3):500-9

Sakamoto N, Ikunaga K, Nojima T, et al: [Biochemical studies on acidic glycosaminoglycans in gingiva and dental pulp. 4. Beta-glucuronidase activity in dental pulp (author's transl)] Hiroshima Daigaku Shigaku Zasshi 1980;12(2):265-70 **(Jpn)**

Saland LC, Munger AT: Emergence of supraependymal cells in rat third ventricle after administration of p-chloroamphetamine. Brain Res Bull 1981 Jun;6(6):517-24

Salcher O, Lingens F: Metabolism of tryptophan by Pseudomonas aureofaciens and its relationship to pyrrolnitrin biosynthesis. J Gen Microbiol 1980 Dec;121(Pt. 2):465-71

El-Salhy M, Grimelius L: Immunohistochemical localization of gastrin C-terminus, gastric inhibitory peptide (GIP) and endorphin in the pancreas of lizards with special reference to the hibernation period. Regul Pept 1981 May;2(2):97-111

Saligaut C, Moore N, Daoust M, et al: Modifications of the dopaminergic receptors sensitivity and learning of normoxic or hypobaric hypoxic rats. Arch Int Pharmacodyn Ther 1981 May;251(1):80-7

Salinger R, Bond CA: Bipolar affective disorder following coronary bypass surgery. J Clin Psychiatry 1981 Sep;42(9):354-5

Salmerón De Diego J, Rodriguez CA, Orlando AS, et al: Syndrome of 'inappropriate secretion of thyroid-stimulating hormone' by partial target organ resistance to thyroid hormones. Acta Endocrinol (Copenh) 1981;97(3):361-8

Salzman SK, Beckman AL: Effects of thyrotropin releasing hormone on hypothalamic thermosensitive neurons of the rat. Brain Res Bull 1981 Sep;7(3):325-32

Sampaio LO, Dietrich CP: Changes of sulfated mucopolysaccharides and mucopolysaccharidases during fetal development. J Biol Chem 1981 Sep 10;256(17):9205-10

Sampath G, Channabasavanna SM, Rao BS, et al: Lithium excretion and therapeutic response in mania. Indian J Med Res 1981 May;73:768-71

Samson WK, Burton KP, Reeves JP, et al: Vasoactive intestinal peptide stimulates luteinizing hormone-releasing hormone release from median eminence synaptosomes. Regul Pept 1981 Aug;2(4):253-64

Samuelsson LI: Mechanism for exoelectron emission mainly from LiF. Acta Radiol [Suppl] (Stockh) 1979;359:1-93

Sanborn BM, Weisbrodt NW, Sherwood OD: Evidence against an obligatory role for catecholamine release or prostacyclin synthesis in the effects of relaxin on the rat uterus. Biol Reprod 1981 Jun; 24(5):987-92

Sánchez Martin MJ, Sánchez Camazano M, Hernández MT, et al: Interaction of propranolol hydrochloride with montmorillonite. J Pharm Pharmacol 1981 Jun;33(6):408-10

Sandler M: Monoamine oxidase inhibitor efficacy in depression and the 'cheese effect'. Psychol Med 1981 Aug;11(3):455-8

Sandman CA, Kastin AJ: The influence of fragments of the LPH chains on learning, memory and attention in animals and man. Pharmacol Ther [B] 1981;13(1):39-60 (76 ref.)

Sannomiya P, De Moraes S: Effects of denervation, decentralization and cocaine on the responses of the guinea-pig vas deferens to phenylephrine in vivo and in vitro. J Pharm Pharmacol 1981 Jun;33(6):388-9

Sano M, Hollan O, Bombeck CT, et al: Effect of acetylcholine and catecholamines on the enterochromaffin-like cells of the stomach. Surg Gynecol Obstet 1981 Sep;153(3):337-40

Santori EM, Schmidt DE, Kalivas PW, et al: Failure of muscarinic blockade to antagonize analepsis induced by thyrotropin-releasing hormone and MK-771 in the rat. Psychopharmacology (Berlin) 1981; 74(1):13-6

Sapun DI, Farah JM Jr, Mueller GP: Evidence that a serotonergic mechanism stimulates the secretion of pituitary beta-endorphin-like immunoreactivity in the rat. Endocrinology 1981 Aug;109(2):421-6

Sar M, Stumpf WE: Estradiol concentration in dopamine-beta-hydroxylase containing neurons of lower brain stem demonstrated by combined autoradiography and immunohistochemistry. Exp Brain Res 1981;Suppl 3:29-36

Sarhan F, Engasser JM, Batt AM, et al: Effect of diphenylhydantoin and its main hydroxylated metabolite on the pharmacokinetics and the urinary and biliary excretion of phenobarbital and its p-hydroxy metabolite. Eur J Drug Metab Pharmacokinet 1981;6(2):99-108

Sarkar DK, Smith GC, Fink G: Effect of manipulating central catecholamines on puberty and the surge of luteinizing hormone and gonadotropin releasing hormone induced by pregnant mare serum gonadotropin in female rats. Brain Res 1981 Jun 1;213(2):335-49

Sasahara K, Nitanai T, Habara T, et al: Dosage form design for improvement of bioavailability of levodopa IV: Possible causes of low bioavailability of oral levodopa in dogs. J Pharm Sci 1981 Jul; 70(7):730-3

Sassa S, Golde DW, Li CH: Growth hormone stimulates drug-induced porphyrin formation in liver cells maintained in a serum-free medium. J Biol Chem 1981 Sep 10;256(17):8882-4

Sato A, Sakaguchi T, Shimada K: [Quantitative measurement of phenytoin and hydroxyphenytoin in human serum by column extraction-high-performance liquid chromatography (author's transl)] Yakugaku Zasshi 1980 Dec;100(12):1215-9 (Eng. Abstr.) **(Jpn)**

Saul'skaia NB: Soderzhanie dofamina v nigro-striarnoi sisteme pri vyrabotke i realizatsii uslovnoreflektornykh reaktsii izbeganiia razlichnoi slozhnosti u krys. Fiziol Zh SSSR 1981 Jun;67(6):797-803 (Eng. Abstr.) **(Rus)**

Sawas AH, Gilbert JC: Effects of adrenergic agonists and antagonists and of the catechol nucleus on the Na+, K+-ATPase and Mg2+-ATPase activities of synaptosomes. Biochem Pharmacol 1981 Jul 1; 30(13):1799-803

Saxena V, Saksena HK: Induction of pseudo-pregnancy in Saccobranchus fossilis and cytomorphological assay of anomalies. Biochem Exp Biol 1980;16(3):257-60

Saxon ME, Safronova VG, Lazarev AV, et al: Role of neurotransmitter release and cyclic AMP-dependent membrane phosphorylation in low voltage myocardial automaticity. Experientia 1981 Jul 15;37(7):731-4

Scanes CG, Harvey S, Morgan BA, et al: Effect of synthetic thyrotrophin-releasing hormone and its analogues on growth hormone secretion in the domestic fowl (Gallus domesticus). Acta Endocrinol (Copenh) 1981 Aug;97(4):448-53

Scatton B: Differential changes in DOPAC levels in the hippocampal formation, septum and striatum of the rat induced by acute and repeated neuroleptic treatment. Eur J Pharmacol 1981 May 22;71(4):499-503

Schafer DF, Fowler JM, Jones EA: Colonic bacteria: a source of gamma-aminobutyric acid in blood. Proc Soc Exp Biol Med 1981 Jul; 167(3):301-3

Schaffler K, Hörmann E, Arnold H: A pilot study to evaluate the effect of acute and long-term administration of cyclandelate on the vigilance of subjects submitted to hypoxic conditions. Preliminary report. Arzneimittelforsch 1981;31(6):1032-5

Schaldenbrand JD, McClatchey KD, Patel JA, et al: Doxylamine: a cause for false-positive gas chromatographic assay for phencyclidine. Ther Drug Monit 1981;3(2):181-3

Scherman D, Henry JP: pH-dependence of the ATP-driven uptake of noradrenaline by bovine chromaffin-granule ghosts. Eur J Biochem 1981 Jun 1;116(3):535-9

Scherrmann JM, Hoellinger H, Nguyen-Hoang-Nam, et al: Detection and quantitation of cannabinoids in biological fluids: specificity and kinetics after smoking. Clin Toxicol 1981 May;18(5):565-71

Schleyer M, Trah T, Schleyer I, et al: Comparative investigations of human and porcine somatotropin. Hoppe Seylers Z Physiol Chem 1981 Jul; 362(7):875-81

Schmeling WT, Hosko MJ, Hardman HF: Potentials evoked in the intermediolateral column by hypothalamic stimulation - suppression by delta 9-tetrahydrocannabinol. Life Sci 1981 Aug 17;29(7):673-80

Schneck DW, Pritchard JF: The inhibitory effect of propranolol pretreatment on its own metabolism in the rat. J Pharmacol Exp Ther 1981 Sep;218(3):575-81

Schneider AS, Cline HT, Rosenheck K, et al: Stimulus-secretion coupling in isolated adrenal chromaffin cells: calcium channel activation and possible role of cytoskeletal elements. J Neurochem 1981 Sep; 37(3):567-75

Schneider SJ, Kirby EJ, Itil TM: Clinical blood chemistry values and long acting phenothiazines. Pharmacopsychiatria 1981 May;14(3):107-14

Schoemaker H, Berendsen HH, Stevens HJ, et al: Differences in presynaptic alpha-blockade, noradrenaline uptake inhibition, and potential antidepressant activity between (+)- and (-)mianserin. Psychopharmacology (Berlin) 1981;74(2):137-42

Schoenle E, Zapf J, Froesch ER: In vivo control of insulin-sensitive phosphodiesterase in rat adipocytes by growth hormone and its parallelism to glucose transport. Endocrinology 1981 Aug;109(2):561-6

Schoepp DD, Azzaro AJ: Alteration of dopamine synthesis in rat striatum subsequent to selective type A monoamine oxidase inhibition. J Neurochem 1981 Aug;37(2):527-30

Schotman P, Allaart J, Gispen WH: Pineal protein synthesis highly sensitive to ACTH-like neuropeptides. Brain Res 1981 Aug 24; 219(1):121-35

Schousboe A, Larsson OM, Hertz L, et al: Heterocyclic GABA analogues as selective inhibitors of astroglial GABA uptake. Adv Biochem Psychopharmacol 1981;29:135-41 (28 ref.)

Schousboe A: Transport and metabolism of glutamate and GABA in neurons are glial cells. Int Rev Neurobiol 1981;22:1-45 (419 ref.)

Schreiber V, Přibyl T, Štěpán J, et al: Biologická a imunologická aktivita podobná digitálisovým glykosidum syntetického ACTH a některých 14-hydroxyderivátu pohlavních hormonu. Cas Lek Cesk 1981 May 21; 120(20):616-8 (Eng. Abstr.) **(Cze)**

Schröder H, Gerold N, Heym C: Immunofluorescence of dopamine-beta-hydroxylase in small intensely fluorescent cells of human sympathetic ganglia. Acta Anat (Basel) 1981 Jan;109(1):47-50

Schulman JA: Anatomical distribution and physiological effects of enkephalin in rat inferior olive. Regul Pept 1981 May;2(2):125-37

Schulz H, Schwarzberg H, Penzlin H: The insect neuropeptide proctolin can affect the CNS and the smooth=muscle of mammals. Acta Biol Med Ger 1981;40(2):K1-5

Schulz SC, van Kammen DP, Buchsbaum MS, et al: Gamma-hydroxybutyrate treatment of schizophrenia: a pilot study. Pharmacopsychiatria 1981 Jul;14(4):129-34

Schusdziarra V, Rouiller D, Harris V, et al: Effect of prostaglandin E2 upon release of pancreatic somatostatin-like immunoreactivity. Life Sci 1981 May 11;28(19):2099-102

Schusdziarra V, Rouiller D, Harris V, et al: Effect of bombesin upon plasma somatostatin-like immunoreactivity, insulin and glucagon in normal and chemically sympathectomized dogs. Regul Pept 1980 Oct; 1(2):89-96

Schuster P, Schwindl L, Oppenoorth E: Phasenüberdauernde Strukturen der 'depressiven Persönlichkeit' bei Lithiumprophylaxe. Unter besonderer Berücksichtigung des Sozialpartners. Bibl Psychiatr 1981; (161):170-8 (Eng. Abstr.) **(Ger)**

Schuurkes JA, Van Nueten JM: Effects of dopamine and its antagonist domperidone cannot be explained by an effect on alpha 1-adrenergic receptors. Arch Int Pharmacodyn Ther 1981 Apr;250(2):324-7

Schwanzel-Fukuda M, Robinson JA, Silverman AJ: The fetal development of the luteinizing hormone-releasing hormone (LHRH) neuronal systems of the guinea pig brain. Brain Res Bull 1981 Sep;7(3):293-315

Schwartz IR: The differential distribution of label following uptake of 3H-labeled amino acids in the dorsal cochlear nucleus of the cat. An autoradiographic study. Exp Neurol 1981 Sep;73(3):601-17

Schwartz J, Jackson G, Kates RE, et al: A comparison of circulatory responsiveness following the sudden withdrawal from atenolol and propranolol. Eur Heart J 1981 Feb;2(1):31-9

Schwarzberg H, Kovács GL, Szabó G, et al: Intraventricular administration of vasopressin and oxytocin effects the steady-state levels of serotonin, dopamine and norepinephrine in rat brain. Endocrinol Exp (Bratisl) 1981;15(2):75-80

Scott PM, Knigge KM: Immunocytochemistry of luteinizing hormone-releasing hormone, vasopressin, and corticotropin following deafferentation of the basal hypothalamus of the male rat brain. Cell Tissue Res 1981;219(2):393-402

Scott TR, Johnson WA, Satterlee DG, et al: Circulating levels of corticosterone in the serum of developing chick embryos and newly hatched chicks. Poult Sci 1981 Jun;60(6):1314-20

Scotto di Tella AM, Mercier J: Influence du mode d'administration sur l'action de quelques antidépresseurs et neuroleptiques désinhibiteurs sur le comportement de désespoir. J Pharmacol 1981 Apr-Jun;12(2):179-88 (Eng. Abstr.) **(Fre)**

Seegal RF: Selective activation of tuberoinfundibular dopaminergic neurons in the chronically restrained rat. Brain Res 1981 Jul 20; 216(2):460-5

Seeger TF, Gardner EL, Bridger WF: Increase in mesolimbic electrical self-stimulation after chronic haloperidol: reversal by L-DOPA or lithium. Brain Res 1981 Jun 29;215(1-2):404-9

Segal M, Greenberger V, Hofstein R: Cyclic AMP-generating systems in rat hippocampal slices. Brain Res 1981 Jun 1;213(2):351-64

Séguin C, Bélanger A, Cusan L, et al: Relative importance of the adenohypophyseal and gonadal sites in inhibitory action of LHRH agonists. Biol Reprod 1981 May;24(4):889-901

Seidler C: Theoretische Ansätze und eigene Erfahrungen mit der Kombination von Psychopharmaka und Psychotherapie. Z Arztl Fortbild (Jena) 1981 May 1;75(9):412-5 **(Ger)**

Seiger A, Granholm AC: Thyroxin dependency of the developing locus coeruleus. Evidence from intraocular grafting experiments. Cell Tissue Res 1981;220(1):1-15

Seiler N, Sarhan S, Roth-Schechter BF: Developmental changes of the GABA and polyamine systems in isolated neurons in cell culture. Dev Neurosci 1981;4(3):181-7

Seino S, Seino Y, Sakurai H, et al: The effect of ventromedial hypothalamic nuclei destruction on somatostatin and insulin release from the isolated perfused rat pancreas. Life Sci 1981 May 18;28(20):2231-6

Seizinger BR, Höllt V, Herz A: Evidence for an opiate-inactive N-acetylated derivative of leucine-enkephalin in the rat neurointermediate pituitary. Biochem Biophys Res Commun 1981 Jul 16;101(1):289-97

Selinger Z, Cassel D: Role of guanine nucleotides in hormonal activation of adenylate cyclase. Adv Cyclic Nucleotide Res 1981;14:15-22

Semenov VV, Glumova VA, Petrov NM, et al: Morfofunktsional'nye izmeneniia shchitovidnoi zhelezy krysy pri deistvii khlorida litiia. Biull Eksp Biol Med 1981 Jun;91(6):754-7 (Eng. Abstr.) **(Rus)**

Semenova TP, Ivanov VA, Tret'yak TM: Brain levels of noradrenalin, dopamine, and serotonin in rats with different levels of motor activity. Neurosci Behav Physiol 1981 Mar-Apr;11(2):153-5

Semke VIa: O vozmozhnostiakh patogeneticheskoi terapii isterii. Zh Nevropatol Psikhiatr 1981;81(3):420-5 (Eng. Abstr.) **(Rus)**

Semm P, Demaine C, Vollrath L: Electrical responses of pineal cells to melatonin and putative transmitters. Evidence for circadian changes in sensitivity. Exp Brain Res 1981;43(3-4):361-70

AUTHOR SECTION

Sen A: Purified low-molecular-weight protein kinase from murine sarcoma virus particles catalyzes tyrosine phosphorylation endogenously but phosphorylates cellular proteins at serine. J Virol 1981 Aug; 39(2):612-24

Sen S, Bhattacharya S: Role of thyroxine & gonadotropins on the mobilization of ovarian cholesterol in a teleost Anabas testudineus (Bloch). Indian J Exp Biol 1981 May;19(5):408-12

Sergienko NG, Luchko NA, Brovina NN: Spektrofluorimetricheskoe iccledovanie vzaimodeistviia atsetilkholina s belkami mozga.
Ukr Biokhim Zh 1981 May-Jun;53(3):18-21 (Eng. Abstr.) **(Rus)**

Serra G, Melis MR, Argiolas A, et al: REM sleep deprivation induces subsensitivity of dopamine receptors mediating sedation in rats.
Eur J Pharmacol 1981 Jun 10;72(1):131-5

Sette M, Raisman R, Briley M, et al: Localisation of tricyclic antidepressant binding sites on serotonin nerve terminals.
J Neurochem 1981 Jul;37(1):40-2

Sezer Yarimağan H, Bor NM: The effects of epinephrine on guinea pig placental glycogen metabolism and on cellular cyclic AMP.
Biochem Med 1981 Apr;25(2):125-34

Shaffer JE, Kocsis JJ: Taurine mobilizing effects of beta alanine and other inhibitors of taurine transport. Life Sci 1981 Jun 15;28(24):2727-36

Shain W, Carpenter DO: Mechanisms of synaptic modulation.
Int Rev Neurobiol 1981;22:205-50 (254 ref.)

Shalaby IA, Dendel PS, Spear LP: Differential functional ontogeny of dopamine presynaptic receptor regulation. Brain Res 1981 Jun; 227(3):434-9

Shanbaky NM, Wacholtz MC, Sha'afi RI: Further studies of hormone-sensitive sodium and potassium transport in red cells from developing chick embryos. J Cell Physiol 1981 May;107(2):303-8

Shane E, Gammon DE, Bilezikian JP: A cellular activator of catecholamine-sensitive adenylate cyclase in rat reticulocytes and erythrocytes: changes during reticulocyte development and effects on the beta receptor. Arch Biochem Biophys 1981 May;208(2):418-25

Sharer DR, Petit E: Using drug holidays for chronic outpatients.
Hosp Community Psychiatry 1981 Jun;32(6):420-1

Sharp PJ, Van Tijen WF, Van Middelkoop JH, et al: Lack of a relationship between concentrations of plasma luteinising hormone, thyroxine and prolactin at nine week's of age and subsequent egg production in the domestic hen. Br Poult Sci 1981 Jan;22(1):53-8

Sharples D: Photodecomposition of some substituted phenothiazines.
J Pharm Pharmacol 1981 Apr;33(4):242-3

Sharpless NS: Accelerated metabolism of probenecid during long-term treatment of rats with anticonvulsant drugs: effect on central serotonin turnover studies. Neuropharmacology 1981 Mar;20(3):211-6

Shaw SH: Management of depressive neurosis. Practitioner 1981 Feb; 225(1352):228-30

Shears SB, Bronk JR: Ion transport in liver mitochondria from normal and thyroxine-treated rats. J Bioenerg Biomembr 1980 Dec; 12(5-6):379-93

Sheehan MJ: Constructs and 'conflict' in depression. Br J Psychol 1981 May;72(Pt 2):197-209

Shefner SA, North RA, Zukin RS: Opiate effects on rabbit vagus nerve: electrophysiology and radioligand binding. Brain Res 1981 Sep 21; 221(1):109-16

Shen YC: [Clinical manifestations and treatment of addictions to hypnotics and mild tranquilizers]
Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1980 Apr;13(4):200-1 **(Chi)**

Shepperson NB, Purcell T, Massingham R, et al: In vitro studies on 6-fluoronoradrenaline at several peripheral sympathetic neuroeffector junctions. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):1-4

Shibuya M, Kageyama N, Taniguchi T, et al: Effects of CDP-choline on striatal dopamine level and behavior in rats. Jpn J Pharmacol 1981 Feb; 31(1):47-52

Shiio I, Sugimoto S: Effect of enzyme concentration on regulation of dissociable chorismate mutase in Brevibacterium flavum.
J Biochem (Tokyo) 1981 May;89(5):1483-92

Shimomura K, Mori J, Honda F: Backward walking induced by L-5-hydroxytryptophan in mice. Jpn J Pharmacol 1981 Feb;31(1):39-46

Shiomi H, Ueda H, Takagi H: Isolation and identification of an analgesic opioid dipeptide kyotorphin (Tyr-Arg) from bovine brain.
Neuropharmacology 1981 Jul;20(7):633-8

Shiomi H, Kuraishi Y, Ueda H, et al: Mechanism of kyotorphin-induced release of Met-enkephalin from guinea pig striatum and spinal cord. Brain Res 1981 Sep 21;221(1):161-9

Shiosaka S, Takatsuki K, Sakanaka M, et al: New somatostatin-containing sites in the diencephalon of the neonatal rat. Neurosci Lett 1981 Aug 7;25(1):69-73

Shire JG: Corticosterone catabolism by mouse liver homogenate: strain difference in dependence on added NADP. J Endocrinol Invest 1981 Apr-Jun;4(2):193-6

Shirling D, Ashby JP, Baird JD: Effect of progesterone on lipid metabolism in the intact rat. J Endocrinol 1981 Aug;90(2):285-94

Shishkin SB, Baranov AG: Deistvie nonakhlazina na kal'tsievyi mekhanizm reguliatsii tonusa koronarnykh arterii. Farmakol Toksikol 1981 Mar-Apr;44(2):184-7 (Eng. Abstr.) **(Rus)**

Shukla GS, Chandra SV: Striatal dopamine turnover and L-dopa treatment after short-term exposure of rats to manganese. Arch Toxicol 1931 Jun; 47(3):191-6

Shukla JS, Ahmad I: Search for newer substituted, phenoxyacetylethyleneimines as possible CNS, MAO and anticonvulsant agents. Pharmazie 1981 May;36(5):327-8

Shulgin A: Profiles of psychedelic drugs: 10. DOB.
J Psychoactive Drugs 1981 Jan-Mar;13(1):99

Shults T, Kownacki AA, Woods WE, et al: Pharmacokinetics and behavioral effects of methylphenidate in Thoroughbred horses.
Am J Vet Res 1981 May;42(5):722-6

Shuto K, Shiozaki Z, Kojima T, et al: Antagonism of KW-5338 (domperidone) against emesis and depression of intestinal motility induced by L-DOPA. J Pharmacobiodyn 1980 Dec;3(12):709-14

Siegers CP, Biltz H, Pentz R: Effect of diethyldithiocarbamate on the metabolic elimination of hexobarbital, phenazone, tolbutamide and four halogenated hydrocarbons. Eur J Drug Metab Pharmacokinet 1981; 6(2):141-8

Siess W, Roth P, Weber PC: Stimulated platelet aggregation, thromboxane B2 formation and platelet sensitivity to prostacyclin - a critical evaluation. Thromb Haemost 1981 Jun 30;45(3):204-7

Silva Carvalho L, Moniz de Bettencourt J, Silva Carvalho J, et al: Action du propranolol et du pindolol sur les réflexes cartidiens déclenchés par la lobéline. C R Trav Lab Carlsberg 1981;175(3):416-9 (Eng. Abstr.) **(Fre)**

Simionescu S, Bordeianu A, Stancu C, et al: L'action pharmacodynamique non spécifique d'un antagoniste du système neuroadrénergique du type réserpinique (Raunervil) en traitement chronique sur l'équilibre de la fonction sexuelle. Physiologie 1981;18(2):89-97 **(Fre)**

Simmonds MA: Distinction between the effects of barbiturates, benzodiazepines and phenytoin on responses to gamma-aminobutyric acid receptor activation and antagonism by bicuculline and picrotoxin. Br J Pharmacol 1981 Jul;73(3):739-47

Simon L, Talpas GS, Sallai J, et al: Osszefüggés a pentetrazol, az 1,2,3,4-tetrahidro-izokinolin-származékok patkány izolált gyomorfunduscsíkon kifejtett spazmogén hatása és néhány fizikai-kémiai tulajdonsága között. Acta Pharm Hung 1980 May;50(3):123-9 (Eng. Abstr.) **(Hun)**

Simpson DL, Rumack BH: Methylenedioxyamphetamine. Clinical description of overdose, death, and review of pharmacology.
Arch Intern Med 1981 Oct;141(11):1507-9

Singh M: Amylase release from dissociated mouse pancreatic acinar cells stimulated by glucagon: effect of membrane stabilizers.
J Physiol (Lond) 1980 Dec;309:81-91

Singh MM, Kay SR, Pitman RK: Territorial behavior of schizophrenics. A phylogenetic approach. J Nerv Ment Dis 1981 Aug;169(8):503-12

Singh PN, Sharma P, Gupta PK, et al: Clinical evaluation of diazepam for relief of postoperative pain. Br J Anaesth 1981 Aug;53(8):831-6

Singleton C, Marsden CA: Circadian variation in the head twitch response produced by 5-methoxy-N1,N1-dimethyltryptamine and p-chloroamphetamine in the mouse. Psychopharmacology (Berlin) 1981; 74(2):173-6

Sinitskii VN, Usherenko LS: Mekhanizmy tsentral'nogo deistviia litiia. Zh Nevropatol Psikhiatr 1981;81(4):567-75 (Eng. Abstr.) **(Rus)**

Siomopoulos V: Violence: the ugly face of amphetamine abuse. IMJ 1981 Jun;159(6):375-7

Siris SG, Rifkin A: The problem of psychopharmacotherapy in the medically ill. Psychiatr Clin North Am 1981 Aug;4(2):379-90 (48 ref.)

Skolinick P, Paul S, Crawley J, et al: 3-hydroxymethyl-beta-carboline antagonizes some pharmacologic actions of diazepam.
Eur J Pharmacol 1981 Feb 19;69(4):525-7

Skotland T: Studies on the interaction of Cibacron Blue and Procion Red with dopamine beta-monooxygenase. Biochim Biophys Acta 1981 Jun 15;659(2):312-25

Skudlarek MD, Swank RT: Turnover of two lysosomal enzymes in macrophages. J Biol Chem 1981 Oct 10;256(19):10137-44

Skutsch GM: Manic depression—a disorder of central dopaminergic rhythm. Med Hypotheses 1981 Jun;7(6):737-46

Sly J, Bell FR: Effect of lithium intake on sodium and lithium appetite in sodium deficient cattle. Physiol Behav 1981 Jul;27(1):147-52

Small JG, Kellams JJ, Dennis JL, et al: Comparison of molindone and tranylcypromine in the treatment of refractory depression.
J Clin Pharmacol 1981 Aug-Sep;21(8-9):351-8

Smedley HM: Malignant breast change in man given two drugs associated with breast hyperplasia [letter] Lancet 1981 Sep 19;2 Pt 1(8247):638-9

Smirnov VB, Ponomarenko VV: Vliianie mutatsii, blokiruiushchikh kinureninovyi put' obmena triptofana, na neironal'nuiu aktivnost'u Drosophila melanogaster. Dokl Akad Nauk SSSR 1981;258(2):489-91 **(Rus)**

Smith CP, Ellis DB, Meyerson LR: Dopaminergic agonist and antagonist effects on striatal tyrosine hydroxylase distribution. Life Sci 1981 Jan 12;28(2):193-7

Smith DF, Strömgren LS: Influence of unilateral ECT on tryptophan metabolism in endogenous depression. Pharmacopsychiatria 1981 Jul; 14(4):135-8

Smith FP, Pomposini DA: Detection of phenobarbital in bloodstains,

AUTHOR SECTION

semen, seminal stains, saliva, saliva stains, perspiration stains, and hair. J Forensic Sci 1981 Jul;26(3):582-6

Smith JE: Improving drug knowledge in psychiatric patients. J Psychiatr Nurs 1981 Apr;19(4):16-8

Smith MS: Site of action of prolactin in the suppression of gonadotropin secretion during lactation in the rat: effect on pituitary responsiveness to LHRH. Biol Reprod 1981 Jun;24(5):967-76

Smith MT, Wills ED: Effects of dietary lipid and phenobarbitone on the distribution and concentration of cytochrome P-450 in the liver studied by quantitative cytochemistry. FEBS Lett 1981 May 5;127(1):33-6

Smith SA, Pogson CI: Effects of benserazide and carbidopa on the metabolism of L-tryptophan by isolated rat liver cells. Biochem Pharmacol 1981 Mar 15;30(6):623-8

Snead OC 3d, Morley BJ: Ontogeny of gamma-hydroxybutyric acid. I. Regional concentration in developing rat, monkey and human brain. Brain Res 1981 Jul;227(4):579-89

Soldin SJ, Chan YP, Hill BM, et al: Liquid-chromatographic analysis for methylphenidate (Ritalin) in serum. Clin Chem 1979 Mar;25(3):401-4

Soll AH, Rodrigo R, Ferrari JC: Effects of chemical transmitters on function of isolated canine parietal cells. Fed Proc 1981 Aug; 40(10):2519-23

Solomon PR, Crider A, Winkelman JW, et al: Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. Biol Psychiatry 1981 Jun;16(6):519-37

Somoza E, Franco C, Laviña M, et al: Clozapine inhibition of metenkephalin binding to synaptosome-enriched fractions of rat whole brain and hippocampus. Neurochem Res 1981 Apr;6(4):413-24

Sonntag WE, Forman LJ, Miki N, et al: Effects of CNS active drugs and somatostatin antiserum on growth hormone release in young and old male rats. Neuroendocrinology 1981 Aug;33(2):73-8

Sono A, Kobayashi Y, Yamamoto H, et al: [Mutagenicity tests on mequitazine (author's transl)] J Toxicol Sci 1981 May;6(2):123-8 (Eng. Abstr.) **(Jpn)**

Sorrentino F, Fella A, Pota A: Effetto preventivo di alcune sostanze sulla calcolosi ossalica sperimentale della rana. Minerva Nefrol 1979 Jul-Sep; 26(3):329-31 (Eng. Abstr.) **(Ita)**

Sotsky SM, Lake CR, Goodwin FK: Adrenocortical function and plasma norepinephrine in normal human subjects. Biol Psychiatry 1981 Jul; 16(7):643-51

Soubrié P, Montastruc JL, Bourgoin S, et al: In vivo evidence for GABAergic control of serotonin release in the cat substantia nigra. Eur J Pharmacol 1981 Feb 19;69(4):483-8

Southwick S, Anderson RJ: Antagonism of reserpine rigidity without inducing sedation. Psychopharmacology (Berlin) 1981;74(1):29-32

Spanne P: Thermoluminescence dosimetry in the muGy range. Theoretical and experimental investigations of the optimum performance of a LiF-TLD system. Acta Radiol [Suppl] (Stockh) 1979;360:1-118

Spatz M, Maruki C, Abe T, et al: The uptake and fate of the radiolabeled 5-hydroxytryptamine in isolated cerebral microvessels. Brain Res 1981 Sep 7;220(1):214-9

Spear LP, Ristine LA: Quipazine-induced behavior in neonatal rat pups. Pharmacol Biochem Behav 1981 Jun;14(6):831-4

Specht LA, Pickel VM, Joh TH, et al: Light-microscopic immunocytochemical localization of tyrosine hydroxylase in prenatal rat brain. I. Early ontogeny. J Comp Neurol 1981 Jun 20;199(2):233-53

Specht LA, Pickel VM, Joh TH, et al: Light-microscopic immunocytochemical localization of tyrosine hydroxylase in prenatal rat brain. II. Late ontogeny. J Comp Neurol 1981 Jun 20;199(2):255-76

Specht LA, Pickel VM, Joh TH, et al: Fine structure of the nigrostriatal anlage in fetal rat brain by immunocytochemical localization of tyrosine hydroxylase. Brain Res 1981 Aug 10;218(1-2):49-65

Sperschneider H, Spustova V, Neumann J, et al: Middle molecular weight substances and tryptophan in cerebrospinal fluid of schizophrenic patients. Artif Organs 1981 May;5(2):177-8

Spiegel R: On predicting therapeutic usefulness of psychotropic drugs from experiments in health persons. Rev Pure Appl Pharmacol Sci 1980 Jul-Sep;1(3):215-91 (163 ref.)

Spindel ER, Lakber M, Wurtman RJ: Formation and degradation of deamido-TRH (pyroglutamyl-histidyl-proline) in rat brain after intraventricular injection of TRH. Brain Res 1981 Jul 20;216(2):343-50

Spindel ER, Pettibone DJ, Wurtman RJ: Thyrotropin-releasing hormone (TRH) content of rat striatum: modification by drugs and lesions. Brain Res 1981 Jul 20;216(2):323-31

Sporn A, Pinsker H: Use of stimulant medication in treating pervasive developmental disorder [letter] Am J Psychiatry 1981 Jul;138(7):997

Springer AD, Fraley SM: Extinction of a conditioned taste aversion in young, mid-aged, and aged C57/BL6 mice. Behav Neural Biol 1981 Jul;32(3):282-94

Springer J, Hannigan JH Jr, Isaacson RL: Changes in dopamine and DOPAC following systemic administration of apomorphine and 3,4-dihydroxyphenylamino-2-imidazoline (DPI) in rats. Brain Res 1981 Sep 7;220(1):226-30

Srikant CB, Patel YC: Somatostatin receptors: identification and characterization in rat brain membranes. Proc Natl Acad Sci USA 1981 Jun;78(6):3930-4

Srivastava VK, Satsangi RK, Shankar K, et al: Some new 5-substituted benzylidene-1-phenyl-3-(2'-pyridinobutan-4'-yl) thiobarbituric acids as psychopharmacological agents. Pharmazie 1981 Apr;36(4):252-3

St-Pierre S, Lalonde JM, Gendreau M, et al: Synthesis of peptides by the solid-phase method. 6. Neurotensin, fragments, and analogues. J Med Chem 1981 Apr;24(4):370-6

Staak R: Uber den Einfluss der Karotissinusdruckbelastung und der lokalen Adrenalinapplikation am Karotissinus auf den Perfusionsdruck der durchströmten Hinterextremität des Hundes. Acta Biol Med Ger 1981;40(2):189-99 (Eng. Abstr.) **(Ger)**

Starling JR, Weese JL, Norback DH: Pulmonary alveolar macrophage lysosomal enzyme activity after sublethal rotational trauma. J Surg Res 1981 Aug;31(2):128-35

Starr MS, Kilpatrick IC: Distribution of gamma-aminobutyrate in the rat thalamus: specific decreases in thalamic gamma-aminobutyrate following lesion or electrical stimulation of the substantia nigra. Neuroscience 1981;6(6):1095-104

Starr MS, Kilpatrick IC: Bilateral asymmetry in brain GABA function? Neurosci Lett 1981 Sep 1;25(2):167-72

Steer ML, Wood A: Inhibitory effects of sodium and other monovalent cations on human platelet adenylate cyclase. J Biol Chem 1981 Oct 10;256(19):9990-3

Steiner RA, Bremner WJ: Endocrine correlates of sexual development in the male monkey, Macaca fascicularis. Endocrinology 1981 Sep; 109(3):914-9

Stenchever MA, Smith WD: The effect of diazepam on meiosis in the CF-1 mouse. Teratology 1981 Apr;23(2):279-81

Stengaard-Pedersen K, Larsson LI: Localization and opiate receptor binding of enkephalin, CCK and ACTH/beta-endorphin in the rat central nervous system. Peptides (Fayetteville) 1981;2 Suppl 1:3-19 (53 ref.)

Sternberg DE, van Kammen DP, Lake CR, et al: The effect of pimozide on CSF norepinephrine in schizophrenia. Am J Psychiatry 1981 Aug; 138(8):1045-50

Stetler-Stevenson MA, Yang DC, Lipkowski A, et al: An approach to the elucidation of metabolic breakdown products of the luteinizing hormone-releasing hormone. J Med Chem 1981 Jun;24(6):688-92

Stetler-Stevenson MA, Flouret G, Peterson DR: Handling of luteinizing hormone-releasing hormone by renal proximal tubular segments in vitro. Am J Physiol 1981 Aug;241(2):F117-22

Stewart JK, Koerker DJ, Goodner CJ, et al: Regulation by catecholamines of spontaneous growth hormone secretion in the baboon. Am J Physiol 1981 Sep;241(3):E196-9

Stoeckel ME, Schmitt G, Porte A: Fine structure and cytochemistry of the mammalian pars intermedia. Ciba Found Symp 1981;(81):101-27

Stone TW: The effects of morphine and methionine-enkephalin on the release of purines from cerebral cortex slices of rats and mice. Br J Pharmacol 1981 Sep;74(1):171-6

Stone TW: The effects of 4-aminopyridine on the isolated vas deferens and its effects on the inhibitory properties of adenosine, morphine, noradrenaline and gamma-aminobutyric acid. Br J Pharmacol 1981 Jul; 73(3):791-6

Stone TW: Studies with excitatory amino acid antagonists in rat CNS: 2-amino-5-phosphonovaleric acid, phenytoin, and benzodiazepines. Adv Biochem Psychopharmacol 1981;29:223-30

Story DF, McCulloch MW, Rand MJ, et al: Conditions required for the inhibitory feedback loop in noradrenergic transmission. Nature 1981 Sep 3;293(5827):62-5

Stotter ML: Propranolol and epinephrine [letter] JAMA 1981 Oct 16; 246(16):1772

Stratone A, Roşca V, Mitrofan A, et al: Activitatea bioelectrică cerebrală şi eliminarea catecolaminelor urinare în stressul termic la copil. Rev Med Chir Soc Med Nat Iasi 1981;85(1):113-6 (Eng. Abstr.) **(Rum)**

(Stretch R), In memoriam. Roger Stretch. June 9, 1935-June 18, 1980. Prog Neuropsychopharmacol 1981;5(1):107-9

Strombeck DR, Rogers QR, Stern JS: Effects of ammonia infusion on plasma glucagon, insulin, and amino acids in intact, pancreatectomized, and adrenalectomized dogs. Am J Vet Res 1981 May;42(5):810-8

Sturgeon D, Kuipers L, Berkowitz R, et al: Psychophysiological responses of schizophrenic patients to high and low expressed emotion relatives. Br J Psychiatry 1981 Jan;138:40-5

Subramoniam A, Ramakrishnan CV: Influence of thyroxine on suckling rat intestinal alkaline phosphatase and effects of undernutrition on the same. J Exp Zool 1980 Dec;214(3):317-22

Suckow RF, Cooper TB: Simultaneous determination of imipramine, desipramine, and their 2-hydroxy metabolites in plasma by ion-pair reversed-phase high-performance liquid chromatography with amperometric detection. J Pharm Sci 1981 Mar;70(3):257-61

Sugrue MF: Current concepts of the mechanisms of action of antidepressant drugs. Pharmacol Ther 1981;13(2):219-47 (262 ref.)

Sumirtapura Y, Rigault JP, Cano JP, et al: Pharmacocinétique clinique du flunitrazépam (Narcozep) chez de malades en réanimation (résultats préliminaires). Ann Anesthesiol Fr 1981;22(2):180-4 (Eng. Abstr.) **(Fre)**

Summers MC, Lightman SL: A reaction of acetaldehyde with enkephalins and related peptides. Biochem Pharmacol 1981 Jun 15;30(12):1621-7

Sendin U: GDP binding to rat brown fat mitochondria: effects of thyroxine at different ambient temperatures. Am J Physiol 1981 Sep;241(3):C134-9

Supavilai P, Karobath M: Action of pyrazolopyridines as modulators of [3H]flunitrazepam binding to the gaba/benzodiazepine receptor complex of the cerebellum. Eur J Pharmacol 1981 Mar 12;70(2):183-93

Supple EW, Powell WJ Jr: Effect of acetylcholine on vascular capacity in the dog. J Clin Invest 1981 Jul;68(1):64-74

Susic H, Malik KU: Prostacyclin and prostaglandin E2 effects on adrenergic transmission in the kidney of anesthetized dog. J Pharmacol Exp Ther 1981 Sep;218(3):588-92

Susic H, Nasjletti A, Malik KU: Bradykinin effects on adrenergic transmission in the canine kidney: relation to prostaglandins. Am J Physiol 1981 Sep;241(3):R146-51

Suzuki O, Katsumata Y, Oya M: Characterization of eight biogenic indoleamines as substrates for type A and type B monoamine oxidase. Biochem Pharmacol 1981 Jun 1;30(11):1353-8

Suzuki O, Katsumata Y, Oya M, et al: Inhibition of type A and type B monoamine oxidases by naturally occurring xanthones. Planta Med 1981 May;42(1):17-21

Suzuki T: [Present status of studies on peptides with biological activity] (Jpn) Nippon Rinsho 1980 Oct;38(10):4230-7 (42 ref.)

Suzuki T, Ohkuma T, Isozaki S: Nonlinear first-pass metabolism of propranolol in the rat. J Pharmacobiodyn 1981 Feb;4(2):131-41

Sved A, Fernstrom J: Tyrosine availability and dopamine synthesis in the striatum: studies with gamma-butyrolactone. Life Sci 1981 Aug 17;29(7):743-8

Svendsen H, Greibrokk T: High-performance liquid chromatographic determination of biogenic amines. II. Comparison of detection methods. J Chromatogr 1981 Sep 4;213(3):429-37

Sverdlov LS: O dinamike obratnogo razvitiia ostrykh shizofrenicheskikh pristupov pri psikhofarmakologicheskom lechenii. (Rus) Zh Nevropatol Psikhiatr 1981;(5):737-43 (Eng. Abstr.)

Svestka J. Náhunek K, Cesková E: Clinical experience with some beta blocking agents and their derivatives in endogenous depressions. Agressologie 1979;20(D):295-8

Swaab DF, Martin JT: Functions of alpha-melanotropin and other opiomelanocortin peptides in labour, intrauterine growth and brain development. Ciba Found Symp 1981;(81):196-217

Swaminathan R, Morgan DB, Hill GL, et al: Blood concentration and disappearance of injected alanine and beta-hydroxybutyrate in surgical patients. Horm Metab Res 1981 Jul;13(7):383-6

Swarup G, Cohen S, Garbers DL: Selective dephosphorylation of proteins containing phosphotyrosine by alkaline phosphatases. J Biol Chem 1981 Aug 10;256(15):8197-201

Swiątecka G: Badania nad wpływem propranololu, nifedipiny i aminofiliny na zmiany odcinka ST i zalamka T elektrokardiogramu w ewolucjach rytmu wlasnego u chorych ze wszczepionym rozrusznikiem serca. (Pol) Kardiol Pol 1981;24(5):343-8 (Eng. Abstr.)

Swiatek KR, Dombrowski GJ Jr, Chao KL, et al: Metabolism of L-and D-3-hydroxybutyrate by rat liver during development. Biochem Med 1981 Apr;25(2):160-7

Switzman L, Fishman B, Amit Z: Pre-exposure effects of morphine, diazepam and delta 9-THC on the formation of conditioned taste aversions. Psychopharmacology (Berlin) 1981;74(2):149-57

Szabadi E, Gaszner P, Bradshaw CM: Interaction of desipramine and amitriptyline with adrenergic mechanisms in the human iris in vivo. Eur J Clin Pharmacol 1981;19(6):403-8

Szutowicz A, Bielarczyk H, Lysiak W: The role of citrate derived from glucose in the acetylcholine synthesis in rat brain synaptosomes. Int J Biochem 1981;13(8):887-92

Szydlowska H, Kowalska Z, Vetulani J: The effect of drugs on accumulation of exogenous norepinephrine in nervous tissue cultured in vitro. IV. The effect of clonidine. Folia Histochem Cytochem (Krakow) 1981;19(2):93-8

T

Taché Y, Rivier J, Vale W, et al: Is somatostatin or a somatostatin-like peptide involved in central nervous system control of gastric secretion? Regul Pept 1981 Feb;1(5):307-15

Tachibana S: [Dynorphin---A potent opioid peptide (author's transl)] (Jpn) Tanpakushitsu Kakusan Koso 1981 Feb;26(2):115-24 (20 ref.)

Tackett RL, Webb JG, Privitera PJ: Cerebroventricular propranolol elevates cerebrospinal fluid norepinephrine and lowers blood pressure. Science 1981 Aug 21;213(4510):911-3

Takács M, Kertész P, Graczáné LM: Csapadékleválás fenotiazin-származékot és novamidazofent tartalmazó injekciós oldatban. Acta Pharm Hung 1981 Mar;51(2):55-60 (Eng. Abstr.) (Hun)

Takagi A: [Studies on the situational factors affecting the effect of psychotropic drugs. II. Circadian fluctuation of sedative and anti-apomorphine effects of chlorpromazine (author's transl)] (Jpn) Seishin Shinkeigaku Zasshi 1981;83(4):236-50

Takai Y, Kishimoto A, Kawahara Y, et al: Calcium and phosphatidylinositol turnover as signalling for transmembrane control of protein phosphorylation. Adv Cyclic Nucleotide Res 1981;14:301-13

Takáts G: A vér kolinészteráz-aktivitás értékelése foszforsavészter-mérgezések posztmortális diagnosztikájában. (Hun) Morphol Igazsagugyi Orv Sz 1980 Jan;20(1):22-5

Takeda T, Honda T, Takeda Y, et al: Failure of chlorpromazine to inhibit fluid accumulation caused by Escherichia coli heat-stable enterotoxin in suckling mice. Infect Immun 1981 May;32(2):480-3

Takeda Y, Kanaya H: Formation of nitroso compounds and mutagens from tranquilizers by drug/nitrite interaction. Cancer Lett 1981 Mar;12(1-2):81-6

Tamir A, Righi M, Levitzki A: The interaction of chlorpromazine and butyrophenones with glutamate dehydrogenase. Biochem Pharmacol 1981 Jun 15;30(12):1469-73

Tamura S, Matsumoto Y: Effect of organic thio-compounds on detoxication of glucuronyltransferase and beta-glucuronidase in the rat liver. J Toxicol Sci 1981 Feb;6(1):19-16

Tan CT, Chan SW, Hsia JC: Specific anti-thyroxine antisera induced by thyroxine sensitized liposomes. Immunol Commun 1981;10(1):27-34

Tan KN, Tashjian AH Jr: Receptor-mediated release of plasma membrane-associated calcium and stimulation of calcium uptake by thyrotropin-releasing hormone in pituitary cells in culture. J Biol Chem 1981 Sep 10;256(17):8994-9002

Tapper EJ, Lewand DL: Actions of a nicotinic agonist, DMPP, on intestinal ion transport in vitro. Life Sci 1981 Jan 12;28(2):155-62

Tapper EJ, Bloom AS, Lewand DL: Endogenous norepinephrine release induced by tyramine modulates intestinal ion transport. Am J Physiol 1981 Sep;241(3):G264-9

Taverner MR, Hume ID, Farrell DJ: Availability to pigs of amino acids in cereal grains. 2. Apparent and true ileal availability. Br J Nutr 1981 Jul;46(1):159-71

Taylor A: Role of cytosolic calcium and sodium-calcium exchange in regulation of transepithelial sodium and water absorption. Soc Gen Physiol Ser 1981;36:233-59 (117 ref.)

Taylor MW, Smith CC, Hern JE: An unexpected reaction to carbamazepine. Practitioner 1981 Feb;225(1352):219-20

Taylor RL, Burt DR: Properties of [3H](3-Me-His2)TRH binding to apparent TRH receptors in the sheep central nervous system. Brain Res 1981 Aug 10;218(1-2):207-17

Tegeler J, Lehmann E: A follow-up study of schizophrenic outpatients treated with depot-neuroleptics. Prog Neuropsychopharmacol 1981;5(1):79-90

Teichberg VI, Cohen S, Blumberg S: Distinct classes of substance P receptors revealed by a comparison of the activities of substance P and some of its segments. Regul Pept 1981 Feb;1(5):327-33

Teixeira F, Macedo TR: Influence of deaminated metabolites on the relaxing effect of dopamine on dog saphenous vein. J Pharm Pharmacol 1981 Aug;33(8):529-33

Telner JI, Singhal RL: Effects of nortriptyline treatment on learned helplessness in the rat. Pharmacol Biochem Behav 1981 Jun;14(6):823-6

Terenina NB: Identifikatsiia katekholaminov v tkanevykh ékstraktakh trematody Fasciola hepatica. (Rus) Zh Evol Biokhim Fiziol 1981 Jul-Aug;17(4):342-7 (Eng. Abstr.)

Terry LC, Epelbaum J, Martin JB: Monosodium glutamate: acute and chronic effects on rhythmic growth hormone and prolactin secretion, and somatostatin in the undisturbed male rat. Brain Res 1981 Jul 27;217(1):129-42

Terry WS, McCorkle DL: Effects of pentobarbital on delayed alternation performance. Behav Neural Biol 1981 Jul;32(3):380-5

Tervo K, Tervo T, Eränkö L, et al: Immunoreactivity for substance P in the Gasserian ganglion, ophthalmic nerve and anterior segment of the rabbit eye. Histochem J 1981 May;13(3):435-43

Tervo K, Tervo T, Eränkö L, et al: Substance P immunoreactive nerves in the rodent cornea. Neurosci Lett 1981 Aug 7;25(1):95-7

Teufel H, Joseph W, Loeschke K, et al: Das Verhalten zellulärer zyklischer Nucleotide nach hydrokinetischer und ekbolischer Stimulierung des Hundepankreas. (Ger) Hoppe Seylers Z Physiol Chem 1981 May;362(5):481-97 (Eng. Abstr.)

Teufel S, Schöny W, Hofmann G: Klinisch-psychopathologische Verlaufsuntersuchung unter prophylaktischer Lithium-Therapie. (Ger) Bibl Psychiatr 1981;(161):58-62

Thackray RI: The stress of boredom and monotony: a consideration of the evidence. Psychosom Med 1981 Apr;43(2):165-76

Tharandt L, Rosanowski C, Windeck R, et al: The metabolic serum clearance of GnRH. Relationship to age, sex and male puberty. Horm Metab Res 1981 May;13(5):277-82

Theron CN, Neethling AC, Taljaard JJ: Sex-dependent differences in phenobarbitone-induced oestradiol-2-hydroxylase activity in rat liver. S Afr Med J 1981 Aug 15;60(7):279-282

Thiede HM, Kehr W: Endogenous dopa in rat brain. Occurrence, distribution and relationship to changes i catecholamine synthesis. Naunyn Schmiedebergs Arch Pharmacol 1981 Jul;316(4):299-303

Thomas EM, Templeton D: Noradrenergic innervation of the villi of rat jejunum. J Auton Nerv Syst 1981 Feb;3(1):25-9

Thomsen K, Olesen OV: Determination of lithium-induced impairment of distal water reabsorption. J Psychiatr Res 1981;16(2):79-85

AUTHOR SECTION

Thurlby PL, Samanin R: Effects of anorectic drugs and prior feeding on food-rewarded runway behavior. Pharmacol Biochem Behav 1981 Jun;14(6):799-804

Ticku MK: Interaction of depressant, convulsant, and anticonvulsant barbiturates with the [3H]diazepam binding site of the benzodiazepine-GABA-receptor-ionophore complex.
Biochem Pharmacol 1981 Jun 15;30(12):1573-9

Tilders FJ, Post M, Jackson S, et al: beta-Adrenergic stimulation of the release of ACTH- and LPH-related peptides from the pars intermedia of the rat pituitary gland. Acta Endocrinol (Copenh) 1981;97(3):343-51

Tindula RJ: Generic phenytoin versus dilantin for once-a-day dosing [letter] Am J Hosp Pharm 1981 Aug;38(8):1114, 1116

Tjälve H, Nilsson M, Larsson B: Studies on the binding of chlorpromazine and chloroquine to melanin in vivo. Biochem Pharmacol 1981 Jul 1; 30(13):1845-7

Tobias H, Carr LA, Voogt JL: Effect of estradiol benzoate and clomiphene on tyrosine hydroxylase activity and on luteinizing hormone and prolactin levels in ovariectomized rats. Life Sci 1981 Aug 17;29(7):711-6

Todescan GC, de Faveri Tron M: Prime osservazioni sulla escrezione di sostanze coloranti da parte della mucosa gastrica di coniglio in condizioni sperimentali. (Nota tecnica). Boll Soc Ital Biol Sper 1981 Mar 30;57(6):656-8 (Eng. Abstr.) **(Ita)**

Togari A, Kato T, Nagatsu T: Effect of substance P C-terminal heptapeptide on amylase release in rat parotid gland.
Arch Oral Biol 1980;25(8-9):597-600

Tohyama M, Shiosaka S, Takagi H, et al: Somatostatin-like immunoreactivity in the facial, glossopharyngeal and vagal lobes of the carp. Neurosci Lett 1981 Jul 17;24(3):233-6

Toivonen H, Hartiala J, Bakhle YS: Effects of high oxygen tension on the metabolism of vasoactive hormones in isolated perfused rat lungs. Acta Physiol Scand 1981 Feb;111(2):185-92

Tokimasa T, Hasuo H, Koketsu K: Desensitization of the muscarinic acetylcholine receptor of atrium in bullfrogs. Jpn J Physiol 1981; 31(1):83-97

Tolis G, Comaru-Schally AM, Mehta AE, et al: Failure to interrupt established pregnancy in humans by D-tryptophan-6-luteinizing hormone-releasing hormone. Fertil Steril 1981 Aug;36(2):241-2

Tolis G, Mehta A, Comaru-Schally AM, et al: Suppression of androgen production by D-tryptophan-6-luteinizing hormone-releasing hormone in man. J Clin Invest 1981 Sep;68(3):819-22

Tolochko ZS: Uchastie noradrenergicheskikh struktur gipotalamusa v protsessakh vosproizvedeniia uslovnoĭ reaktsii 'passivnogo' izbeganiia. Zh Vyssh Nerv Deiat 1981;31(2):267-70 (Eng. Abstr.) **(Rus)**

Tondlová H, Vrzal K, Bastecky J, et al: Tricyclic antidepressants and distortions of urination in men. Agressologie 1979;20(D):291-3

Tonini M, Frigo G, Lecchini S, et al: Hyoscine-resistant peristalsis in guinea-pig ileum. Eur J Pharmacol 1981 May 22;71(4):375-81

Topall G, Laborit H: Action de la minaprine sur le métabolisme de la tyrosine chez le rat. Agressologie 1981;22(2):55-7 (Eng. Abstr.) **(Fre)**

Törk I, Turner S: Histochemical evidence for a catecholaminergic (presumably dopaminergic) projection from the ventral mesencephalic tegmentum to visual cortex in the cat. Neurosci Lett 1981 Jul 17; 24(3):215-9

Torres M, [illegible]rvisalo J, Hakim J: The liver-protective enzymes against reduced forms of oxygen in phenobarbital-treated rats. Enzyme 1981; 26(3):129-35

Torres Ruiz A, Galván Gómez L, Nieto D: Clomacrán en el tratamiento de pacientes esquizofrénicos. Estudio transcultural.
Arch Neurobiol (Madr) 1981 Mar-Apr;44(2):117-24 (Eng. Abstr.) **(Spa)**

Towell JF, Erwin VG: Determination of the primary metabolite of central nervous system norepinephrine,
3-methoxy-4-hydroxy-phenethyleneglycol, in mouse brain and brain perfusate by high-performance liquid chromatography with electrochemical detection. J Chromatogr 1981 May 8;223(2):295-303

Toyosawa K, Sitizyo K, Fukunishi K, et al: Augmentation of thoracic duct lymph flow induced by adrenaline in the rabbits treated previously with propranolol. Nippon Seirigaku Zasshi 1981;43(2):44-5

Tramu G, Beauvillain JC, Croix D, et al: Comparative immunocytochemical localization of enkephalin and somatostatin in the median eminence, hypothalamus and adjacent areas of the guinea-pig brain. Brain Res 1981 Jun 29;215(1-2):235-55

Trapani A, Matsuki N, Abel PW, et al: Norepinephrine produces tension through electromechanical coupling in rabbit ear artery.
Eur J Pharmacol 1981 Jun 10;72(1):87-91

Treasure P: Effects of fluoride, lithium and strontium on extracellular polysaccharide production by Streptococcus mutans and Actinomyces viscosus. J Dent Res 1981 Aug;60 Spec No C:1601-10

Treiser SL, Cascio CS, O'Donohue TL, et al: Lithium increases serotonin release and decreases serotonin receptors in the hippocampus.
Science 1981 Sep 25;213(4515):1529-31

Tresguerres JA, Esquifino AI: Dissociation in the regulation of luteinizing hormone and follicle-stimulating hormone in a hyperprolactinaemic rat model: interrelationships between gonadotrophin and prolactin control. J Endocrinol 1981 Jul;90(1):41-51

Tret'iak TM, Arkhipova LV, Ivanov VA: Vzaimodeistvie dioksifenilalanina s kislymi belkami khromatina golovnogo mozga krys.
Dokl Akad Nauk SSSR 1981;257(5):1262-4 **(Rus)**

Trippodo NC: Total circulatory capacity in the rat. Effects of epinephrine and vasopressin on compliance and unstressed volume. Circ Res 1981 Oct;49(4):923-31

Troillard AM: Les psychotropes aux urgences. Soins Psychiatr 1980 Apr 30;(2):33-8 **(Fre)**

Truex LL, Schmidt MJ: 3H-amphetamine concentrations in the brains of young and aged rats: implications for assessment of drug effects in aged animals. Neurobiol Aging 1980 Summer;1(1):93-5

Trzeciak HI: Metabolism of rat brain phospholipids after prolonged treatment with psychotropic drugs. Pol J Pharmacol Pharm 1980 May-Jun;32(3):319-26

Tsiantis J, Blackburn IM, Lyketsos GC: Changes in the hostility of schizophrenic patients during treatment. Br J Med Psychol 1981 Sep; 54(Pt 3):251-8

Tsuzuki Y: Effect of chronic methylmercury exposure on activities of neurotransmitter enzymes in rat cerebellum.
Toxicol Appl Pharmacol 1981 Sep 15;60(2):379-81

Tuček S, Doležal V, Sullivan AC: Inhibition of the synthesis of acetylcholine in rat brain slices by (-)-hydroxycitrate and citrate.
J Neurochem 1981 Apr;36(4):1331-7

Tukiainen E: Effect of hypophysectomy and adrenalectomy on 5-hydroxytryptamine uptake by rat hypothalamic synaptosomes and blood platelets. Acta Pharmacol Toxicol (Copenh) 1981 Feb; 48(2):139-44

Tupin JP: Use of psychotropic drugs in psychiatric conditions; psychiatric problems - recent advances in diagnosis and treatment.
Proc Annu Meet Med Sect Am Counc Life Insur 1980;5:67-85

Turner P: Some methods to assess the autonomic effects of psychotropic drugs in man. Rev Pure Appl Pharmacol Sci 1980 Oct-Dec;1(4):343-56 (50 ref.)

Turski L, Turski W, Czuczwar SJ, et al: Evidence against the involvement of serotonergic mechanisms in wet dog shake behavior induced by carbachol chloride in rats. Psychopharmacology (Berlin) 1981; 73(4):376-80

U

Uchikura K, Horikawa R, Tanimura T, et al: Determination of catecholamines by radioenzymatic assay using ion-pair liquid chromatography. J Chromatogr 1981 Apr 10;223(1):41-50

Uchiyama Y, von Mayersbach H: Circadian changes of lysosomal enzyme activities in rat hepatocytes using ultracytochemistry.
Prog Clin Biol Res 1981;59C(00):117-24

Uddman R, Malm L, Sundler F: Peptide containing nerves in the nasal mucosa. Rhinology 1981 Jun;19(2):75-9

Ueda M: Effets des ions calcium et magnésium sur l'interaction de la corticostérone avec le(s) récepteur(s) cytosolique(s) de cerveau de Rat. C R Trav Lab Carlsberg 1981;175(3):372-6 (Eng. Abstr.) **(Fre)**

Ueda Y: [Effects of diazepam and thiamylal on reticular multi-unit activity, visual evoked responses, EEG and arterial blood pressure in rabbits (author's transl)] Nippon Geka Hokan 1980 Sep 1;49(5):595-607 (Eng. Abstr.) **(Jpn)**

Uekama K, Irie T, Sunada M, et al: Protective effects of cyclodextrins on drug-induced hemolysis in vitro. J Pharmacobiodyn 1981 Feb; 4(2):142-4

Uguru-Okorie DC: Effects of chronic haloperidol treatment on ingestive behaviour and body weight regulation in the rat.
Psychopharmacology (Berlin) 1981;73(4):384-7

Uguru-Okorie DC, Arbuthnott GW: Altered paw preference after unilateral 6-hydroxy-dopamine injections into lateral hypothalamus.
Neuropsychologia 1981;19(3):463-7

Ulmar G: Rat undercut cortex as a model for the study of central amino acid transmission. Adv Biochem Psychopharmacol 1981;29:105-13

Umemoto M, Olds ME: Presynaptic alpha-adrenergic mediation of self-stimulation in locus coeruleus in rats treated neonatally with 6-hydroxydopamine. Brain Res 1981 Aug 24;219(1):107-19

Unger PD, Salerno AJ, Friedman MA: Disposition of [14C]caprolactam in the rat. Food Cosmet Toxicol 1981 Aug;19(4):457-62

Unger WG, Butler JM, Cole DF, et al: Substance P, vasoactive intestinal polypeptide (VIP) and somatostatin levels in ocular tissue of normal and sensorily denervated rabbit eyes. Exp Eye Res 1981 Jun; 32(6):797-801

Unnerstall JR, Kuhar MJ, Niehoff DL, et al: Benzodiazepine receptors are coupled to a subpopulation of gamma-aminobutyric acid (GABA) receptors: evidence from a quantitative autoradiographic study.
J Pharmacol Exp Ther 1981 Sep;218(3):797-804

Uphouse LL, Bondy SC: The maturation of cortical serotonin binding sites. Brain Res 1981 Jun;227(3):415-7

Urakov AL, Baranov AG: Zashchita proizvodnymi izokhinolina i fenotiazina mitokhondriĭ miokarda ot proniknoveniia v nikh ionov kal'tsiia. Farmakol Toksikol 1981 Jan-Feb;44(1):60-2 (Eng. Abstr.) **(Rus)**

Ursin R: Does para-chlorophenylalanine produce disturbed waking,

AUTHOR SECTION

disturbed sleep or activation by ponto-geniculo-occipital waves in cats? Waking Sleeping 1980 Jul-Sep;4(3):211-21

Urwyler S, Tabakoff B: Stimulation of dopamine synthesis and release by morphine and D-ala2-D-leu5-enkephalin in the mouse striatum in vivo. Life Sci 1981 May 18;28(20):2277-86

Uzbekov MG, Murfi Sh, Rouz SP, et al: O roli serotonina neironov i neiropilia v zritel'nom analizatore. Biull Eksp Biol Med 1981 Apr; 91(4):389-90 (Eng. Abstr.) (Rus)

V

Vaatstra WJ, Deiman-Van Aalst WM, Eigeman L: Du 24565, a quipazine derivative, a potent selective serotonin uptake inhibitor. Eur J Pharmacol 1981 Mar 12;70(2):195-202

Vale W, Spiess J, Rivier C, et al: Characterization of a 41-residue ovine hypothalamic peptide that stimulates secretion of corticotropin and beta-endorphin. Science 1981 Sep 18;213(4514):1394-7

Valentino RJ, Lockridge O, Eckerson HW, et al: Prediction of drug sensitivity in individuals with atypical serum cholinesterase based on in vitro biochemical studies. Biochem Pharmacol 1981 Jun 15; 30(12):1643-9

Valzelli L, Garattini S, Bernasconi S, et al: Neurochemical correlates of muricidal behavior in rats. Neuropsychobiology 1981;7(4):172-8

Valzelli L, Kostowski W, Bernasconi S, et al: Effect of chloro-N-desmethyldiazepam on serum and brain tryptophan and serotonin in relation to the activity of central serotonergic neurons. Pol J Pharmacol Pharm 1981 Jan-Feb;33(1):37-42

van Breemen C, Hwang O, Meisheri KD: The mechanism of inhibitory action of diltiazem on vascular smooth muscle contractility. J Pharmacol Exp Ther 1981 Aug;218(2):459-63

Vandenburg MJ, Conlon C, Ledingham JM: A comparison of the effects of propranolol and oxprenolol on forearm blood flow and skin temperature. Br J Clin Pharmacol 1981 May;11(5):485-90

van der Heyden JA, Venema K, Lebrun P, et al: Release of endogenous GABA from the rat brain: methodological aspects and the effects of catecholamines. Adv Biochem Psychopharmacol 1981;29:193-203

van der Hoeven T: Testosterone oxidation by rat liver microsomes: effects of phenobarbital pretreatment and the detection of seven metabolites by HPLC. Biochem Biophys Res Commun 1981 Jun 16;100([illegible]):1285-91

Van der Laan JW, Bruinvels J: A dual role for GABA in quasi-morphine abstinence behavior induced by di-n-propylacetate involving both initiation and termination. Psychopharmacology (Berlin) 1981; 74(2):143-8

van Dieten JA, van Valkenburg CF, de Koning J, et al: Dopaminergic and adrenergic effects on plasma LH levels in rats with hypothalamic islands. Acta Endocrinol (Copenh) 1981;97(3):289-96

van Dongen PA: The central noradrenergic transmission and the locus coeruleus: a review of the data, and their implications for neurotransmission and neuromodulation. Prog Neurobiol 1981; 16(2):117-43 (303 ref.)

Vanhoutte PM, Collis MG, Janssens WJ, et al: Calcium dependence of prejunctional inhibitory effects of adenosine and acetylcholine on adrenergic neurotransmission in canine saphenous veins. Eur J Pharmacol 1981 Jun 19;72(2-3):189-98

van Kammen DP, Docherty JP, Marder SR, et al: Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients. Psychiatry Res 1981 Jun; 4(3):313-25

Van Orden DE, Clancey CJ, Farley DB: Uterine serotonin and receptor blockade during estrogen-induced uterine hyperemia. Proc Soc Exp Biol Med 1981 Sep;167(4):469-74

Van Ree JM, Wolterink G: Injection of low doses of apomorphine into the nucleus accumbens of rats reduces locomotor activity. Eur J Pharmacol 1981 Jun 10;72(1):107-11

Van Vossel-Daeninck J, Dierickx K, Vandesande F, et al: Electron-microscopic immunocytochemical demonstration of separate vasotocinergic, mesotocinergic and somatostatinergic neurons in the hypothalamic magnocellular preoptic nucleus of the frog. Cell Tissue Res 1981;218(1):7-12

Van Wijk M, Korf J: Postmortem changes of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in mouse brain and their prevention by pargyline and microwave irradiation. Neurochem Res 1981 Apr; 6(4):425-30

Vargas AM, Lupiani MJ, Lupiañez JA, et al: Stimulation of rat renal phosphoenolpyruvate carboxykinase activity after an intravenous lactic acid load. FEBS Lett 1981 May 5;127(1):121-4

Varotto M, Roman G, Battistin L: Influenze farmacologiche sul livello e trasporto cerebrale del GABA. - I) Effetto di alcuni farmaci antiepilettici sul livel-lo cererale del GABA. Boll Soc Ital Biol Sper 1981 Apr 30;57(8):904-8 (Eng. Abstr.) (Ita)

Vartanian FE: The role of information exchange in psychopharmacology. Prog Neuropsychopharmacol 1981;5(2):201-3

Vasconcelos JA, Enns JW: Does lithium prevent neutropenia caused by antidepressants? [letter] Can Med Assoc J 1981 Jul 1;125(1):20

Vayssse N, Chayvialle JA, Pradayrol L, et al: Somatostatin 28: comparison with somatostatin 14 for plasma kinetics and low-dose effects on the exocrine pancreas in dogs. Gastroenterology 1981 Oct;81(4):700-6

Vazir H, Whitehouse BJ, Vinson GP, et al: Effects of prolonged ACTH treatment on adrenal steroidogenesis and blood pressure in rats. Acta Endocrinol (Copenh) 1981 Aug;97(4):533-42

Veber DF, Freidlinger RM, Perlow DS, et al: A potent cyclic hexapeptide analogue of somatostatin. Nature 1981 Jul 2;292(5818):55-8

Vecchione A, Buccolo M: La nostra esperienza sulla inibizione della lattazione Studio clinico controllato con bromocriptina, metergolina e piridossina). Riv Ital Ginecol 1980;59(2-3):311-9 (Eng. Abstr.) (Ita)

Veldhuis JD, Sweinberg S: Multihormonal regulation of ornithine decarboxylase activity in highly differentiated porcine granulosa cells in vitro. J Cell Physiol 1981 Aug;108(2):213-20

Velley L, Cardo B, Kempf E: Amélioration des performances lors d'un apprentissage, 4 semaines après stimulation du locus coeruleus chez le rat : absence d'effet de la lésion du faisceau noradrénergique dorsal. C R Acad Sci [D] (paris) 1981 May 4;292(16):943-6 (Eng. Abstr.) (Fre)

Vendepette-van Messom G, Burvenich C: Antidiuretic effects of intracerebroventricular infusion of adrenaline in conscious goats. Arch Int Pharmacodyn Ther 1981 Mar;250(1):137-46

Venturini PL, Horowski R, Maganza C, et al: Effects of lisuride and bromocriptine on inhibition of lactation and on serum prolactin levels: comparative double-blind study. Eur J Obstet Gynaecol Reprod Biol 1981 May;11(6):395-400

Verbanck PM, Mendlewicz J: Cell membrane anomaly in genetically determined manic-depressive illness. Neuropsychobiology 1981; 7(4):185-7

Verhoeven WM: Werkingsmechanisme an indicaties van psychofarmaca; mogelijkheden en beperkingen bij bejaarden. Gerontologie 1981 Aug; 12(3):126-38 (Eng. Abstr.) (Dut)

Vestergaard P, Schou M: Kidney morphology and function in lithium-treated patients. Bibl Psychiatr 1981;(161):104-14 (17 ref.)

Vetulani J, Antkiewicz-Michaluk L, Golembiowska-Nikitin K, et al: The effect of multiple imipramine administration on monoaminergic systems of the rat brain. Pol J Pharmacol Pharm 1980 Jul-Aug;32(4):523-30

Viby-Mogensen J: Succinylcholine neuromuscular blockade in subjects heterozygous for abnormal plasma cholinesterase. Anesthesiology 1981 Sep;55(3):231-5

Vickroy TW, Johnson KM: Stimulation of synaptosomal tyrosine hydroxylation by phencyclidine in vitro. Eur J Pharmacol 1981 May 22;71(4):463-73

Vidal y Plana RR, Cifarelli A, Setnikar I: Mechanism of smooth muscle relaxation by tiropramide. J Pharm Pharmacol 1981 Jan;33(1):19-24

Vieth WR, Ciftçi T: Transport models of the neurotransmitter-receptor interaction. Ann NY Acad Sci 1981;369:99-111

Vijayan E, McCann SM: Acetylcholine (Ach) induced alterations of plasma growth hormone (GH) in normal and pimozide-treated ovariectomized rats. Brain Res Bull 1981 Jul;7(1):11-5

Villani L, Poli A, Contestabile A, et al: Effect of kainic acid on ultrastructure and gamma-aminobutyrate-related circuits in the optic tectum of the goldfish. Neuroscience 1981;6(7):1393-403

Vincent SR, Kimura H, McGeer EG: Organization of substance P fibers within the hippocampal formation demonstrated with a biotin-avidin immunoperoxidase technique. J Comp Neurol 1981 Jun 10;199(1):113-23

Vincent SR, McGeer EG: A substance P projection to the hippocampus. Brain Res 1981 Jun 29;215(1-2):349-51

Virion A, Pommier J, Deme D, et al: Kinetics of thyroglobulin iodination and thyroid hormone synthesis catalyzed by peroxidases: the role of H2O2. Eur J Biochem 1981 Jun;117(1):103-9

Virtanen R: Radioimmunoassay for tricyclic antidepressants. Scand J Clin Lab Invest 1980 Apr;40(2):191-7

Vitto A, Mandell AJ: Stability properties of activated tryptophan hydroxylase from rat midbrain. J Neurochem 1981 Sep;37(3):601-7

Vlachoyannis J, Hoppe D, Meyer T, et al: Hämoperfusion und forcierte Diurese bei Dibenzepin-Intoxikation. Dtsch Med Wochenschr 1981 Oct 2;106(40):1314-5 (Ger)

Volkmar FR, Bacon S, Shakir SA, et al: Group therapy in the management of manic-depressive illness. Am J Psychother 1981 Apr;35(2):226-34

Vollmer KO: Zur pharmakokinetischen Differenzierung von Benzodiazepinen. Fortschr Med 1981 Jun 4;99(21):829-34 (Ger)

Vonderlage M: Spread of contraction in rabbit ear artery preparations in response to stimulation by norepinephrine. Circ Res 1981 Sep; 49(3):600-8

von Littrow C: Tinocromid ein Psychopharmakon mit Antidepressiver Wirkung. Agressologie 1979;20(D):299-302 (Ger)

Vorob'ev VV, Nesterova IV: Recovery cycles of visual cortical primary responses during pharmacological and electrical intervention on monoaminergic systems of the rat brain. Neurosci Behav Physiol 1981 Mar-Apr;11(2):129-33

Voronina TA, Toshanova NM: Vliianie stimuliatorov na trankviliziruiushchee, snotvornoe i miorelaksantnoe deistvie fenazepama. Farmakol Toksikol 1981 Mar-Apr;44(2):155-9 (Eng. Abstr.) (Rus)

Vozeh S, Muir KT, Sheiner LB, et al: Predicting individual phenytoin dosage. J Pharmacokinet Biopharm 1981 Apr;9(2):131-46

AUTHOR SECTION

W

Wachtel RE, Wilson WA Jr: Use of the single electrode voltage clamp to perform noise and relaxation studies of acetylcholine-activated channels in Aplysia neurons. J Neurosci Methods 1981 Jun;4(1):87-103

Wachtmeister L: Further studies of the chemical sensitivity of the oscillatory potentials of the electroretinogram (ERG). II. Glutamate-aspartate-and dopamine antagonists. Acta Ophthalmol (Copenh) 1981 Apr;59(2):247-58

Waddington G, Banks P: The development of pre- and postsynaptic components of the noradrenergic system in the rat cerebellum. J Neurochem 1981 Sep;37(3):576-81

Waddington JL, Gamble SJ, Bourne RC: Sequelae of 6 months continuous administration of cis(Z)- and trans(E)-flupenthixol in the rat. Eur J Pharmacol 1981 Feb 19;69(4):511-3

Wahlin A, Bucht G: Case 17-1981: chronic interstitial nephritis from lithium therapy [letter] N Engl J Med 1981 Aug 13;305(7):408

Wahlin A, Bucht G, von Knorring L, et al: Kidney function in patients with affective disorders with and without lithium therapy. Int Pharmacopsychiatry 1980;15(4):253-9

Wainer IW, Schneider LC, Weber JD: Application of chiral lanthanide nuclear magnetic resonance shift reagents to pharmaceutical analysis. II. Determination of dextro- and levoamphetamine mixtures. J Assoc Off Anal Chem 1981 Jul;64(4):848-50

Wakabayashi M, Higa H, Kushiya E, et al: gamma-Aminobutyric acid system in isolated dorsal and ventral horn neurons from bovine spinal cord. Neurochem Res 1981 Jun;6(6):659-71

Wakade AR, Wakade TD: Enhancement of 3H-noradrenaline overflow from cardiac sympathetic nerves by low Ca and tetraethylammonium. Naunyn Schmiedebergs Arch Pharmacol 1981 Jul;316(4):273-7

Wakade AR: Studies on secretion of catecholamines evoked by acetylcholine or transmural stimulation of the rat adrenal gland. J Physiol (Lond) 1981;313:463-80

Wakade AR: Facilitation of secretion of catecholamines from rat and guinea-pig adrenal glands in potassium-free medium or after ouabain. J Physiol (Lond) 1981;313:481-98

Waldbillig RJ, Bartness TJ, Stanley BG: Increased food intake, body weight, and adiposity in rats after regional neurochemical depletion of serotonin. J Comp Physiol Psychol 1981 Jun;95(3):391-405

Waldbillig RJ, Bartness TJ, Stanley BG: Disproportionate increases in locomotor activity in response to hormonal and photic stimuli following regional neurochemical depletion of serotonin. Brain Res 1981 Jul 27; 217(1):79-91

Walicke PA, Patterson PH: On the role of Ca2+ in the transmitter choice made by cultured sympathetic neurons. J Neurosci 1981 Apr;1(4):343-50

Walker CH, Faustman WO, Fowler SC, et al: A multivariate analysis of some operant variables used in behavioral pharmacology. Psychopharmacology (Berlin) 1981;74(2):182-6

Walker CR, Peacock JH: Diazepam binding of dissociated hippocampal cultures from fetal mice. Brain Res 1981 Jul;227(4):565-78

Walker P, Weichsel ME Jr, Hoath SB, et al: Effect of thyroxine, testosterone, and corticosterone on nerve growth factor (NGF) and epidermal growth factor (EGF) concentrations in adult female mouse submaxillary gland: dissociation of NGF and EGF responses. Endocrinology 1981 Aug;109(2):582-7

Wallace JE, Shimek EL Jr, Stavchansky S, et al: Determination of promethazine and other phenothiazine compounds by liquid chromatography with electrochemical detection. Anal Chem 1981 Jun; 53(7):960-2

Wallace SM, Suveges LG, Blackburn JL, et al: Oral fluphenazine and tea and coffee drinking [letter] Lancet 1981 Sep 26;2(8248):691

Walle UK, Wilson MJ, Walle T: Propranolol, alprenolol and oxprenolol metabolism in the dog. Identification of N-methylated metabolites. Biomed Mass Spectrom 1981 Feb;8(2):78-84

Waloch M, Gilman D, Whitmoyer D, et al: The effects of stimulation and lesion of raphe nuclei on luteinizing hormone release in estrogen-progesterone-treated ovariectomized rats. Brain Res 1981 Aug 3;217(2):305-13

Walsh RA, Badke FR, O'Rourke RA: Differential effects of systemic and intracoronary calcium channel blocking agents on global and regional left ventricular function in conscious dogs. Am Heart J 1981 Sep;102(3 Pt 1):341-50

Walther H, Meyer FP, Leuschner U: Verbrauchsentwicklung von Sedativa/Hypnotika und Psychopharmaka in der DDR mit internationalen Vergleichen unter Verwendung von Defined Daily Doses (DDD). Psychiatr Neurol Med Psychol (Leipz) 1981 Apr; 33(4):218-29 (Eng. Abstr.) (Ger)

Walther H, Meyer FP: Zum Einfluss von Phenobarbital auf die Selbstbeurteilung gesunder Probanden im Vergleich zur objektiven Beeinträchtigung ihrer Leistungsfähigkeit. Acta Biol Med Ger 1980; 39(8-9):949-60 (Eng. Abstr.) (Ger)

Wang IY: Effects of phenobarbital, 3-methylcholanthrene and beta-naphthoflavone pretreatment on mouse liver microsomal enzymes and on metabolite patterns of benzo[a]pyrene. Biochem Pharmacol 1981 Jun 1;30(11):1337-43

Warberg J: Potentiation of prostaglandin E2-induced release of LH by the prostaglandin analogue, 7-oxa-13-prostynoic acid. Acta Endocrinol (Copenh) 1981;97(3):297-304

Ward DP, Trevor AJ: Chronic phencyclidine induced changes in rat central cholinergic receptor regulation. Proc West Pharmacol Soc 1981; 24:3-4

Ward HE Jr, Kosh JW, Freeman JJ: Antagonism of methylphenidate-induced behavior by neostigmine or hemicholinium-3. Neuropharmacology 1981 Jul;20(7):703-9

Warembourg M, Otten U, Schwab ME: Labelling of Schwann and satellite cells by [3H]dexamethasone in a rat sympathetic ganglion and sciatic nerve. Neuroscience 1981;6(6):1039-43

Waszczak BL, Hume C, Walters JR: Supersensitivity of substantia nigra pars reticulata neurons to GABAergic drugs after striatal lesions. Life Sci 1981 May 21;28(21):2411-20

Watanabe H, Menzies JA, Jordan N, et al: Identification of hydrazone of norethindrone, a metabolic product resulting from the interaction between isoniazid and norethindrone. Res Commun Chem Pathol Pharmacol 1981 Mar;31(3):435-42

Watanabe H, Ikeda M, Watanabe K, et al: Effects on central dopaminergic systems of d-coclaurine and d-reticuline, extracted from Magnolia salicifolia. Planta Med 1981 Jul;42(3):213-22

Watanabe K, Yamamoto I, Oguri K, et al: Metabolic disposition of delta 8-tetrahydrocannabinol and its active metabolites, 11-hydroxy-delta 8-tetrahydrocannabinol and 11-oxo-delta 8-tetrahydrocannabinol, in mice. Drug Metab Dispos 1981 May-Jun;9(3):261-4

Watanabe K, Hiroshige T: Phase relation between episodic fluctuations of spontaneous locomotor activity and plasma corticosterone in rats with suprachiasmatic nuclei lesions. Neuroendocrinology 1981 Jul; 33(1):52-9

Watanabe K, Yamamoto I, Oguri K, et al: Identification and determination of 11-oxo-delta8-tetrahydrocannabinol as an intermediate metabolite of delta8-tetrahydrocannabinol in the mouse brain and liver. J Pharmacobiodyn 1980 Dec;3(12):686-91

Watanabe M, Yonezawa Y: Biphasic dose-response relationship for acetylcholine in the chick jugular vein. Life Sci 1981 Aug 10; 29(6):619-26

Watanabe S, Muraki H, Tsutsui K, et al: [Studies on the measurement of serum thyroxine with 'Amerlex T4 RIA' kit (author's transl)] Kaku Igaku 1981 Apr;18(3):333-8 (Jpn)

Watkins JC: Pharmacology of excitatory amino acid transmitters. Adv Biochem Psychopharmacol 1981;29:205-12 (31 ref.)

Watson DM, Uden DL: Promotion of intramuscular diazepam questioned [letter] Am J Hosp Pharm 1981 Jul;38(7):968, 970-1

Watts AD, Feniuk W, Humphrey PP: A pre-junctional action of 5-hydroxytryptamine and methysergide on noradrenergic nerves in dog isolated saphenous vein. J Pharm Pharmacol 1981 Aug;33(8):515-20

Webb JG, Newman WH, Walle T, et al: Myocardial sensitivity to isoproterenol following abrupt propranolol withdrawal in conscious dogs. J Cardiovasc Pharmacol 1981 May-Jun;3(3):622-35

Wehrenberg WB, McNicol D, Wardlaw SL, et al: Dopaminergic and serotonergic involvement in opiate-induced prolactin release in monkeys. Endocrinology 1981 Aug;109(2):544-7

Weiershausen U: Zur klinischen Relevanz pharmakokinetischer Unterschiede bei Benzodiazepinen. Fortschr Med 1981 Jun 28; 99(23):919-24 (Eng. Abstr.) (Ger)

Weihe E, Reinecke M, Opherk D, et al: Peptidergic innervation (substance P) in the human heart. J Mol Cell Cardiol 1981 Mar;13(3):331-3

Weindl A, Sofroniew MV: The morphology of LRH and oxytocin neurons. Exp Brain Res 1981;Suppl 3:1-17 (37 ref.)

Weinfeld RE, Miller KF: Determination of the major urinary metabolite of flurazepam in man by high-performance liquid chromatography. J Chromatogr 1981 Apr 10;223(1):123-30

Weinstock M, Roll D, Zilberman Y: An analysis of the respiratory stimulant effect of physostigmine and neostigmine in the conscious rabbit. Clin Exp Pharmacol Physiol 1981 Mar-Apr;8(2):151-8

Weiss RD, Goldenheim PD, Mirin SM, et al: Pulmonary dysfunction in cocaine smokers. Am J Psychiatry 1981 Aug;138(8):1110-2

Wernberg M, Petersen TK, Kristensen HK: Forgiftning med karbamazepin (Tegretol). Ugeskr Laeger 1981 Mar 2;143(10):619-20 (Eng. Abstr.) (Dan)

Wertheimer J: Les médicaments spychotropes en gériatrie. Ther Umsch 1981 Jan;38(1):26-31 (Eng. Abstr.) (Fre)

Wesemann W, von Pusch I: 5-hydroxytryptamine and adenine uptake by human blood platelets following the release reaction. Thromb Res 1981 Feb-Mar;21(4-5):367-74

West MJ, Blessing WW, Chalmers J: Arterial baroreceptor reflex function in the conscious rabbit after brainstem lesions coinciding with the A1 group of catecholamine neurons. Circ Res 1981 Oct;49(4):959-70

Wester R, Noonan P, Markos C, et al: Identification of carbamate derivatives formed during chloroform extraction of tricyclic antidepressants from urine. J Chromatogr 1981 May 22;209(3):463-6

Westerink BH, Mulder TB: Determination of picomole amounts of dopamine, noradrenaline, 3,4-dihydroxyphenylalanine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, and 5-hydroxyindolacetic acid in nervous tissue after one-step purification on Sephadex G-10, using high-performance liquid chromatography

AUTHOR SECTION

with a novel type of electrochemical detection. J Neurochem 1981 Apr; 36(4):1449-62

Westermann KH: Supersensitivität durch Reserpin und deren Beeinflussbarkeit. Acta Biol Med Ger 1980;39(8-9):941-7 (Eng. Abstr.) (Ger)

Wetli CV, Mittleman RE: The 'body packer syndrome'-toxicity following ingestion of illicit drugs packaged for transportation. J Forensic Sci 1981 Jul;26(3):492-500

Wetzel CD, Squire LR, Janowsky DS: Methylphenidate impairs learning and memory in normal adults. Behav Neural Biol 1981 Apr;31(4):413-24

Whalley LJ, Roberts DF, Wentzel J, et al: Antinuclear antibodies and histocompatibility antigens in patients on long-term lithium therapy. J Affective Disord 1981 Jun;3(2):123-30

Wheatley D: Trazodone in depression. Int Pharmacopsychiatry 1980; 15(4):240-6

White JH: The hyperactive child in adolescence: some pharmacologic approaches. J Adolesc 1981 Mar;4(1):79-86

White WF, Dichter MA, Snodgrass SR: Benzodiazepine binding and interactions with the GABA receptor complex in living cultures of rat cerebral cortex. Brain Res 1981 Jun 29;215(1-2):162-76

Wickings EJ, Zaidi P, Brabant G, et al: Stimulation of pituitary and testicular functions with LH-RH agonist or pulsatile LH-RH treatment in the rhesus monkey during the non-breeding season. J Reprod Fertil 1981 Sep;63(1):129-36

Wiegant VM, Zwiers H, Gispen WH: Neuropeptides and brain cAMP and phosphoproteins. Pharmacol Ther 1981;12(3):463-90

Wielosz M, Przegalinski E, Kleinrok Z: In vivo effect of danitracen on the uptake mechanism in monoaminergic neurons and platelets in rats. Agressologie 1979;20(D):253-7

Wieneke GH, Verhoeven WM, Westenberg HG, et al: The effects of haloperidol on the EEG spectrum. Psychopharmacology (Berlin) 1981; 74(1):33-4

Wikberg JE, Hede AR: Characterization of 5-hydroxytryptamine uptake in sliced rat lung. Acta Pharmacol Toxicol (Copenh) 1981 Feb; 48(2):151-6

Wildt L, Häusler A, Marshall G, et al: Frequency and amplitude of gonadotropin-releasing hormone stimulation and gonadotropin secretion in the rhesus monkey. Endocrinology 1981 Aug;109(2):376-85

Wilkinson M, Moger WH: Development of a quotidian increase in pituitary responsiveness to GnRH in prepubertal female rats. J Reprod Fertil 1981 Jul;62(2):393-8

Willcockson WS, Kahlid M, Ahmed AE, et al: Effects of acetylcholine mustard analogs on schistosome and vertebrate neuromuscular preparations. J Pharmacol Exp Ther 1981 Aug;218(2):330-6

Williams BJ, Droge MH, Hester K, et al: Induction of swimming in the high spinal stingray by L-DOPA. Brain Res 1981 Sep 7;220(1):208-13

Williford DJ, Ormsbee HS 3d, Norman W, et al: Hindbrain GABA receptors influence parasympathetic outflow to the stomach. Science 1981 Oct 9;214(4517):193-4

Willow M, Morgan IG, Johnston GA: Phenobarbitone binding sites in rat brain synaptosomal membranes. Neurosci Lett 1981 Jul 17; 24(3):301-6

Wilson WH, Petrie WM, Ban TA, et al: The effects of amoxapine and ethanol on psychomotor skills related to driving: a placebo and standard controlled study. Prog Neuropsychopharmacol 1981;5(3):263-70

Winkler ME, Yanofsky C: Pausing of RNA polymerase during in vitro transcription of the tryptophan operon leader region. Biochemistry 1981 Jun 23;20(13):3738-44

Winquist RJ, Bevan JA: Relative location of alpha- and beta-adrenoceptors to sites of release of sympathetic transmitter in the rabbit facial vein. Circ Res 1981 Aug;49(2):486-92

Wirz-Justice A, Tobler I, Kafka MS, et al: Sleep deprivation: effects on circadian rhythms of rat brain neurotransmitter receptors. Psychiatry Res 1981 Aug;5(1):67-76

Wise PM, Camp-Grossman P, Barraclough CA: Effects of estradiol and progesterone on plasma gonadotropins, prolactin, and LHRH in specific brain areas of ovariectomized rats. Biol Reprod 1981 May;24(4):820-30

Witiak DT, Tomita K, Patch RJ, et al. Epimeric cis-decahydroquinoline-5-carboxylic acids: effects on gamma-aminobutyric acid uptake and receptor binding in vitro. J Med Chem 1981 Jul;24(7):788-94

Witzgall H, Hassan-Ali S: A simultaneous radioimmunoassay for aldosterone and its precursors: human plasma levels following the inhibition of converting enzyme, before and after blockade of prostaglandin biosynthesis. J Clin Chem Clin Biochem 1981 Jun; 19(6):387-94

Wold F: In vivo chemical modification of proteins (post-translational modification). Annu Rev Biochem 1981;50:783-814 (199 ref.)

Wolfarth S, Kolasiewicz W, Sontag KH: The effects of muscimol and picrotoxin injections into the cat substantia nigra. Naunyn Schmiedebergs Arch Pharmacol 1981 Aug;317(1):54-60

Wolff JR: Evidence for a dual role of GABA as a synaptic transmitter and a promoter of synaptogenesis. Adv Biochem Psychopharmacol 1981;29:459-65 (29 ref.)

Wollemann M: Endogenous opioids and cyclic AMP. Prog Neurobiol 1981;16(2):145-54 (76 ref.)

Wondrák E: Zur Problematik der Sudeckschen Dystrophie am Handgelenk. Zentralbl Chir 1981;106(10):641-8 (Eng. Abstr.) (Ger)

Wong DS, Hochstein P: The potentiation of ozone toxicity by thyroxine. Res Commun Chem Pathol Pharmacol 1981 Mar;31(3):483-92

Wong DT, Reid LR: Activation of adenylate cyclase in rat striatum by an ergoline dopamine agonist, pergolide. Commun Psychopharmacol 1980;4(4):269-75

Wong PC, Lai JC, Lim L, et al: Selective inhibition of L-glutamate and gammaaminobutyrate transport in nerve ending particles by aluminium, manganese, and cadmium chloride. J Inorg Biochem 1981 Jun; 14(3):253-60

Wong PT, McGeer EG: Postnatal changes of GABAergic and glutamatergic parameters. Brain Res 1981 Jul;227(4):519-29

Woods WT, Urthaler F, James TN: Electrical Activity in canine sinus node cells during arrest produced by acetylcholine. J Mol Cell Cardiol 1981 Apr;13(4):249-57

Wray BB, Guill MF: Emergency treatment of insect sting reactions -- should adrenaline be available in schools and camps? J Med Assoc Ga 1981 Aug;70(8):551-2

Wrenn RW, Katoh N, Schatzman RC, et al: Inhibition by phenothiazine antipsychotic drugs of calcium-dependent phosphorylation of cerebral cortex proteins regulated by phospholipid or calmodulin. Life Sci 1981 Aug 17;29(7):725-33

Wright KC, Hedge GA: Effects of various prostanoids on thyrotropin secretion by superfused anterior pituitary cells. Endocrinology 1981 Aug;109(2):637-43

Wright PJ, Findlay JK, Anderson GA: The failure of prolactin to enhance the inhibitory effect of oestradiol-17 beta on LH synthesis and release in ewes. J Reprod Fertil 1981 Jul;62(2):537-42

Wright PJ, Jenkin G, Heap RB: Prolactin and LH release in response to LH-RH and TRH in ewes during dioestrus, pregnancy and post partum. J Reprod Fertil 1981 Jul;62(2):447-53

Wszolek PC, LaFaunce NA, Wachs T, et al: Studies of possible bovine urinary excretion and rumen decomposition of fenvalerate insecticide and metabolite. Bull Environ Contam Toxicol 1981 Feb;26(2):262-6

Wu AM, Christie GE, Platt T: Tandem termination sites in the tryptophan operon of Escherichia coli. Proc Natl Acad Sci USA 1981 May; 78(5):2913-7

Wu PH, Phillis JW: The effect of noradrenaline on Na-K transport in rat cerebral cortical slices. Eur J Pharmacol 1981 Feb 19;69(4):529-31

Wu ZC, Gaginella TS: Functional properties of noradrenergic nervous system in rat colonic mucosa: uptake of [3H]norepinephrine. Am J Physiol 1981 Aug;241(2):G137-42

Wuerthele SM, Freed WJ, Olson L, et al: Effect of dopamine agonists and antagonists on the electrical activity of substantia nigra neurons transplanted into the lateral ventricle of the rat. Exp Brain Res 1981; 44(1):1-10

Wünsch E, Jaeger E, Moroder L, et al: Somatostatin-28: a conformational analysis. Biopolymers 1981 Aug;20(8):1741-5

Wustmann C, Rudolph E, Fischer HD, et al: Einfluss von Piracetam und Dihydroergotoxin auf die Freisetzung von Dopamin aus striatumschnitten der Ratte. Acta Biol Med Ger 1980;39(8-9):383-5 (Ger)

Wuttke W, Mansky T: Gonadal steroids and brain monoamines: how do they interact? Exp Brain Res 1981;Suppl 3:130-41

Y

Yamada K, Kayama E, Aizawa Y, et al: Determination of vanillylmandelic acid in urine by pre-column dansylation using micro high-performance liquid chromatography with fluorescence detection. J Chromatogr 1981 Apr 10;223(1):176-8

Yamada K, Furukawa T: Barrel rotation induced by vasopressin and involvement of dopaminergic and cholinergic functions in rats. Arch Int Pharmacodyn Ther 1981 May;251(1):88-94

Yamada S, Mikami S: Immunocytochemical localization of neurotensin-containing neurons in the hypothalamus of the Japanese quail, Coturnix coturnix japonica. Cell Tissue Res 1981;218(1):29-39

Yamamoto T, Takahashi T, Kawamura Y: Access to the cerebral cortex of extra-lingual taste inputs in the rat. Neurosci Lett 1981 Jul 2; 24(2):129-32

Yamasaki K, Lico MC: Electroencephalographic serotonin synchronization: area postrema and solitary tract nucleus. Am J Physiol 1981 Sep;241(3):R158-62

Yamauchi J: Thyrotropin releasing hormone (TRH): its changes in discrete hypothalamic areas after treatment with triiodothyronine, thyroidectomy and acute cold exposure. Acta Med Okayama 1981 Feb; 35(1):61-76

Yamauchi T, Fujisawa H: Tyrosine 3-monoxygenase is phosphorylated by Ca2+-, calmodulin-dependent protein kinase, followed by activation by activator protein. Biochem Biophys Res Commun 1981 May 29; 100(2):807-13

Yamauchi T, Fujisawa H: A calmodulin-dependent protein kinase that is involved in the activation of tryptophan 5-monooxygenase is specifically distributed in brain tissues. FEBS Lett 1981 Jun 29;

AUTHOR SECTION

129(1):117-9

Yamaya R: [Effects of intrathecal injection of beta-endorphin on endocrine function in man (author's transl)] Masui 1981 May;30(5):445-52 (Eng. Abstr.) (Jpn)

Yanagi S, Sasaki K, Yamamoto N: Induction by phenobarbital of ornithine decarboxylase activity in rat liver after initiation with diethylnitrosamine. Cancer Lett 1981 Mar;12(1-2):87-91

Yanagihara N: Stimulatory effect of ouabain on catecholamine synthesis in bovine adrenal medullary slices. Tokushima J Exp Med 1980 Dec;27(3-4):63-8

Yanai J, Bergman A: Neuronal deficits after neonatal exposure to phenobarbital. Exp Neurol 1981 Jul;73(1):199-208

Yanuka Y, Yosselson-Superstine S, Geryes A, et al: Assignment of conformation and configuration to potassium permanganate oxidation products of quinidine. J Pharm Sci 1981 Jun;70(6):675-9

Yassa R: Leukocytosis during long-term lithium treatment.
NY State J Med 1981 Sep;81(10):1479-80

Al-Yassiri MM, Ankier SI, Bridges PK: Trazodone—a new antidepressant.
Life Sci 1981 Jun 1;28(22):2449-58 (106 ref.)

Yazulla S: GABAergic synapses in the goldfish retina: an autoradiographic study of 3H-muscimol and 3H-GABA binding. J Comp Neurol 1981 Jul 20;200(1):63-93

Yen MH, Reed DJ: Regulation of lithium in cerebrospinal fluid of the cat by the choroid plexus isolated in situ.
Arch Int Pharmacodyn Ther 1981 Jun;251(2):217-27

Yesavage JA, Holman CA, Cohn R: Correlation of thiothixene serum levels and age. Psychopharmacology (Berlin) 1981;74(2):170-2

Yokoyama H, Hiai S, Oura H: Chemical structures and corticosterone secretion-inducing activities of saikosaponins.
Chem Pharm Bull (Tokyo) 1981 Feb;29(2):500-4

Yorek MA, Rufo GA Jr, Blair JB, et al: Gluconeogenesis in rabbit liver. IV. The effects of glucagon, epinephrine, alpha- and beta-adrenergic agents on gluconeogenesis and pyruvate kinase in hepatocytes given dihydroxyacetone or fructose. Biochim Biophys Acta 1981 Jul 17;675(3-4):309-15

Yoshida M, Yokoo H, Kojima H, et al: The acute effects of sulpiride on the central dopamine turnover in rats: a quantitative histochemical study. Experientia 1981 May 15;37(5):491-2

Yoshida M, Ariga T, Kanazawa I, et al: Topographical distribution of gamma-aminobutyric acid within the cat thalamus in relation to the basal ganglia, as determined by mass fragmentometry. J Neurochem 1981 Sep;37(3):670-6

Yoshida Y, Takayanagi I, Murakami H: Dopamine and its antagonists on molluscan smooth muscle. J Pharmacobiodyn 1981 Mar;4(3):226-8

Yoshimura H, Ueki S: Regional changes in brain norepinephrine content in relation to mouse-killing behavior by rats. Brain Res Bull 1981 Aug;7(2):151-5

Young AB, Bromberg MB, Penney JB Jr: Decreased glutamate uptake in subcortical areas deafferented by sensorimotor cortical ablation in the cat. J Neurosci 1981 Mar;1(3):241-9

Young RF, Oleson TD, Perryman KM: Effect of trigeminal tractotomy on behavioral response to dental pulp stimulation in the monkey.
J Neurosurg 1981 Sep;55(3):420-3

Young-Karlan BR, Ashman RF: Order of events leading to surface immunoglobulin capping: analysis of a transmembrane signal.
J Immunol 1981 Sep;127(3):1177-81

Yu PH: Some effects of non-ionic detergent Triton X-100 on rat liver monoamine oxidase. Biochem Pharmacol 1981 Jun 1;30(11):1283-7

Yu WH, Srinivasan R: Effect of thyroid hormone on the regeneration of the hypoglossal nerve in rats. Exp Neurol 1981 Jul;73(1):325-9

Yuhas EM, Lofton FT, Baldinus JG, et al: Cimetidine hydrochloride compatibility with preoperative medications. Am J Hosp Pharm 1981 Aug;38(8):1173-4

Z

Zábojníková M, Kovalčík V: Interferencia magnézia v interakcii rezerpínu s aminofenazónom. Bratisl Lek Listy 1981;75(6):677-80 (Eng. Abstr.) (Slo)

Zaitsev AA, Tsyrlin VA: Vliianie nekotorykh neiromediatornykh sredstv na segmentarnye mekhanizmy vazomotornoi reguliatsii.
Farmakol Toksikol 1981 Mar-Apr;44(2):178-81 (Eng. Abstr.) (Rus)

Zakusov VV, Ostrovskaia RU: Novye dokazatel'stva
GAMK-ergicheskogo komponenta v mekhanizme deistviia
benzdiazepinovykh trankvilizatorov. Biull Eksp Biol Med 1981 May;91(5):571-4 (Eng. Abstr.) (Rus)

Zanchin G, Rigotti P, Dussini N, et al: Effect of L-dopa treatment on cerebral amino acid levels in rats after portocaval anastomosis.
Neurochem Res 1981 Jun;6(6):649-58

Zandomeneghi R, Tortorelli I, Sticchi G, et al: Ruolo 'in vitro' di alcuini ormoni entero-insulari sui recettori periferici dell'insulina.
Boll Soc Ital Biol Sper 1981 Apr 15;57(7):723-9 (Eng. Abstr.) (Ita)

Zapletálek M, Libiger J, Kaspárková E, et al: Pyrazidol v léčbe endogenni deprese: kontrolovaná studie. Cesk Psychiatr 1981 Feb;77(1):31-7 (Eng. Abstr.) (Cze)

Zapletálek M, Hanus H, Kindernayová H, et al: Klinické zkušenosti s preparátem lithium carbonicum retard v psychiatrii. Cesk Psychiatr 1981 Apr;77(2):110-5 (Eng. Abstr.) (Cze)

Zarevics P, Setler PE: Effects of GABAergic drugs on brain stimulation reward as assessed by a 'threshold' method. Brain Res 1981 Jun 29;215(1-2):201-9

Zarrindast MR: Dopamine-like properties of ephedrine in rat brain.
Br J Pharmacol 1981 Sep;74(1):119-22

Zavecz JH, Yellin TO: Interaction of alpha-adrenergic imidazolines with cardiac histamine H2-receptors. Eur J Pharmacol 1981 May 8;71(2-3):297-306

Zebrowska-Lupina I, Kozyrska C, Stelmasiak M: Interaction between antidepressants and alpha-adrenergic receptor blocking agents.
Pol J Pharmacol Pharm 1980;32(5):673-80

Zeisel SH, Mauron C, Watkins CJ, et al: Developmental changes in brain indoles, serum tryptophan and other serum neutral amino acids in the rat. Brain Res 1981 Jul;227(4):551-64

Zelger JL, Schorno HX, Carlini EA: Behavioural effects of cathinone, an amine obtained from Catha edulis Forsk.: comparisons with amphetamine, norpseudoephedrine, apomorphine and nomifensine.
Bull Narc 1980;32(3):67-81

Zeller FJ, Breneman WR: The in-vivo effect of Lithospermum ruderale on LHRH activity in the chick. Contraception 1981 Jul;24(1):77-81

Zerbe RL, Feuerstein G, Kopin IJ: Effect of captopril on cardiovascular, sympathetic and vasopressin responses to hemorrhage.
Eur J Pharmacol 1981 Jul 10;72(4):391-5

Zerbi F, Clemente E, Bezzi G, et al: Memory performances in depressed patients during prophylactic treatment with lithium salts.
Bibl Psychiatr 1981;(161):190-6

Zerr C, Apoil E, Poulain D, et al: Diltiazem et anesthésie.
Ann Cardiol Angeiol (Paris) 1981 Mar-Apr;30(2):133-7 (Fre)

Zetin M, Rubin HR, Rydzewski R: Tricyclic antidepressant sample stability and the vacutainer effect. Am J Psychiatry 1981 Sep;138(9):1247-8

Zhang F, Tang J: [Endogenous opiate-like substances and cardiovascular activity (author's transl)] Sheng Li Ko Hsueh Chin Chan 1980 Apr;11(4):365-7 (Chi)

Zhang ZX, Yi QC, Zou G: [Immunohistochemical localization of neuropeptides in mammalian brain (author's transl)]
Sheng Li Ko Hsueh Chin Chan 1980 Apr;11(4):342-7 (Chi)

Zhu WY: [The relation between nerves and gastrointestinal peptides]
Sheng Li Ko Hsueh Chin Chan 1980 Mar;11(3):259-62 (Chi)

Zhu YQ, Wu YZ, Li ZY: [Study on antiradiation drugs. II. Synthesis of N,N-substituted aminoalkyl 2-phenyl (or
2-chlorophenyl)-thiomorpholine and some of its derivatives (author's transl)] Yao Hsueh Hsueh Pao 1980 Oct;15(10):603-8 (Eng. Abstr.) (Chi)

Zhukotskii AV, Istomin VV: Primenenie televizionnogo analizatora 'Mikrovideomat' dlia otsenki funktsional'nogo sostoianiia populiatsii énterokhromaffinnykh kletok dvenadtsatiperstnoi kishki krysy.
Biull Eksp Biol Med 1981 May;91(5):628-30 (Eng. Abstr.) (Rus)

Zipfel E, Grezes JR, Seiffert W, et al: Über Romanowsky-Farbstoffe und den Romanowsky-Giemsa-Effekt. 1. Mitteilung: Azur B, Reinheit und Gehalt von Farbstoffen, Assoziation. Histochemistry 1981;72(2):279-90 (Eng. Abstr.) (Ger)

Zisook S, Overall JE, Click MA Jr: Treatment validity of different diagnostic concepts of depression. Psychiatry Res 1981 Aug;5(1):77-85

Zühlke H, Poltorak V, Schröder D, et al: Biosynthesis of somatostatin in pancreatic islets of Wistar rats and its regulation by glucose.
Acta Biol Med Ger 1981;40(1):99-103

Zumstein A, Karduck W, Starke K: Pathways of dopamine metabolism in the rabbit caudate nucleus in vitro.
Naunyn Schmiedebergs Arch Pharmacol 1981 Jun;316(3):205-17

Zvartau EE, Sheremet VV, Malinina VN: Vliianie élforiziruiushchikh sredstv na émotsional'no-pozitivnye sistemy mozga.
Zh Vyssh Nerv Deiat 1981;31(2):308-14 (Eng. Abstr.) (Rus)

Zwiers H, Aloyo VJ, Gispen WH: Behavioral and neurochemical effects of the new opioid peptide dynorphin—(1-13): comparison with other neuropeptides. Life Sci 1981 Jun 1;28(22):2545-51

ANONYMOUS

AUTHOR SECTION

Acta Med Scand
Guidelines for the prescription of psychotropic drugs.
Acta Med Scand 1981;209(6):437-8

Adv Biochem Psychopharmacol
Amino acid neurotransmitters. Adv Biochem Psychopharmacol 1981;
29:1-572

Agressologie
IInd Czechoslovakian Symposium of Psychopharmacology, Smolenice,
28th-30th September 1977. Agressologie 1979;20(D):235-318 (Mul)

Am J Psychiatry
Neuroleptic drug effects on neurotransmitter receptors [letter]
Am J Psychiatry 1981 Jul;138(7):991-2

Bibl Psychiatr
Current perspectives in lithium prophylaxis. International symposium,
Vienna, October 19-20, 1979. Bibl Psychiatr 1981;(161):1-248
(Eng, Mul)

Br Med J [Clin Res]
The new psychiatry [editorial] Br Med J [Clin Res] 1981 Aug 22;
283(6290):513-4
The psychiatrically violent patient [letter] Br Med J [Clin Res] 1981 Apr
11;282(6271):1232

Lancet
The how of anxiety [editorial] Lancet 1981 Aug 1;2(8240):237-9
Multicentre depression [editorial] Lancet 1981 Sep 12;2(8246):563-4

Med J Aust
John Frederick Joseph Cade. Med J Aust 1981 May 2;1(9):489

N Engl J Med
Endorphins and ventilatory control [letter] N Engl J Med 1981 Oct 15;
305(16):958-60

Nutr Rev
Dietary tryptophan and aggressive behavior in rats. Nutr Rev 1981 Jul;
39(7):284-5

Pharmacopsychiatria
Guidelines for the evaluation of drugs in the elderly neuropsychiatric
patient (demented and non-demented). Pharmacopsychiatria 1981 Jul;
14(4):150-4 contd

Prog Neuropsychopharmacol
In memoriam. Roger Stretch. June 9, 1935-June 18, 1980.
Prog Neuropsychopharmacol 1981;5(1):107-9

Psychol Med
Continuation therapy with lithium and amitriptyline in unipolar depressive
illness: a controlled clinical trial. A report by the Medical Research
Council Drug Trials Subcommittee. Psychol Med 1981 May;
11(2):409-16

S Afr Med J
Die bensodiasepiene in 1981. S Afr Med J 1981 Aug 22;60(8):301(Afr)
Dieet, senuwee-oordragstowwe en breinfunksie. S Afr Med J 1981 Aug
8;60(6):221 (Afr)

Tanpakushitsu Kakusan Koso
[Metabolism of biogenic amines and related enzymes]
Tanpakushitsu Kakusan Koso 1981 Jul;26(9 Suppl):1289-484 (Jpn)
[Progress in biochemical studies for biogenic amines]
Tanpakushitsu Kakusan Koso 1981 Jul;26(9 Suppl):1071-288 (Jpn)
[Biogenic amines and biological control] Tanpakushitsu Kakusan Koso
1981 Jul;26(9 Suppl):1065-484 (Jpn)

West J Med
Alkalinization therapy for tricyclic antidepressant overdose [letter]
West J Med 1981 May;134(5):450-2

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-180/102

The *Psychopharmacology Bulletin* is prepared by the Pharmacologic and Somatic Treatments Research Branch of the National Institute of Mental Health. Its purpose is to facilitate the dissemination and exchange of information among the national and international scientific community. The emphasis is on rapid, informal reporting of work which has not appeared in the more formal literature. We invite contributions such as original articles, brief reports, review articles, letters to the Editor, news items, books for review, and announcements appropriate for the *Bulletin*.

All material published in the *Psychopharmacology Bulletin* is in the public domain unless otherwise noted. Publication in the *Bulletin* therefore does not preclude publication elsewhere.

Individuals interested in submitting material to the *Psychopharmacology Bulletin* should contact:

Allen Raskin, Ph.D.
Editor-in-Chief
Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

We respectfully ask you to adhere to the following guidelines when preparing a paper for the *Psychopharmacology Bulletin:*

1. Manuscript Format: Manuscripts should be typed double-spaced with ample margins, and submitted in triplicate. Do not split paragraphs from one page to another, even if this makes page lengths uneven. Also, do not hyphenate words at the end of a line, even if this makes uneven lines.

Title page should include each author's name, degree, and full address.

Papers should be written in *third* person, e.g., the investigators found, *Not*: I found, we found. Contents should be *substantive*, not indicative, e.g., the investigator used the gas chromatography method to determine the three molecular structures, *Not*: The author described the method for determining the structure of the drug.

2. Figures: Figures, charts, or graphs should be submitted as glossies (photographs printed on smooth shiny paper) or should be professionally prepared using black ink on white paper. Only one copy is needed. Indicate in the text where these figures and their legends should be placed.

3. References: References mentioned in the text should appear as full citations in the **References** following the text with *all* authors cited in the reference list, e.g., Simpson, G.M., Lee, L.H., Zubok, B, and Gardos. A rating scale for tardive dyskinesia. *Psychopharmacology (Berlin)*, 64(2):171-179, 1979.

If a work has two authors, always cite both names every time the reference occurs in the text, e.g. (Swanson & Cole 1974). If more than two authors, cite only the surname of the first author in the text followed by et al., e.g., Williams et al. 1963.

4. Abbreviations: Abbreviations should appear in parentheses after the first time they are mentioned in the paper, ie., Brief Psychiatric Rating Scale (BPRS).

Use generic names in referring to drugs; trade names may be given in parenthesis the first time a drug is mentioned only.

Journal titles should be abbreviated in the *References* according to the National Library of Medicine's Index Medicus.

5. Brief Reports: Authors wishing very rapid reporting of new work may submit manuscripts of up to five typed double-spaced pages for inclusion as Brief Reports. If accepted, these results would appear in the next issue of the *Bulletin*. In preparing a manuscript for publication as a Brief Report, please follow the format cited above.

DEPARTMENT OF
HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20857

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.H.S.
HHS 396

THIRD CLASS
BULK RATE

U.S.MAIL

DHHS Publication No. (ADM) 82 - 173
Printed 1982

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20857

18/3

National Institute of Mental Health

NEWARK PUBLIC LIBRARY
OCT 28 1982
U. S. GOVT. PUBS.
DEPOSITORY 376

Psychopharmacology Bulletin

Vol. 18, No. 3
July 1982

HE 20.8109:

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

Contributions and inquiries should be sent to:

Allen Raskin, Ph.D.
Editor-in-Chief

Lillian Altman
Managing Editor

Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

The *Psychopharmacology Bulletin* is available on subscription from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402. Subscription price $11.00 per year for the United States. All other countries add $2.75 for postage. Please make check or money order payable to the Superintendent of Documents. An annual subscription for four quarterly issues begins with the next issue following receipt of the order. Single copies and back issues may also be ordered from the Superintendent of Documents. The expiration date is printed on the top line of the address label. Change of address and complaints about non-receipt of issues should be sent to the Superintendent of Documents, and should include the old address, preferably a mailing label, as well as the new address.

ORDER FORM Mail To: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Enclosed is $________ ☐ check,
(U.S. Currency Only)
☐ money order, or charge to my
Deposit Account No.
☐☐☐☐☐☐☐–☐

Order No.____________

VISA

master charge

Credit Card Orders Only

Total charges $________ Fill in the boxes below.

Credit Card No. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Expiration Date Month/Year ☐☐☐☐

Please enter my subscription to: **PSYCHOPHARMACOLOGY BULLETIN** [*PSBU*]
@ $11.00 domestic, @ $13.75 foreign.

Name—First, Last

Street address

Company name or additional address line

City **State** **ZIP Code**

(or Country)

PLEASE PRINT OR TYPE

For Office Use Only.

	Quantity	Charges
Enclosed		
To be mailed		
Subscriptions		
Postage		
Foreign handling		
MMOB		
OPNR		
UPNS		
Discount		
Refund		

Psychopharmacology Bulletin

CONTENTS

Vol. 18, No. 3 **July 1982**

Page

Addendum 1
Meeting Announcements 1

20th Annual Meeting of the ACNP—Abridged Proceedings—

Positron Emission Tomography (PET) and Cortical Localization: Clinical Studies in Psychiatry and Neurology—

Positron Emission Tomographic Studies of Epilepsy, Brain Tumors, and Alzheimer's Disease—*Thomas N. Chase, Rodney A. Brooks, Robert L. DeLaPaz, Alessandro Denaro, Giovanni DiChiro, Reymon Durso, Paul Fedio, Norman L. Foster, Robert M. Kessler, Paul L. Kornblith, Conrad V. Kufta, Ronald G. Manning, Michael E. Newmark, Nicholas J. Patronas, Roger Porter, Sumio Sato, Barry H. Smith, and William H. Theodore* 3
Cerebral Blood Flow in Depression and Mania—*A. John Rush, Michael A. Schlesser, Ernest Stokely, Frederick R. Bonte, and Kenneth Z. Altshuller* 6

Biochemical and Behavioral Studies of Anxiety—

Convulsive Benzodiazepine Receptor Ligands—*Claus Braestrup, Erling N. Petersen, and Mogens Nielsen* 8
Benzodiazepine Receptor: Interaction of a Selective Benzodiazepine Antagonist, Ro 15-1788—*H. Möhler and J. G. Richards* 10

Psychopharmacologic Treatment of Obsessive-Compulsive Disorder—

Clomipramine Treatment of Obsessive Disorder—Biochemical and Clinical Aspects—*Marie Åsberg, Peter Thorén, and Leif Bertilsson* 13

Quo Vadis—Biology of Schizophrenia—

Introductory Comments—*Edward F. Domino* 21
Two Dimensions of Pathology in Schizophrenia: Dopaminergic and Non-Dopaminergic—*Timothy J. Crow* 22
Schizophrenia and Late Maturational Brain Changes in Man—*Irwin Feinberg* 29

Dopamine and the Neural Substrates of Depression—

Evidence in Support of a Role of Dopamine in Affective Illness—*Angelos E. Halaris* 31
Mania, Depression, and Brain Dopamine: An Overview—*Axel Randrup, Ib Munkvad, and Rasmus Fog* 35

Nonlinear Dynamics in Brain Processes—

A Mathematical Model for the Effect of Tetrahydrobiopterin Level on Tyrosine Hydroxylase Kinetic Fluctuations—*Patrick V. Russo* 36
Ordering the Fluctuations of Tryptophan Hydroxylase: Lithium and Chlorimipramine—*Suzanne Knapp* 39
Characterization of Drug Effects on the EEG by Power Spectral Band Time Series Analysis—*Cindy L. Ehlers and James W. Havstad* 43
Variational and Probabilistic Aspects of Exploratory Behavior in Space: Four Stimulant Styles—*Mark A. Geyer* 48
Heart Rate Variational Characteristics in Psychopathology: A Pilot Study—*Michael R. Blackburn* 51

Page

Attending or Discriminating 40 Hz-Modulated Tones Induces Phase-Locked Subharmonic Resonances in the EEG—*Scott D. Makeig and Robert Galambos* 55

Nonlinear Dynamics in Brain Processes—*Arnold J. Mandell* 59

Interaction Among Government, Industry, and Extramural Investigators: New Developments and Problems—

An Investigator's View—*Arthur Rifkin* 64

Industry's Response to New Drug Development—*Victor B. Slotnick* 66

The Balance Sheet (The Other Side of the Ledger)—*Paul Leber* 68

New Biological Approaches to Schizophrenia—

Dopamine Neuronal Instability: A Model for the Schizophreniform Psychoses—*Roy J. King, Joachim D. Raese, Bernard A. Huberman, and Jack D. Barchas* 70

Retinal Oscillatory Potentials in Schizophrenia: Implications for the Assessment of Dopamine Transmission in Man—*Joachim D. Raese, Roy J. King, Debbie Barnes, Philip A. Berger, Jack D. Barchas, Michael Marmor, and Peggy Hock* 72

A Convergence of Findings in the Psychophysiology of Schizophrenia—*Walton T. Roth and Jared R. Tinklenberg* 78

What Is Vital Depression (Endogenous Depression or Melancholia), and How Can It Be Reliably Assessed?—

Pituitary-Adrenal Assessment in Identifying Subtypes of Depression—*Walter Armin Brown and C. Brandon Qualls* 84

Benzodiazepine Abuse: What Are the Data?—

Subjective Effects of Benzodiazepines and Methaqualone in Recreational Sedative Users—*Jonathan O. Cole, Maressa Hecht Orzack, Francine M. Benes, Barbara J. Beake, Michael P. Bird, Yoram Bar Tel, and Martin Ionescu-Pioggia* 87

What Is the Effect of "Stress" on Neuroendocrine Function? In-Depth Consideration of Recent Theorizing—

Heterogeneity in the Response Pattern of Organ Systems to Stress: Mediators and Mechanisms—*Cynthia M. Kuhn, Alberto Grignolo, Mark Johnson, and Saul M. Schanberg* 96

Neurotransmitter Receptors: Heterogeneity, Regulation, and Function—

Correlation Between Pharmacological Activity and the Influence of GABA on the Binding of Flunitrazepam and the Specific Benzodiazepine Antagonist, Ro 15-1788—*Frederick J. Ehlert, William R. Roeske, Andrew Chen, and Henry I. Yamamura* 100

Down Regulation and Heterogeneity of Opiate Receptors—*Kwen-Jen Chang and Steven G. Blanchard* 102

Alpha Adrenergic Receptor Subtypes: Physiological Relationships and Mechanisms—*Brian B. Hoffman* 107

Psychobiology of Premenstrual Change—

Retrospective Report of Premenstrual Depressive Changes: Factors Affecting Confirmation by Daily Ratings—*Jean Endicott and Uriel Halbreich* 109

Premenstrual Tension in Biochemical and Psychotropic Drug Assessment—*Richard I. Shader and Jerold S. Harmatz* 113

Future Directions in the Study of Premenstrual Changes—*Uriel Halbreich and Jean Endicott* 121

Page

Child Psychopharmacology—

Methylphenidate in Adults with MBD Symptomatology—*Jeffrey A. Mattes, Lane Boswell, and Herman Oliver* 124
Lithium and Haloperidol in Hospitalized Aggressive Children—*Magda Campbell, Arthur M. Small, Wayne H. Green, Susan J. Jennings, Richard Perry, Walter G. Bennett, Maria Padron-Gayol, and Lillian Anderson* 126

Monoamine Receptor Sensitivity and the Mechanism of Action of Antidepressant Treatment—

The Monoamine Receptor Sensitivity Hypothesis of Antidepressant Drug Action—*George R. Heninger and Dennis S. Charney* 130
Catecholamine-Stimulated Production of Melantonin After Administration of Antidepressants—*William E. Heydorn, Stanley Caroff, and Alan Frazer* 135
Agonist-Induced Changes in Behavior as a Measure of Functional Changes in Receptor Sensitivity Following Chronic Antidepressant Treatments—*Michael Davis* 137
Antidepressant Treatment and Central Adrenergic and Histamine Receptors—*Ghanshyam N. Pandey, P. Sudershan, and John M. Davis* 147
Assessment of Adrenergic and Serotonergic Receptor Function: Implications for the Etiology and Treatment of Depression—*Dennis S. Charney and George R. Heninger* 151

Protein Phosphorylation and Synaptic Mechanisms—

Introductory Comments—*Walter Lovenberg* 156
The Possible Role of Phosphorylation of Tyrosine Hydroxylase in Catecholaminergic Neurons—*Mitchell A. Lazar and Jack D. Barchas* 157
Calcium-Dependent Phosphorylation and the Regulation of Serotonin Synthesis—*Donald M. Kuhn* 161
Control of Phosphorylation of a Vesicle-Associated Protein, Synapsin I—*Mary B. Kennedy* 165

The Indole Hallucinogens—A New Look at Their Mechanisms of Action—

Action of Hallucinogenic Drugs at Postsynaptic Serotonergic Receptors—*Barry L. Jacobs, James Heym, and Kurt Rasmussen* 168
Interaction of Monoamine Blocking Agents with Behavioral Effects of N,N-Dimethyltryptamine—*David M. Stoff, Dilip V. Jeste, Egidio A. Moja, Ken A. Stauderman, and Richard J. Wyatt* 173
Evidence for Opioids as Partial Antagonists for Indole Hallucinogens—*Edward F. Domino and Diane M. Ruffing* 175
In Vitro Models to Examine Regulation of Transmitter Content and Adenylatecyclase Coupled Receptors in Neurons—*David C. U'Prichard, Karen M. Braas, and Deborah J. Kahn* 180

Mental Illness in Pregnancy and the Puerperium—

Model Utility in Postpartum Psychosis—*James A. Hamilton* 184
Hormonal Modulation of Central Dopamine Receptor Sensitivity in the Postpartum Period—*Umberto Scapagnini, Filippo Drago, Ferdinando Nicoletti, Francesco Patti, Mario Matera, and Pier L. Canonico* 187

Membrane Lipids in Neuropsychiatric Disorders—

Membrane Abnormalities in Schizophrenia—*Robert Hitzemann and David Garver* 190
Phospholipids and Phospholipid Methylation in Platelets and Brain—*Donna Mandio Cordasco, David Wazer, David J. Segarnick, Andrew Lautin, Arnold Lippa, and John Rotrosen* . . . 193

Page

Occurrence and Significance of Beta-Carbolines and Tetrahydroisoquinolines—

Cellular Actions and Localization of Beta-Carbolines and Tetrahydroisoquinolines—*Floyd E. Bloom and Jack D. Barchas* 198

Endogenous Opioid Mechanism in Neuroendocrine Regulation in Normal and Psychopathological States—

The Effect of a Methadone Challenge on the Prolactin and Growth Hormone Responses of Psychiatric Patients and Normal Controls—*Lewis L. Judd, S. Craig Risch, Donal C. Parker, David S. Janowsky, David S. Segal, and Leighton Y. Huey* 204

Response of Plasma Cortisol and β-Endorphin Immunoreactivity to Surgical Stress—*David Pickar, Martin R. Cohen, Michel Dubois, and William E. Bunney, Jr.* 208

Elevated Plasma β-Endorphin Concentrations in Depression and Cholinergically Supersensitive Release Mechanisms—*S. Craig Risch, David S. Janowsky, Lewis L. Judd, and Leighton Y. Huey* 211

Endorphins May Be Involved in the Behavioral Response to Dextro-Amphetamine—*Uriel Halbreich, Susanna Goldstein, Ee-Sing Lo, and Jean Endicott* 216

Where Is the "Lesion" in Patients Who Fail to Suppress Plasma Cortisol Concentrations with Dexamethasone?—*Ned H. Kalin, Stephen J. Weiler, William T. McKinney, Gary W. Kraemer, and Steven E. Shelton* 219

The Epidemiology of Mental Disorders: Results from the Epidemiologic Catchment Area Study (ECA)—

An Epidemiologic Perspective on Senile Dementia—Facts and Fragments—*Jacob A. Brody and Lon R. White* 222

Workshop—

Antipsychotics and Clinical Response: An Overview—*John M. Davis, Katherin Hendricks, and Javaid I. Javaid* 225

Measurement of Antipsychotics in Patients—*Javaid I. Javaid, Robert D. Linden, and John M. Davis* 227

ADDENDUM

The October 1981 issue of the *Psychopharmacology Bulletin* (Vol. 17, No. 4, p. 9) included a report on the Clinical Research Center at the Western Psychiatric Institute and Clinic (WPIC) of the University of Pittsburgh Medical School. This report did not include a full description of one of the projects at WPIC, the National Institute of Mental Health (NIMH) Treatment of Depression Collaborative Research Program. This program was initiated and designed by the staff of the NIMH Psychosocial Treatments Research Branch. The program is funded by Cooperative Agreements with the Psychosocial Treatments Research Branch and continues to be coordinated by NIMH staff. The collaborating research sites, in addition to the University of Pittsburgh, include the University of Oklahoma and George Washington University. Three sites are involved in training therapists for the program, Yale University, the University of Western Ontario, and Rush Presbyterian St. Luke's Medical Center. Also collaborating in data management and analysis aspects of the program is the Perry Point Veterans Administration Cooperative Studies Program.

Meeting Announcements

The Brazilian Geriatrics and Gerontology Society (SBGG) will hold its 6th Congress in Belo Horizonte (Minas Gerais), Brazil on October 17-22, 1982. The SBGG is the only scientific and philanthropic society in Brazil carrying out programs for the elderly population. The congress is open to all people involved in the care of the elderly. There will be lectures, debates, and discussions on subjects in the area of geriatrics and basic and social gerontology. Contact Flavio Aluizio Xavier Cancado, Head of the SBGG, Palacio das Artes, Belo Horizonte, MG, Brazil.

* * * *

The 4th Congress of the Latin-American Federation of Geriatrics and Gerontology Societies will be held in Montevideo, Uruguay on October 24-28, 1982.

* * * *

20th Annual Meeting of the ACNP — Abridged Proceedings

The Twentieth Annual Meeting of the American College of Neuropsychopharmacology (ACNP) was held in Coronado, California on December 16-18, 1981.

This Meeting annually brings together investigators actively involved in psychopharmacologic research. The papers presented at the sessions are indicative of the state-of the-art in psychopharmacology in the United States, as well as in some foreign countries.

For those who did not attend the conference, we are again publishing summaries of the presentations given at various sessions. In some cases, not all of the papers were included because they were not received in time. Papers based on poster sessions will be published in Vol. 18, No. 4, October 1982 issue.

Publication of these summaries in the *Bulletin* does not prejudice later publication of the full papers elsewhere.

Positron Emission Tomography (PET) and Cortical Localization: Clinical Studies in Psychiatry and Neurology

Co-Chair: **William E. Bunney, Jr., M.D.**
Adult Psychiatry Branch
National Institutes of Health
Rockville, Maryland

and

Earl Usdin, Ph.D.
Neurosciences Research Branch
National Institute of Mental Health
Rockville, Maryland

best copy available

Positron Emission Tomographic Studies of Epilepsy, Brain Tumors, and Alzheimer's Disease

Thomas N. Chase, M.D.,[1] Rodney A. Brooks, Ph.D.,[1] Robert L. DeLaPaz, M.D.,[2] Alessandro Denaro, M.D.,[3] Giovanni DiChiro, M.D.,[1] Raymon Durso, M.D.,[4] Paul Fedio, Ph.D.,[1] Norman L. Foster, M.D.[1] Robert M. Kessler, M.D.,[5] Paul L. Kornblith, M.D.,[1] Conrad V. Kufta, M.D.,[1] Ronald G. Manning, Ph.D.,[5] Michael E. Newmark, M.D.,[1] Nicholas J. Patronas, M.D.,[1] Roger Porter, M.D.,[1] Susumu Sato, M.D.,[1] Barry H. Smith, M.D.,[1] and William H. Theodore, M.D.[1]

Clinical measurements of local rates of glucose metabolism provide an important new approach to the non-invasive study of human central nervous system function. This procedure, adapted from a model developed by Sokoloff and coworkers (Sokoloff et al. 1977) involves the intravenous administration of 18F-2-fluoro-2-deoxy-D-glucose (FDG) whose phosphorylated metabolite accumulates in brain cells in proportion to their rate of glucose utilization (Reivich et al. 1977; Phelps et al. 1977; Reivich et al. 1979). A positron emission tomography (PET) scanner provides maps of the regional concentration of the radioactively labeled tracer throughout the brain (Ter-Pogossian et al. 1975; Kuhl et al. 1977; Phelps et al. 1978). Since the local metabolic rate for glucose appears to correlate with neuronal firing rates (Sokoloff 1980) as well as with several aspects of normal brain function (Greenberg et al. 1981; Huang et al. 1980; Phelps et al. 1979, 1981), the FDG technique may contribute substantially to the study of neurologic disease. Recent observations by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) investigators of patients with epilepsy, brain tumors, and Alzheimer's disease will be briefly reviewed.

Method

Consenting individuals were admitted to the National Institutes of Health (NIH) Clinical Center for study. FDG was prepared (Ido et al. 1980), with 18F obtained from the Naval Research Center or Brookhaven National Laboratory as previously described (DiChiro et al., submitted). By means of bilateral upper extremity catheters, up to 5 mCi of FDG was rapidly injected intravenously while serial "arterialized" venous blood samples were obtained from the opposite extremity for the determination of FDG and glucose concentrations. Following isotope administration, patients were kept quietly in the recumbent position to minimize external stimuli. PET scans were performed by an Ortec ECAT II tomograph having a spatial resolution of approximately 1.7 cm in the image plane and 1.8 cm in the axial direction. Scanning, usually at 6 sequential levels parallel to the canthomeatal plane, began about 30 minutes after FDG infusion. Calculation of local metabolic rates for glucose in mg per 100g of tissue per minute (Huang et al. 1980; DiChiro et al., submitted) was based on rate constants determined from normal young adults. In some studies comparisons were made between the metabolic rate for glucose in selected brain regions and corresponding contralateral zones.

Epilepsy

PET scanning following FDG adminstration helps identify local alterations in cerebral function in patients with complex partial seizures (Newmark et al. 1981). Previous studies using this method suggested that individuals with focal seizures, when studied interictally, evidenced a region of reduced glucose metabolism that becomes hypermetabolic during a clinical seizure (Kuhl et al. 1980). Subsequent NINCDS investigations have sought to ascertain the usefulness of the FDG technique in patients with diffuse, nonlocalized epileptiform foci, as well as to determine the stability of PET abnormalities in response to changes in various environmental factors.

---

[1] Intramural Research Program, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20205.

[2] George Washington University Medical Center, Washington, D.C. 20037.

[3] Department of Neurology, University of L'Aquila, L'Aquila, Italy.

[4] Boston Veterans Administration Medical Center, Boston, MA 02132.

[5] Department of Nuclear Medicine, National Institutes of Health, Bethesda, MD 20205.

All study subjects had refractory complex partial seizures associated with normal neurologic examinations and computed transmission tomographic (CT) scans. Interictal PET scans in patients with unilateral or predominantly unilateral epileptiform discharges invariably revealed an area of hypometabolism. Moreover, three of the four patients studied who had diffuse or bilateral discharges had a discernible interictal hypometabolic focus.

PET results were substantially influenced by clinical seizures occurring shortly after FDG injection. Individuals with seizures during the 30-minute period of FDG uptake were found to have a hypermetabolic focus in the area that was hypometabolic interictally. A comparison of interictal and ictal scans in such patients allowed a substantially better localization of the seizure focus than either ictal or interictal scans alone. Interictal PET foci did not, however, appear to be affected by the frequency of seizures between scans or the frequency of spike discharges occurring during the 30 minutes following FDG injection. Changes in anticonvulsant medication also failed to modify PET scan results. Similarly, alterations in the patient's state of alertness had no discernible effect on interictal PET abnormalities.

Brain Tumors

Human brain tumors range in malignancy from slow growing, relatively benign lesions (e.g., Grade I or II astrocytomas) to rapidly expanding, highly invasive neoplasms (e.g., glioblastomas). Although current radiologic techniques often provide useful information, diagnostic uncertainties with respect to tumor grade are not uncommon. Moreover, assessment of tumor recurrence after surgical, radiologic, or chemotherapeutic intervention may be difficult. Since available evidence suggests a positive correlation may exist between degree of malignancy and rate of tumor glycolysis (Macbeth & Bekesi 1962; Wolleman 1972), the FDG-PET technique for quantifying local rates of glucose metabolism may afford a more accurate, noninvasive approach to the clinical evaluation of cerebral neoplasms (DiChiro et al., submitted)

NINCDS studies of over 20 patients with primary brain tumors now indicate that a positive correlation does exist between malignancy grade and metabolic rate as determined by the FDG method (DiChiro et al., submitted). On average, Grade III and IV tumors exhibit twice the metabolic rate of the more benign Grade I and II tumors. It now also appears that clinically successful chemotherapeutic or radiologic treatment may be associated with a reduction in the apparent glucose utilization of these tumors.

Alzheimer's Disease

PET evaluations of patients with Alzheimer's disease may eventually provide insight into the pathophysiology of neuronal degenerative disorders as well as into the localization of major human brain functions (Ferris et al.1980; Foster et al. 1982). Right-handed Alzheimer's disease patients with disproportionate failure of visuoconstructive, language, or memory function were selected for initial study (Foster et al. 1982). CT scans from four individuals in whom constructional apraxia was the predominant cognitive impairment revealed diffuse cortical atrophy without focal abnormalities. PET scans of these patients consistently showed a conspicuous focus of low glucose consumption in the right parietal region. Glucose metabolism in this area of the nondominant hemisphere, classically associated with constructional praxis, averaged 24 percent less than the same region in the opposite hemisphere. This right-left difference significantly correlated with various tests of visuoconstructive function (e.g., Rey copy test, block design). Stimulation of one apractic patient by repetitive spatial tasks during the 30-minute period immediately following FDG injection failed to produce a significant increase in the metabolic rate of this area of hypofunction.

Focal right parietal hypofunction was not found on PET scans from Alzheimer's disease patients who were free of clinically significant constructional apraxia. On the other hand, a patient with global receptive and expressive aphasia out of proportion to his other cognitive deficits had a conspicuous focal area of hypometabolism in the left parietal region. This finding was hardly unanticipated, in view of the well-accepted brain localization of language function as well as the results of a previous PET study of aphasic patients (Metter et al. 1981). Considering the entire group of nine Alzheimer's disease patients studied thus far, there was a significant positive correlation between degree of language impairment (as evidenced by tests such as the verbal IQ on the Wechsler Adult Intelligence Scale) and absolute left temporal-parietal metabolism or relative left temporal-parietal reduction compared with the same area in the right hemisphere. Four Alzheimer's patients, clinically selected prior to PET scanning on the basis of disproportionate failure of memory, had no significant left-right differences in the temporal-parietal regions which are classically associated with aphasic disturbances. On the other hand, temporal lobe glucose metabolism, especially medially in the hippocampal area, tended to be reduced bilaterally in these individuals compared with other cortical regions or with the hippocampal regions in Alzheimer's disease patients with predominant apractic or aphasic dysfunction.

Concluding Remarks

Results are briefly presented from three ongoing NINCDS studies of neurologic disorders in which the application of the FDG-PET technique now appears exceptionally promising, not only in relation to direct patient management but also to the broad study of normal and disordered human brain function. Conclusions based on the present limited material must remain highly tentative, especially in view of the relatively poor spatial resolution of available scanning equipment, the lack of appropriate normative data, and the uncertain applicability of some assumptions used in the calculation of metabolic rates. Considering the pace of current investigative efforts, it can be confidently predicted that these limitations will appreciably lessen in the near future. Use of other positron-labeled tracers, alone or in combination with FDG, will further enhance the ultimate clinical usefulness of the PET technique.

References

DiChiro, G., DeLaPaz, R.L., Brooks, R.A., Sokoloff, L., Kornblith, P.L., Smith, B.H., Patronas, N., Kufta, C.V., Kessler, R.M., Johns, G.S., Manning, R.G., Wolf, A.P. Glucose utilization of cerebral gliomas measured by (^{18}F)fluorodeoxyglucose and positron emission tomography. *Neurology*. (In press)

Ferris, S.H., deLeon, M.J., Wolf, A.P., Farkas, T., Christman, D.R., Reisberg, B., Fowler, J.S., MacGregor, R., Goldman, A., George, A.E., and Rampal, S. Positron emission tomography in the study of aging and senile dementia. *Neurobiol. Aging*, 1:127-131, 1980.

Foster, N.L., Patronas, N.J., DeLaPaz, R., DiChiro, G., Brooks, R., Chase, T.N., Fedio, P., Denaro, A., and Durso, R. PET studies of Alzheimer's disease. *Neurology*, 32:A167, 1982.

Greenberg, J.H., Reivich, M., Alavi, A., Hand, P., Rosenquist, A., Rintelmann, W., Stein, A., Tusa, R., Dann, R., Christman, D., Fowler, J., MacGregor, B., and Wolf, A. Metabolic mapping of functional activity in human subjects with the (^{18}F)fluorodeoxyglucose technique. *Science*, 212:678-680, 1981.

Huang, S.C., Phelps, M.E., Hoffman, E.J., Sideris, K., Selin, C.J., and Kuhl, D.E. Noninvasive determination of local cerebral metabolic rate of glucose in man. *Am. J. Physiol.*, 238:E69-82, 1980.

Ido, T., Wan, C-N., Casella, V., Fowler, J.S., and Wolf, A.P. Labeled 2-deoxy-D-glucose analogs. 18-F labeled-2-deoxy-2-fluoro-D-glucose, 2-deoxy-2 fluoro-D-mannose and 14-C-2-deoxy-2-fluoro-D-glucose. *J. Label Comp. Radiopharm.*, 14:175-183, 1978.

Kuhl, D.E., Engel, J. Jr., Phelps, M.E., and Selin, C. Epileptic patterns of local cerebral metabolism and perfusion in humans determined by emission computed tomography of ^{18}FDG and $^{13}NH_3$. *Ann Neurol.*, 8:348-60, 1980.

Kuhl, D.E., Hoffman, E.J., Phelps, M.E., and Ricci, A. Design and application of the Mark IV scanning system for radionuclide computed tomography of the brain. In: *Medical Radionuclide Imaging, Vol. 1.* Vienna: International Atomic Energy Association, 1977, pp. 309-320.

Macbeth, R.A.L., and Bekesi, J.G. Oxygen consumption and anaerobic glycolysis of human malignant and normal tissue. *Cancer Res.*, 22:244-248, 1962.

Metter, E.J., Wasterlain, C.G. Kuhl, D.E., Hanson, W.R., and Phelps, M.E. 18 FDG positron emission computed tomography in a study of aphasia. *Ann. Neurol.*, 10:173-183, 1981.

Newmark, M.E., Theodore, W., DeLaPaz, R., Sato, S., DiChiro, G., Brooks, R.A., Kessler, R.M., and Porter, R.J. Positron emission computed tomography (PECT) in refractory complex partial seizures. *Ann. Neurol.*, 10:73-74, 1981.

Phelps, M.E., Hoffman, E.J., Huang, S.C., and Kuhl, D.E. ECAT: A new computerized tomographic imaging system for positron emitting radiopharmaceuticals. *J. Nucl. Med.*, 19:635-647, 1978.

Phelps, M.E., Hoffman, E.J., Huang, S.C., and Kuhl, D.E. Positron tomography: an "in vivo" autoradiographic approach to measurement of cerebral hemodynamics and metabolism. *Acta Neurol. Scand.* 56, (Suppl. 64):446-447, 1977.

Phelps, M.E., Huang, S.C., Hoffman, E.J., Selin, C., Sokoloff, L., and Kuhl, D.E. Tomographic measurement of local cerebral glucose metabolic rate in humans with (F-18)2-fluoro-2-deoxy-D-glucose: Validation of method. *Ann. Neurol.*, 6:371-388, 1979.

Phelps, M.E., Mazziotta, J.C., Kuhl, D.E., Nuwer, M., Packwood, J., Metter, J., and Engei, J. Tomographic mapping of human cerebral metabolism: Visual stimulation and deprivation. *Neurology (NY)*, 31:517-529, 1981.

Reivich, M., Greenberg, J., Alavi, A., Christman, D., Fowler, J., Hand, P., Rosenquist, A., Rintelmann, W., and Wolf, A. The use of ^{18}F-fluorodeoxyglucose technique for mapping functional neural pathways in man. *Acta Neurol. Scand. 60,* (Suppl. 72):198-199, 1979.

Reivich, M., Kuhl, D., Wolf, A., Greenberg, J., Phelps, M., Ido, T., Casella, V., Fowler, J., Gallagher, B., Hoffman, E., Alavi, A., and Sokoloff, L. Measurement of local cerebral glucose metabolism in man with ^{18}F-2-fluoro-2-deoxy-D-glucose. *Acta Neurol. Scand.* 56, (Suppl. 64):190-191, 1977.

Sokoloff, L. Relationship between functional activity and energy metabolism in the CNS. *Trans. Am. Soc. Neurochem.*, 11:171, 1980.

Sokoloff, L., Reivich, M., Kennedy, C., Des Rosiers, M.H., Patlak, C.S., Pettigrew, K.D., Sakurada, O., and Shinohara, M. The (^{14}C) deoxyglucose method for the measurement of local cerebral glucose utilization: Theory and normal values in the conscious and anesthetized albino rat and normal values in the conscious and anesthetized albino rat. *J. Neurochem.*, 28:897-916, 1977.

Ter-Pogossian, M.M., Phelps, M.E., Hoffman, E.J., and Mullani, N.A. A positron emission transaxial tomography for nuclear imaging (PETT). *Radiology,* 114:89-98, 1975.

Wolleman, M. Biochemistry of brain tumors. In: Lajtha, A. (ed.), *Handbook of Neurochemistry.* New York: Plenum Press, 1972, pp. 502-542.

Cerebral Blood Flow in Depression and Mania[1]

A. John Rush, M.D.,[2] Michael A. Schlesser, M.D.,[2] Ernest Stokely, Ph.D.,[3] Frederick R. Bonte, M.D.,[3] and Kenneth Z. Altshuller, M.D.[2]

Various investigations suggest patients with affective disorders suffer impairment of higher cortical functions (Ross & Rush 1981). Measures of regional cerebral blood flow (rCBF) provide methods that may potentially tell us, albeit indirectly, about the functional activity and/or capacity of specific regions in the brain. Until recently, such measures were restricted to information derived from lateral views of both hemispheres. Stokely et al. (1980) have developed a single photon emission tomograph method using inhaled 133 Xenon gas that provides views of three cross-sectional brain slices (4 cm apart) with a resolution of 1.7 cm (Lassen et al. 1981).

Twenty-six adult male and female patients, aged 19-69, were evaluated with Research Diagnostic Criteria (Spitzer, Endicott, & Robins 1978), Diagnostic and Statistical Manual-III (DSM-III) (APA 1980), and the 1 mg Dexamethasone Suppression Test (DST) (Carroll et al. 1981). Whenever feasible, subjects ($N = 17$) were studied at two points in time (when acutely ill and later when in clinical remission). Symptom severity was gauged by the 17-item Hamilton Rating Scale for Depression (HRS-D) (Hamilton 1960). Treatment varied across subjects and included electroconvulsive therapy (ECT), tricyclic antidepressants, alprazolam, monoamine oxidase inhibitors (MAOIs), lithium, or haloperidol. Treatment was ongoing when the repeat measurement of rCBF was made for those taking medication. For those receiving ECT, no less than 2, and most typically 5 days, elapsed between the last ECT treatment and the second rCBF determination. Treatment selection was independent of rCBF findings.

---

[1] This study was supported in part by grants from The Meadows Foundation and The Biohumanics Foundation.

[2] Department of Psychiatry and Affective Disorders Unit, University of Texas Health Science Center, Dallas, TX 75235.

[3] Department of Radiology and Nuclear Medicine Center, University of Texas Health Science Center, Dallas, TX 75235.

RCBF in ml/100 gm/min was determined using a single photon emission computerized tomographic scanner (Stokely et al. 1980). Values reported were derived from the mid slice for both whole brain and/or right and left hemisphere values separately. The algorithm used to calculate flow is still undergoing revision; thus, the actual numbers shown likely exceed actual flow in all subjects. However, the same algorithm was used in all subjects, so that comparisons between subject groups and within subjects over time are likely to be valid. Controls were gathered from volunteers at the medical center who reported themselves to be free of psychiatric symptomatology, medical illnesses, and medications.

Results

Ten unipolar depressed subjects who were both endogenous by RDC and melancholic by DSM-III were studied (UP-ED). Six Bipolar I or II subjects in the depressed phase (BP-D); four nonendogenous, nonmelancholic, unipolar patients (UP-NED); and six Bipolar I patients in mixed or manic phases (BP-MM) were studied.

RCBF was lower for the UP-ED group ($t = 2.10$, $p < .05$) and higher for the BP-MM group ($t = 2.97$, $p < .01$) compared to controls. The BP-D group did not differ from controls ($t = 0.09$, $p < .50$). Flow in UP-NED patients was higher than controls, although the sample size precludes meaningful statistical evaluation.

A significant *increase* in whole brain rCBF ($N = 8$) was found with treatment and complete clinical response (HRS-D score of 6 or less) in the UP-ED group (paired *t*-test, $t = 2.62$, $p < .04$). The type of treatment (ECT vs. medication) did not relate to this finding.

RCBF changes in treated BP-D patients were more heterogenous (three showing increases and three with decreases in whole brain rCBF). Two of the three with decreases subsequently relapsed in the following 2 months. No significant pre- or posttreatment differences for the groups as a whole were found (paired *t*-test, $t = -9.546$, $p < .65$).

Taken together, these data suggest that a) whole brain cerebral blood flow is low in melancholic, endogenous UP patients compared to controls and compared to themselves when later clinical remission; and b) whole brain cerebral blood flow is elevated in BP-MM patients compared to controls. To determine the differential contribution of the left and right hemispheres to these findings, flow rates for each hemisphere, as seen from the mid-slice, were calculated. The increases or decreases in whole brain rCBF found in the above diagnostic groups profoundly involved *both* left and right hemispheres.

While the majority of controls (14/16) showed a very slightly greater flow to the right hemisphere when at rest with eyes open, the majority of all UP-ED, BP-MM, and BP-D patients (13/22) showed a slightly greater flow on the left when acutely ill. This was significantly different from normals by chi-square ($X^2 = 7.26$, $p < .01$).

While both between-group and within-subject comparisons for UP-ED patients suggest that a lower rCBF is found during this illness and between-group comparisons suggest a higher rCBF in BP-MM and a lower rCBF in UP-ED patients, these findings are only preliminary. Samples are small; flow computations are still under investigation; more extensive control data are needed; better controls for age effect and Pa CO_2 are needed; and the effect of medications on rCBF deserves closer scrutiny.

One group (Risberg 1980) suggests no differences between depressed and controls, whereas another group (Matthews et al. 1980) did find a lower left hemisphere flow in their depressed subjects and a trend toward lower right hemisphere flow. While these data demonstrate the feasibility of rCBF determinations by inhaled 133-Xenon, the findings must be replicated.

References

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders (DSM III).* Washington, D.C., APA, 1980.

Bonte, F.J., and Stokely, E.M. Single-photon tomographic study of regional cerebral blood flow in stroke. *J. Nucl. Med.* (In press)

Bonte, F.J., and Stokely, E.M. Measurement of regional cerebral blood flow with dynamic single-photon tomography. *J. Clin. Radio.* (Submitted)

Carroll, B.J., Feinberg, M., Greden, J.F., Tarika, J., Albala, A.A., Haskett, R.F., James, N.M., Kronfol, Z., Lohr, N., Steiner, M., de Vigne, J.P., and Young, E. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry,* 138:1182-1187, 1981.

Gruzelier, J., and Flor-Henry, P., (eds.), *Hemispheric Asymmetries of Functions in Psychopathology.* Amsterdam: Elsevier, 1979.

Hamilton, M. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry,* 23:56-62, 1960.

Lassen, N.A., Henriksen, L., and Paulson, O. Regional cerebral blood flow in stroke by 133-Xenon inhalation and emission tomography. *Stroke,* 12:284-288, 1981.

Matthew, R.J., Meyer, J.S., Francis, D.J., Semchuk, K.M., Mortel, K., and Claghorn, J.L. Cerebral blood flow in depression. *Am. J. Psychiatry,* 137:1449-1450, 1980.

Risberg, J. Regional cerebral blood flow measurements by 133 Xe-inhalation: Methodology and applications in neuropsychology and psychiatry. *Brain Lang.,* 9:9-34, 1980.

Ross, E.D., and Rush, A.J. Diagnostic issues and neuroanatomical correlates of depression in brain damaged patients: Implications for a neurology of depression. *Arch. Gen. Psychiatry,* 38:1344-1354, 1981.

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry,* 35:773-782, 1978.

Stokely, E.M., Sveinsdottir, E., Lassen, N.A., and Rommer, P. A single photon dynamic computer assisted tomograph (DCAT) for imaging brain function in multiple cross-sections. *J. Comput. Assist. Tomogr.,* 4:230-240, 1980.

Biochemical and Behavioral Studies of Anxiety

Chair: Erminio Costa, M.D.
Preclinical Pharmacology
National Institute of Mental Health
St. Elizabeth Hospital
Washington, D.C.

Convulsive Benzodiazepine Receptor Ligands

Claus Braestrup, M.D.,[1] Erling N. Petersen, Ph.D.,[2] and Mogens Nielsen, Ph.D.[1]

It is generally believed that the benzodiazepine group of minor tranquilizers exert their pharmacological and clinical effects by an interaction with specific benzodiazepine (BZ) receptors located on neurons in the central nervous system (CNS) (Braestrup & Squires 1978).

It was believed that agents that interacted with benzodiazepine receptors would have benzodiazepine-like pharmacological effects. Recently, however, it was observed that the very potent BZ receptor ligand ethyl β-carboline-3-carboxylate (β-CCE) (Braestrup et al. 1980) failed to elicit benzodiazepine-like actions but that β-CCE, on the other hand, antagonized effects of benzodiazepines (Tenen & Hirsch 1980; Cowen et al. 1981). More recently, an imidazodiazepine carboxylic acid ethyl ester has been described (Ro 15-1788) which also antagonizes the effects of benzodiazepines (Hunkeler et al. 1981). These findings indicate that BZ receptor ligands bind in different ways to BZ receptors. Thus ligands may have different efficacies without differences in affinity.

During structural modifications of β-CCE we observed that the corresponding methyl ester, β-CCM [10-50 mg/kg intraperitoneally (i.p.)] and, in particular, methyl 4-ethyl-6, 7-dimethoxy-β-carboline-3-carboxylate (DMCM, Figure) (5-15 mg/kg, i.p.) produced convulsions in mice and rats when given i.p. Convulsions produced by DMCM (15 mg/kg, i.p.) were similar in quality to convulsions produced by bicuculline and pentylenetetrazol.

Convulsions produced by β-CCM and DMCM

---

[1] Sct. Hans Hospital, DK-4000 Roskilde, Denmark.

[2] A/S Ferrosan, Research Division, DK-2860 Soeborg, Denmark.

DMCM

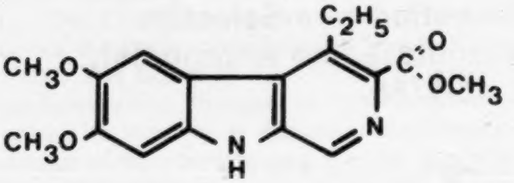


FIGURE. Chemical Structure of DMCM (methyl 4-ethyl-6, 7-demethoxy-β-carboline-3-carboxylate; ZK 90798)

are probably the consequence of BZ receptor interaction for reasons cited below:

1. β-CCM and DMCM have high affinity in vitro for BZ receptors, IC50 values for inhibition of specific [^{3}H]-flunitrazepam (^{3}H-FNM) binding to rat cerebellar membranes are 3 nM and 11 nM, respectively.

2. β-CCM and DMCM occupy BZ receptors in the brain of living animals after systemic administration. The dose that inhibits by 50 percent the BZ binding sites available for [^{3}H]-FNM intraventricularly) (i.v.) is 22 mg/kg (i.p., 35 min) for β-CCM and 4 mg/kg (i.p., 35 min) for DMCM in mouse forebrain.

3. The occurrence of clonic convulsions, tonic convulsions, and death, produced by 15 mg/kg, i.p., of DMCM in mice, can be antagonized by β-CCE (70 mg/kg, i.p.) and Ro 15-1788 [7 mg/kg, orally (p.o.)]. These agents are *not* general anticonvulsants but share the ability to occupy BZ receptors without producing overt pharmacological actions when given alone. Barbiturates and benzodiazepines likewise inhibit convulsions produced by DMCM.

4. Alternative mechanisms of action of β-CCM and DMCM have not been suggested by pharmacological and biochemical studies. When investigated with affinity binding techniques *in vitro*, DMCM, for example, does not interact with serotonin, dopamine (D-2), noradrenaline (α_1), gamma aminobutyric acid (GABA), glutamate, opiate (μ), or cholinergic (muscarinic) receptors.

5. GABA and BZ receptors are functionally coupled at the molecular level. It has been suggested that the effect of GABA agonist on the affinity of a particular BZ receptor ligand for BZ receptors may reflect the pharmacological profile of that agent (Ehlert et al. 1981; Braestrup & Nielsen 1981; Möhler & Richards 1981). Thus, GABA enhances the affinity *in vitro* of one group of BZ ligands, which consists mainly of conventional benzodiazepines (Group I) and this group of ligands exert benzodiazepine like anticonvulsant and anxiolytic activity in animals and man. For ligands in Group II, GABA has no major effect on the affinity of the ligands for BZ receptors, and members of this group antagonize effects exerted via BZ receptors without having overt pharmacological effects when given alone (examples are several β-carbolines and Ro 15-1788). In Group III, GABA agonists reduce the affinity of the ligands for BZ receptors and ligands in this group. For example β-CCM and, in particular, DMCM, have pharmacological effects opposite to those of the benzodiazepines. Thus, β-CCM and DMCM produce convulsions in rats and mice and in addition produce effects in rats that may be interpreted as anxiogenic (Petersen et al., submitted).

The affinity of DMCM for cerebellar BZ$_1$ receptors *in vitro* in chloride-containing buffer is reduced to 50 percent of the normal value by adding the GABA agonist muscimol (10^{-5}M) to the assay; this effect of muscimol is antagonized by bicuculline (10^{-5}M). The convulsant effect of DMCM and β-CCM is consistent with the BZ receptor/GABA receptor model. Consonant with these conjectures, it has also been observed that DMCM reduces the electrophysiological effects of GABA in cultured spinal neurons from the mouse (J. Lambert, unpublished).

In conclusion, BZ receptor ligands can be divided into at least three groups relating to the coupling between BZ receptors and GABA receptors. Further subclassification according to a chloride channel coupling has also been proposed (Fujimoto et al. 1982). Probably, the BZ receptor can exist in at least two conformations. It was surmised that when Group I ligands bind to the resting state of the receptor, they install a shift in direction of one particular conformational state of the receptor. This new state of the receptor-ligand complex is permissible for chloride channel opening by GABA receptor stimulation. No conformational shift occurs when Group II ligands bind to the receptor. Thus, binding has no overt consequences other than inhibiting access of Groups I and III ligands to receptors. When Group III ligands bind, the receptor attains yet a new conformation which now is inhibitory for chloride channel opening by GABA (GABAergic transmission is reduced). It is not known whether these two assumedly distinct conformations of BZ receptor exist in equilibrium under normal physiological conditions, or whether the resting state of the receptor, found in normal, undrugged individuals, represents a third conformational state.

It should be noted that the experiments described above were conducted using rat cerebellar membranes. Cerebellum is known only to contain one class of BZ receptors, BZ_1 receptors. The present considerations are not related to a BZ_1/BZ_2 receptor subclassification.

References

Braestrup, C., and Nielsen, M. GABA reduces binding of [^{3}H]-methyl β-carboline-3-carboxylate to brain benzodiazepine receptors. *Nature,* 294:472-474, 1981.

Braestrup, C., Nielsen, M., and Olsen, C.E. Urinary and brain β-carboline-3-carboxylates as potent inhibitors of brain benzodiazepine receptors. *Proc. Natl. Acad. Sci. USA,* 77:2288-2292, 1980.

Braestrup, C., and Squires, R.F. Brain specific benzodiazepine receptors. *Br. J. Psychiatry,* 133:249-260, 1978.

Cowen, P.J., Green, A.R., and Nutt, D.J. Ethyl β-carboline carboxylate lowers seizure threshold and antagonizes flurazepam-induced sedation in rats. *Nature,* 290:54-55, 1981.

Ehlert, F.J., Roeske, W.R., Braestrup, C., Yamamura, S.H., and Yamamura, H.I. γ-Aminobutyric acid regulation of the benzodiazepine receptor: Biochemical evidence for pharmacologically different effects of benzodiazepines and propyl β-carboline-3-carboxylate. *Eur. J. Pharmacol.,* 70:593-596, 1981.

Fujimoto, M., Hirai, K., and Okabayashi, T. Comparison of the effects of GABA and chloride ion on the affinities of ligands for the benzodiazepine receptor. *Life Sci.,* 30:51-57, 1982.

Hunkeler, W., Möhler, H., Pieri, L., Polc, P., Bonetti, E.P., Cumin, R., Schaffner, R., and Haefely, W. Selective antagonists of benzodiazepines. *Nature,* 290:514-516, 1981.

Möhler, H., and Richards, J.G. Agonist and antagonist benzodiazepine receptor interaction in vitro. *Nature,* 294:763-765, 1981.

Tenen, S.S., and Hirsch, J.D. Antagonism of diazepam activity by β-carboline-3-carboxylic acid ethyl ester. *Nature,* 288:609-610, 1980.

Benzodiazepine Receptor: Interaction of a Selective Benzodiazepine Antagonist, Ro 15-1788

H. Möhler, Ph.D.,[1] and J.G. Richards, Ph.D.[1]

Introduction

Recently, Ro 15-1788, a representative of a novel series of imidazodiazepines, was found to selectively antagonize all major central actions of benzodiazepines by competitive high affinity interaction with benzodiazepine receptors in the central nervous system (Hunkeler et al. 1981). Ro 15-1788 itself is not pharmaceutically active in doses sufficient to antagonize benzodiazepine actions in animals and man (Darragh et al. 1981; Haefely et al. 1982; Hunkeler et al. 1981; Möhler et al. 1981; Polc et al. 1981). Ro 15-1788 may find therapeutic application as an antidote in cases of intoxication involving overdoses of benzodiazepines, and in anaethesiology for terminating benzodiazepine-induced sedation (Haefely et al. 1982, Hunkeler et al. 1981).

Difference in Receptor Interaction of Benzodiazepine Agonists and Ro 15-1788

Benzodiazepines and the antagonist Ro 15-1788 interact with the same benzodiazepine receptor sites (Möhler & Richards 1981) as shown, for example, by light-microscopic autoradiography (Figure 1). The mode of receptor interaction, however, must be different, since benzodiazepine agonists trigger a biological response while Ro 15-1788 does not. This different receptor interaction is reflected in the different susceptibility of agonists and antagonists to conformational changes of the benzodiazepine receptor. It is known that, *in vitro,* GABA and some other compounds can alter the affinity of the

---

[1] Pharmaceutical Research Department, F. Hoffmann-La Roche & Co., Ltd., CH-4002 Basle, Switzerland.

benzodiazepine receptors for agonists. The affinity of Ro 15-1788, however, remained unchanged under the same conditions (Möhler & Richards 1981). The failure of Ro 15-1788 to respond to conformational changes of the receptor may reflect its inability to induce a conformational change of the receptor and thereby to trigger a biological response.

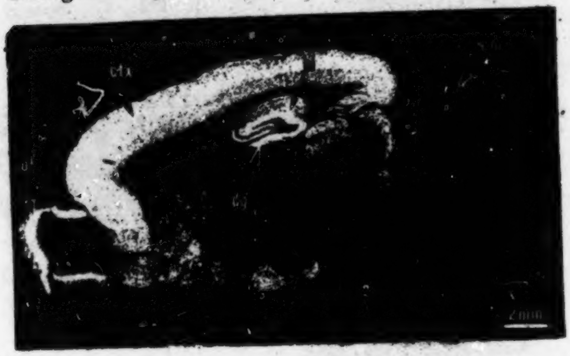


FIGURE 1. Autoradiogram of high affinity binding sites of ^{3}H-Ro 15-1788 in a sagittal section of rat brain. The slide-mounted cryostat section was incubated with 1 nmol·l^{-1} of the radioligand for 40 min at 4°C, washed, rapidly dried and then exposed to LKB Ultrofilm® for 14 days at 4°C. White areas correspond to the presence of the radioligand. Note the high density of binding sites in several brain regions, e.g. olfactory bulb (ol, external plexiform and glomerular layers), cerebral cortex (ctx, particularly layer IV), molecular layers of hippocampus (hi), dentate gyrus (dg), and cerebellum (cm). The same distribution pattern was found when the benzodiazepine agonist ^{3}H-clonazepam was used as radioligand.

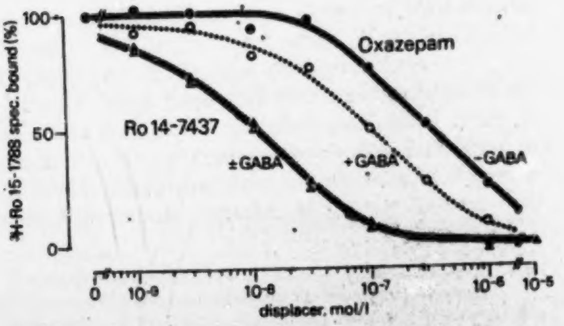


FIGURE 2. ^{3}H-Ro 15-1788 binding in the presence (open symbols) and absence (solid symbols) of 100 μmol·l^{-1} GABA: Inhibition by the agonist oxazepam (circles) and the benzodiazepine antagonist Ro 14-7437 (triangles).

The different receptor interaction of agonists and Ro 15-1788 *in vitro* can be used as a test to distinguish benzodiazepine agonists from antagonists (Möhler & Richards 1981). Their IC_{50} values are determined in ^{3}H-Ro 15-1788 binding in the presence and absence of 100μm .1^{-1} GABA. For agonists but not antagonists, the IC_{50} value in ^{3}H-Ro 15-1788 binding is reduced in the presence of GABA (Figure 2 and Table). For methyl-β-carboline-3-carboxylate, a convulsant benzodiazepine antagonist, the IC_{50} value was even increased in the presence of GABA (Table).

Table

The Inhibitory Potency (IC_{50}) of Various Benzodiazepine Receptor Agonists and Antagonists in ^{3}H-Ro 15-1788 Binding Tested in the Absence and Presence of GABA

	IC_{50}-ratio ± SEM
Agonists	
Flunitrazepam	2.7 ± 0.3
Diazepam	2.9 ± 0.1
Oxazepam	2.7 ± 0.2
Zopiclone	1.6 ± 0.1
CL 118 872	1.6 ± 0.1
Antagonists	
Ro 15-1788	1.0 ± 0.1
Ro 14-7437	0.9 ± 0.1
Propyl-βCC*	1.0 ± 0.1
Methyl-βCC*	0.6 ± 0.05

*β-carboline-3-carboxylate

According to the different types of response to the presence of GABA, several states of the benzodiazepine receptor may be distinguished: The agonist state characterized by an enhancement of the receptor affinity by GABA, the antagonist state in which the affinity remains unaffected by GABA, and an antagonist/convulsant state in which the affinity of the receptor is reduced by GABA.

Model of Ligand-Receptor Interaction

Based mainly on thermodynamic data, a two-step model of ligand receptor interaction was proposed for benzodiazepine receptors (Möhler & Richards 1981),

$$\begin{array}{l} L + R \overset{1}{\rightleftharpoons} LR \overset{2}{\rightleftharpoons} LR' \\ \qquad\qquad\qquad\; \overset{3}{\rightleftharpoons} LR'' \end{array}$$

in which L is the ligand and R the receptor. Agonists and antagonists participate in reaction (1). Due to their structural properties, agonists but not antagonists can participate in reaction (2) by inducing a conformational change of the receptor to an activated state R′, a prerequisite for the initiation of the agonist drug response. Convulsant receptor ligands induce different conformational change of the receptor reaction (3). Effects opposite to those of benzodiazepine agonists are triggered by these compounds.

References

Darragh, A., Scully, M., Lambe, R., and Brick, I. Investigation in man of the efficacy of a benzodiazepine antagonist, Ro 15-1788. *The Lancet*, II(7):8-10, 1981.

Haefely, W., Bonetti, E.-P., Burkard, W.P., et al. Benzodiazepine antagonists. In: Costa, E., et al. (eds.), *Benzodiazepines: From Molecular Biology to Clinical Practice.* New York: Raven Press. (In press)

Hunkler, H., Möhler, H., Pieri, L., Polc, C., Bonetti, E.-P., Cumin, R., Schaffner, R., and Haefely, W. Selective antagonists of benzodiazepines. *Nature*, 290:514-516, 1981.

Möhler, H., and Richards, J.G. Agonist and antagonist benzodiazepine receptor interaction in vitro. *Nature*, 294: 763-765, 1981.

Möhler, H., Burkard, W.P., Keller, H.H., Richards, J.G., and Haefely, W. Benzodiazepine antagonist Ro 15-1788: Binding characteristics and interaction with drug-induced changes in dopamine turnover and cerebellar cGMP levels. *J. Neurochem.*, 37:714-722, 1981.

Polc, P., Laurent, J.-P., Scherschlicht, R., and Haefely, W. Electrophysiological studies on the specific benzodiazepine antagonist, Ro 15-1788. *Naunyn Schmiedeberg's Arch. Pharmacol.*, 316:317-325, 1981.

Vol. 18, No. 3, July 1982

Psychopharmacologic Treatment of Obsessive-Compulsive Disorder

Chair: Dennis Murphy, M.D.
Clinical Neuropharmacology Branch
National Institute of Mental Health
Bethesda, Maryland

Clomipramine Treatment of Obsessive Disorder—Biochemical and Clinical Aspects[1]

Marie Åsberg, M.D.,[2] Peter Thorén, M.D.,[3] and Leif Bertilsson, M.D.[2]

Chronic obsessive-compulsive disorder, a crippling illness in its more severe form, socially disruptive and connected with intense suffering, has long been conceived of as one of the most treatment-resistant conditions known to psychiatry (Goodwin et al. 1969). It is therefore encouraging that a range of new treatments has recently been reported to be effective. Exposure treatment, a variety of behavior therapy, has thus been found to be superior to relaxation procedures (used as a placebo control) in controlled trials (Marks et al. 1980). Among the drugs claimed to be effective are the monoaminoxidase inhibitors (MAOIs), high doses of imipramine (Freed et al. 1972), tryptophan (Yaryura-Tobias & Bhavagan 1977), and clomipramine.

These drugs have different mechanisms of action, but they have one pharmacological effect in common: they potentiate serotonin functions in the brain. Clomipramine, for instance, is the most potent serotonin uptake inhibitor among the tricyclic antidepressants (Carlsson et al. 1969). The MAOIs inhibit enzymatic degradation of serotonin. The serotonin precursor, tryptophan, accelerates synthesis of the transmitter.

These drugs also have (or are claimed to have) antidepressant properties. The tricyclics and the MAOIs have long been used as antidepressants, while tryptophan has been found to potentiate the effect of other antidepressant treatments such as the MAOIs (Coppen et al. 1963), clomipramine (Wålinder et al. 1976), and electroconvulsive therapy (ECT) (d'Elia et al. 1977) in controlled trials.

This pattern of effects raises a number of questions. Is the antiobsessive effect (if any) related to the drugs' effect on serotonin neurons? Is it secondary to amelioration of depression in the obsessive-compulsive patients? What is the relationship between depression and obsessive-compulsive disorder? A close connection between depression and obsessive-compulsive disorder has been recognized since at least the turn of the century (Gadelius 1896). Is obsessive-compulsive disorder merely a variety of depression or are the two disorders different manifestations of a common underlying biochemical abnormality?

As yet, there are not sufficient research data to answer any of these questions, but there is some suggestive evidence which will be discussed in this paper. To the authors' knowledge, placebo-controlled trials have only been published with clomipramine, and the discussion will therefore be limited to studies of this drug.

The Controlled Trials

In 1980, three double-blind, placebo-controlled clinical trials of clomipramine in obsessive-compulsive disorder were published. Although their designs differed, they complemented each other in a number of ways.

---

[1] This study was supported by the Swedish Medical Research Council Grant #5454 and by funds from the Karolinska Institute.

[2] Department of Psychiatry, Karolinska Hospital, Stockhom, and the Department of Clinical Pharmacology, Huddinge Hospital, Huddinge, Sweden.

Address correspondence to Dr. Åsberg at the Department of Psychiatry, Karolinaka Hospital, S-104 01 Stockholm, Sweden.

Thorén et al. (1980a) studied antiobsessive effects in 24 hospitalized patients with severe, chronic (median duration 11 years) obsessive-compulsive disorder. After a drug-free "washout" period, the patients were randomly allocated to one of three treatment groups, clomipramine (150 mg/day divided in three doses), nortriptyline (150 mg/day), or placebo. Treatment was continued on a fixed dosage for 5 weeks. With the exception of occasional low doses of benzodiazepines, no concomitant drug treatment was allowed.

All patients met Research Diagnostic Criteria (RDC) (Spitzer et al. 1978) for obsessive-compulsive disorder. Particular efforts were made to exclude patients with a *primary* depressive illness (as defined by Feighner et al. 1972) from the study. Six patients were diagnosed by the RDC as suffering from a *secondary* depressive condition superimposed on the obsessive-compulsive disorder.

An eight-item subscale for obsessive-compulsive disorder (the OCD Scale, Table 1) derived from the Comprehensive Psychopathological Rating Scale (CPRS; Åsberg et al. 1978) was used to assess effects. After 5 weeks of treatment, clomipramine was significantly superior to placebo, both on the two core obsessive-compulsive symptoms (Rituals and Compulsive Thoughts) and on the entire OCD scale. Nortriptyline effects were in between clomipramine and placebo and did not differ significantly from either. The effect in the placebo-treated group was very small in spite of the supportive hospital environment. The mean score on obsessional symptoms after 6 weeks of placebo treatment was 96 percent of the pretreatment score.

After the controlled phase of the trial, all patients but two were given clomipramine *openly* in a flexible dosage (maximum 225 mg/day). During this phase, behavior therapy, according to the principles laid down by Marks (1973), was also given. On the combined treatment, 12 out of 22 patients could be classified as responders. Clinical and demographic data (including the presence or absence of secondary depression) did not predict response to the combination of clomipramine and behavior therapy.

Table 1

Items of the CPRS-Derived Rating Scales for Obsessive-Compulsive Disorder and Depression

OCD Scale	Depression Scale
1. Rituals	1. Apparent sadness
2. Inner tension	2. Reported sadness
3. Compulsive thoughts	3. Inner tension
4. Concentration difficulties	4. Reduced sleep
5. Worrying over trifles	5. Reduced appetite
6. Reported sadness	6. Concentration difficulties
7. Lassitude	7. Lassitude
8. Indecision	8. Inability to feel
	9. Pessimistic thoughts
	10. Suicidal thoughts

Both scales consist of items drawn from a larger rating instrument, the CPRS (Åsberg et al. 1978). The construction of the two subscales is similar and partially based on the incidence of symptoms in the respective disorders. Note the overlap—half of the items in the OCD scale occur in the depression scale as well.

Marks et al. (1980) compared clomipramine and placebo, with and without exposure treatment. Relaxation procedures were used to control for the time spent with the therapist. The 40 patients studied were all chronic cases with a mean duration of illness similar to those studied by Thorén et al. (1980a). Depressive symptoms were not an exclusion criterion, and pretreatment scores on a depression inventory suggested that only 2 of the 40 patients were not depressed.

The patients were given placebo or clomipramine (flexible dosage up to 225 mg/day given as a single dose at night) on an outpatient basis for 4 weeks. On subsequent admission to hospital, drug treatment was continued without further changes of dosage, and the patients were given either exposure or relaxation sessions. After 6 weeks of psychological treatment, the patients were released from hospital to continue on the drug (or placebo) treatment for another 26 weeks. Final followup was after 2 years.

A series of ratings was used to assess rituals, mood, and general adjustment. Compared to placebo, clomipramine produced significantly more improvement of all these aspects. Severity of the mood symptoms in this patient group predicted response to clomipramine. In the least dysphoric patients only the time spent on target rituals showed a significant advantage of the active drug over placebo. Exposure was connected with an amelioration of rituals. The best effect was obtained in patients who had both drug and exposure, and the effects of the two treatments appeared to be additive. Compliance with the psychological treatments was better in the patients who had received an active drug.

Montgomery (1980) studied 14 patients with severe and chronic obsessive-compulsive disorder, diagnosed by the RDC of Spitzer et al. (1978). In this study, primary and secondary depressive illness were both exclusion criteria. A crossover design was used, where each patient received either placebo or 75 mg clomipramine (given as a single dose by night) for 4 weeks, and was then crossed over to the other treatment for another 4-week period. Behavior therapy was given once weekly to all patients during the entire trial.

A six-item CPRS subscale for obsessive-compulsive disorder, and a CPRS-derived scale for depression (Montgomery & Åsberg 1979) were used to assess effects. Clomipramine was significantly better than placebo for compulsive thoughts, but not for rituals. There was no significant change in scores on the depression scale with any of the treatments.

Effects on the Serotonin System

Clomipramine is not a "pure" serotonin uptake inhibitor. It is metabolized in the body, and the main metabolite demethylclomipramine is a potent inhibitor of noradrenaline uptake (Träskman et al. 1979). The plasma concentrations of the metabolite are almost always higher than those of the parent compound after oral administration.

Clomipramine's lack of selectivity suggests that the pattern of neuronal effects may be complicated. It is, however, possible to some extent to disentangle the effects of the parent compound from those of the metabolite.

When a monoamine uptake inhibitor is given to a patient, the turnover of the respective amine is changed. This is reflected in a decreased concentration of its metabolite in the spinal fluid. Nortriptyline, for instance, is a preferential inhibitor of noradrenaline uptake and causes a reduction of the noradrenaline metabolite 4-hydroxy-3-methoxyphenylglycol (HMPG) in the spinal fluid (Bertilsson et al. 1974). Zimelidine, which is a relatively selective serotonin uptake inhibitor, causes a decrease in the spinal fluid level of the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) (Bertilsson et al. 1980).

During clomipramine treatment of depression, both 5-HIAA and HMPG concentrations are reduced. The extent of the HMPG reduction is correlated to the plasma concentration of the demethyl metabolite, and the 5-HIAA reduction is a function of the plasma concentration of the parent compound. The latter association is not linear but U-shaped (Figure 1). Both very low and very high concentrations of clomipramine are associated with a smaller reduction in 5-HIAA than intermediate concentrations (Träskman et al. 1979; Thorén et al. 1980b).

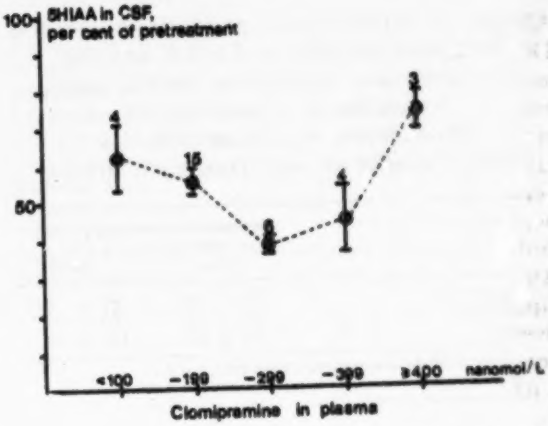


FIGURE 1. Concentrations of 5-HIAA in CSF during treatment with clomipramine (as percent of the pretreatment concentration) in relation to plasma level of clomipramine. Means, standard deviations, and number of patients are given. Both depressed $N = 24$) and obsessive-compulsive ($N = 8$) patients are included.

Thorén and co-workers (1980b) measured spinal fluid concentration of monoamine metabolites before and during treatment with clomipramine, nortriptyline, and placebo in their obsessive-compulsive patients. As expected, nortriptyline caused a reduction in HMPG, clomipramine reduced both HMPG and 5-HIAA, and placebo treatment did not change the metabolite concentrations (Table 2).

The change in 5-HIAA, but not that in HMPG, appeared to be important for the treatment outcome. There was a significant correlation between reduction in 5-HIAA and effect on the two core obsessive symptoms, rituals and compulsive thoughts—the more pronounced the reduction of 5-HIAA, the better was the effect.

This was in contrast to the effect on the remaining, "dysphoric" symptoms of the OCD scale (see Table 1), which *increased* with decreasing HMPG levels, although not significantly (Table 3). This is also in striking contrast to the pattern described in endogenous depression, where amelioration during clomipramine treatment has been found to be correlated to HMPG reduction, but not to change in 5-HIAA (Träskman et al. 1979).

Table 2

Changes in Spinal Fluid Concentrations of the Serotonin Metabolite, 5-HIAA, and the Noradrenaline Metabolite, HMPG, after Three Weeks' Treatment for Obsessive-Compulsive Disorder (Eight Patients in Each Treatment Group)

Treatment	Metabolite concentration, percent of pretreatment (mean ± SD) 5-HIAA	HMPG
Clomipramine	61 ± 14*	68 ± 6**
Nortriptyline	95 ± 16	68 ± 10*
Placebo	91 ± 27	102 ± 8

*Significant reduction compared to pretreatment, $p < 0.01$.
**Significant reduction compared to pretreatment, $p < 0.001$.
Data from Thorén et al. (1980)

Thorén et al. (1979) also correlated the treatment effect with the plasma concentrations of clomipramine and its metabolite and found a significant negative relationship between the parent compound and the effect (once more for the core symptoms only). This may seem surprising. If the best effect is obtained with a maximal reduction of 5-HIAA, and if the relationship between clomipramine concentration and 5-HIAA reduction is curvilinear, the relationship between clomipramine and effect should also be curvilinear. Closer examination of the range of levels found in the obsessive-compulsive patients explains the apparent contradiction, since almost all patients had plasma levels in the high range (and thus lie on the right limb of the U-shaped curve in Figure 1).

A curvilinear relationship between clomipramine in plasma and the effect on rituals was indeed found by Stern, Marks, Mawson, and Luscombe in their analysis of 20 of the patients studied by Marks et al. (1980). These authors also found a relationship between demethylclomipramine and one effect—the reduction of scores on the Hamilton Depression Scale. This suggests that clomipramine may account for the anti-obsessive effect and the metabolite for the antidepressant effect. (It may be recalled that depression was not an exclusion criterion in this study.)

Taken together, these findings seem to support the hypothesis of a relationship between amelioration of core obsessive symptoms (in particular, rituals) and a drug effect on serotonin neurons. The number of patients studied is, however, still too small to permit definitive conclusions. The obvious test of the hypothesis would be to try a selective serotonin uptake inhibitor, for instance, zimelidine, in a controlled trial.

Depression, Dysphoria, and Treatment Outcome

The study of Marks et al. (1980) suggests that clomipramine treatment may above all be effective in patients who have affective symptoms in addition to their rituals, while those who are not dysphoric react better to exposure. The study by Thorén et al. (1980a) can hardly be used to investigate the importance of pretreatment depressive symptoms for the effect of clomipramine, since those among the eight clomipramine-treated patients who had high scores on the depression scale also had plasma levels of clomipramine outside the "therapeutic range." The study by Montgomery (1980) cannot be used for this purpose, either, since the patients were given both clomipramine and behavior therapy.

The predictive value of pretreatment depression for the effect of the *combination* of clomipramine and behavior therapy can, however, be evaluated from the two latter studies. Montgomery (1980) explicitly excluded patients with a diagnosis of depression and was nonetheless able to demonstrate an effect, but only on obsessive thoughts. Thorén et al. (1980a) included some patients with a secondary depression, and this diagnosis did not predict outcome. The pretreatment depression scores were 14.2 ± 7.9 in the responders, and 13.0 ± 7.9 in the nonresponders to the combined treatment, a nonsignificant difference.

Patients who do not receive a *diagnosis* of depression may still have many symptoms, e.g., depressed mood, that are characteristic of depressive illness but are common in other psychiatric afflictions as well. In order to explore further the importance of pretreatment symptomatology, a factor analysis of the 14 item-scores (Varimax rotation, SPSS) was performed on the combined OCD and depression scales from the patients studied by Thorén et al. (1980). In particular, the authors were interested to see whether "depressive" or dysphoric symptoms are highly loaded in the same factor. This appears not to be the case, since classical "depressive" symptoms load on all four factors found in the analysis (Table 3). The first factor, which accounts for about half of the variance, might be labeled an "obsessive" factor, since it is the only one where rituals load strongly. It is also characterized by pessimistic thoughts, reduced sleep, worry, and a *negative* correlation with compulsive thoughts. The second factor might be described as an "anxiety" factor with high loadings for inner tension, concentration difficulties, inability to feel, and reduced appetite, but also for apparent sadness. The third factor appears to be the most "pure" depression factor with strong loadings for reported sadness, inner tension, suicidal thoughts, and reduced sleep. The fourth factor, finally, could possibly be described as an "asthenia" factor with strong loadings for indecision, lassitude, worry, and compulsive thoughts. Scores on the four factors in patients with and without a diagnosis of secondary depression are shown in Figure 2.

Table 3

Factor Analysis of Scores Given to 24 Untreated Patients with Obsessive-Compulsive Disorder on Items from the CPRS Obsessive-Compulsive Disorder and Depression Scales. Varimax Rotated Factor Matrix

Symptom	Factor 1 (49.8)	Factor 2 (20.7)	Factor 3 (15.7)	Factor 4 (13.7)
Reported sadness	25	24	94	−02
Inner tension	−01	49	55	21
Inability to feel	−12	75	11	11
Pessimistic thoughts	67	21	13	07
Suicidal thoughts	13	−11	49	20
Worrying over trifles	45	26	05	35
Compulsive thoughts	−43	14	26	36
Rituals	59	−03	07	−01
Indecision	10	−16	05	79
Lassitude	02	29	16	61
Concentration difficulties	23	48	−14	−06
Reduced appetite	30	60	24	03
Reduced sleep	62	10	39	03
Apparent sadness	43	36	18	23

The figures within parenthesis are the percentages of variance accounted for by the respective factors.

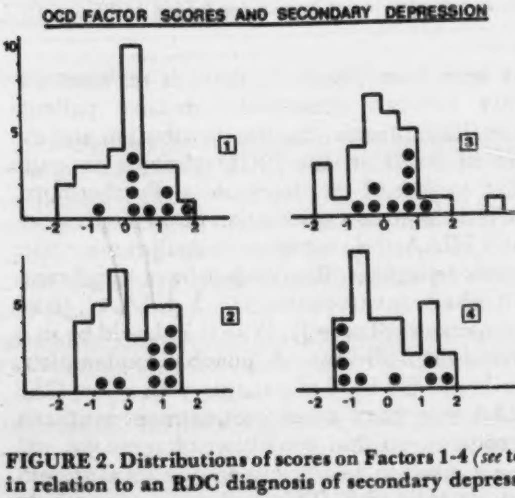


FIGURE 2. Distributions of scores on Factors 1-4 (*see* text) in relation to an RDC diagnosis of secondary depression (filled dots).

Individual factor scores were then related to outcome of the combined treatment with clomipramine and behavior therapy (Table 4, Figure 3). The two "affective" factors, the "anxiety" (2) and "depression" (3) factors correlated positively with outcome, significantly so for Factor 3. The predictive value of the factor scores was low, however and, as seen from Figure 3, some patients with very low scores on the "depression" factor reacted well to the treatment. The outcome of the factor analysis should be regarded with great caution due to the small number of patients ($N = 24$), but would seem to support the contention of Marks and coworkers (1980 and this issue) of a better treatment effect in obsessive-compulsive patients who are also dysphoric.

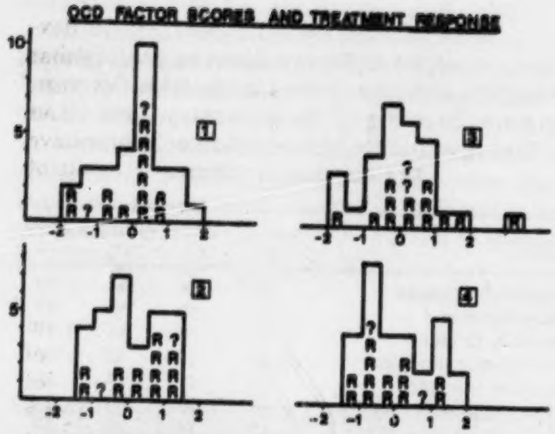


FIGURE 3. Distributions of scores on Factors 1-4 (*see* text) and response category on combined treatment with clomipramine and exposure. R denotes positive response, "?" patients who were included in the pretreatment rating but not given clomipramine plus exposure.

Table 4

Correlations Between Factor Scores and Response to Combined Treatment with Clomipramine and Exposure in 22 Patients with Obsessive-Compulsive Disorder

Factor	Pearson *r*	*p*
1	−0.17	0.38
2	0.36	0.06
3	0.39	0.04
4	−0.27	0.18

Biochemical Disturbances in Depression and Obsessive-Compulsive Disorders

During recent years, research in depression has largely focused on the importance of monoamine neurons and of neuroendocrine functions. Depression, particularly of the endogenous type (melancholia), has been associated with low cerebrospinal fluid (CSF) concentrations of the serotonin metabolite 5-HIAA (*see*, e.g., the review by van Praag 1981; also Åsberg et al. 1982). The low 5-HIAA levels may be characteristic only of a subgroup of patients with melancholia, since the distribution of the metabolite has repeatedly been reported to be nonnormal or bimodal (Åsberg et al. 1976). Melancholia has also been associated with a high frequency of inability to suppress cortisol secretion after administration of dexamethasone (Carroll et al. 1981). In order to elucidate the relationship between melancholia and obsessive-compulsive disorder, it might therefore be of interest to compare distributions of CSF 5-HIAA, and dexamethasone suppression, in obsessive-compulsive disorder and depression.

Figure 4 shows CSF 5-HIAA in patients with melancholia and obsessive-compulsive disorder, and in healthy controls. Only women are shown, since 5-HIAA concentrations differ between sexes, and the group of men with obsessive-compulsive disorder is too small to allow any meaningful comparisons.

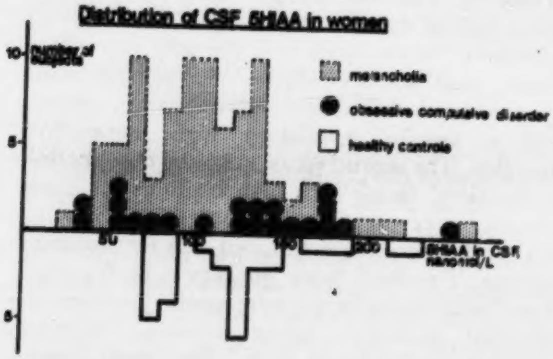


FIGURE 4. Distributions of 5-HIAA in CSF in women with melancholia and obsessive-compulsive disorder, and healthy female controls. Response to clomipramine plus exposure treatment is indicated by R. "?" indicates that response category is not known (*see* legend to Figure 3).

As seen from Figure 4, there is no *mean* difference between obsessive-compulsive patients and healthy controls, but the distribution and the range of levels in the OCD patients is quite similar to that of the depressives. Furthermore, there is a significant association between pretreatment 5-HIAA and response to clomipramine plus behavior treatment. Responders have significantly higher pretreatment 5-HIAA than nonresponders (Table 5). Why this should be so is by no means obvious. A possible explanation, however, might be that patients with a low CSF 5-HIAA may have a low pretreatment synthesis of serotonin, so that inhibition of reuptake still does not result in a sufficient amount of serotonin in the synaptic cleft. This explanation is entirely speculative but it is testable in principle since, if it were true, addition of tryptophan should lead to an increased therapeutic effect.

Table 5

Pretreatment CSF Amine Metabolite Levels in Responders and Nonresponders to Clomipramine Plus Behavior Treatment

Metabolite	Metabolite Concentration, mean ± SD (nanomol/L CSF)	
	Responders	Nonresponders
5-HIAA	137 ± 39	93 ± 49
HVA	339 ± 100	248 ± 91
HMPG	61 ± 23	52 ± 14

Data from Thorén et al. (1980).

Table 6

Dexamethasone Suppression Tests (DST) in 17 Patients with Obsessive-Compulsive Disorder

	Abnormal *N* = 7 (41%)	Normal *N* = 10 (59%)
Age (mean, SD)	44.0 (12.08)	44.90 (8.69)
Sex (women:men)	6:1	8:2
Depression score (mean, SD)	3.43 (3.40)	3.25 (1.34)
OCD scale score (mean, SD)	7.43 (3.88)	7.85 (2.61)
Obsessive symptoms score (mean, SD)	3.14 (1.65)	3.60 (0.88)
Current medication (clomipramine or drug free)	1:6	2:8
Response to clomipramine (responder ornonresponder)	5:1	7:3

None of the differences between patients with normal and abnormal DSTs are statistically significant.

Dexamethasone suppression tests (DSTs) have been performed in 17 patients with obsessive-compulsive disorder according to the RDC criteria. The tests were performed as recommended by Carroll (Carroll et al. 1981), i.e., 1 mg dexamethasone was given at 2300 hours on Day 1 and blood was drawn for analysis of cortisol (by radioimmunoassay) on Day 2 at 0800, 1600, and 2300 hours. The test was regarded as abnormal if any of these cortisol values exceeded 138 nanomol/L. In seven cases the DST was clearly abnormal. None of the background factors listed in Table 6 differed between patients with a normal or an abnormal DST, not even scores on the depression scale. This outcome would seem to cast some doubt on the specificity of the dexamethasone test for melancholia, at least as that disorder is usually defined. It does suggest, however, that some cases of melancholia and some cases of obsessive-compulsive disorder have a biochemical disturbance in common, in spite of the apparent differences in the clinical picture.

Conclusion

There is now good evidence that clomipramine is indeed an effective drug in the treatment of obsessive-compulsive illness. The presence of dysphoria in the patient may be associated with a better chance of recovery on drug treatment, but its absence does not preclude a good effect. There is indirect evidence that the serotonin effects of the drug are important for its effect on rituals, while the noradrenaline effects may be more important for depression. It may be relevant in the context that a low turnover of serotonin, as reflected in low levels of 5-HIAA in the CSF, has been associated with increased anxiety and increased aggression (Banki 1977; Brown et al. 1979, 1981; Rydin et al. 1982)—two factors that psychoanalytic theory have associated with obsessive-compulsive neurosis.

There is no evidence that the effect of clomipramine declines with time. The long-term outcome of the patients studied by our group has generally been favorable in those patients initially classified as responders (Table 7). Most of these patients are still taking the drug, but two have been drug-free for more than a year without a relapse.

Table 7

Long-Term Outcome of Clomipramine Treatment

	Responders	Nonresponders
Lost to followup	1	2
Recovered or better on clomipramine	9*	
Recovered or better, drug free	2†	
Unchanged		3
Psychosurgery		3
Schizophrenic development		1
Depression (periodic)		1

*Episodic treatment in two cases.
†Both made previous attempts to stop taking the drug, but failed. Both were drug free for more than a year.
Data from Thorén et al. (1980). The followup period varies from 5 to 7 years.

There now seems to be enough data on the effect of clomipramine in obsessive-compulsive disorder to allow the formulation of tentative guidelines for its clinical use. In patients with long-standing, severe obsessive-compulsive illness who also are dysphoric, clomipramine appears to be the drug of choice. It can be tried also in patients who are not dysphoric, but the effect is not equally convincing. The treatment effect is not fully apparent until after 5-10 weeks' treatment. Dosage should be individualized. Plasma level determinations may be of help to avoid too high or too low levels, both which seem to be connected with a poorer effect. Combination with exposure treatment is desirable. Treatment should be prolonged, probably over several years. With the exception of dental problems from the reduced production of saliva (which can be avoided by a careful mouth hygiene), no serious long-time side-effects have been described. It is important to assist the patients in recreating meaningful social relationships and activities. A common remark from patients whose symptoms diminish with drug treatment is that they do not quite know what to do with the time that they used to spend on their rituals. A few of our patients have indeed stopped taking the drug, stating that they actually preferred their rituals to an attempt to cope with the demands of an ordinary existence. But for the majority of the responders, the advantages have far outweighed these problems.

Acknowledgment: The assistance of Lisbeth Eriksson in the preparation of this manuscript is greatly appreciated.

References

Åsberg, M., Bertilsson, L., Mårtensson, B., Scalia-Tomba, G.-P., Thorén, P., and Träskman-Bendz, L. CSF monoamine metabolites in melancholia. (Manuscript, 1982.)

Åsberg, M., Montgomery, S., Perris, C., Schalling, D., and Sedvall, G. A comprehensive psychopathological rating scale. *Acta. Psychiatr. Scand. (Suppl.)*, 271:5-27, 1978.

Åsberg, M., Thorén, P., Träskman, L., Bertilsson, L., and Ringberger, V.-A. "Serotonin depression": A biochemical subgroup within the affective disorders? *Science*, 191:478-480, 1976.

Banki, C.M. Correlation of anxiety and related symptoms with cerebrospinal fluid 5-hydroxy-indoleacetic acid in depressed women. *J. Neural Transm.*, 41:135-143, 1977.

Bertilsson, L., Tuck, J.R., and Siwers, B. Biochemical effects of zimelidine in man. *Eur. J. Clin. Pharmacol.*, 18:483-487, 1980.

Bertilsson, L., Åsberg, M., and Thorén, P. Differential effect of chlorimipramine and nortriptyline on cerebrospinal fluid metabolites of serotonin and noradrenaline in depression. *Eur. J. Clin. Pharmacol.*, 7:365-368, 1974.

Brown, G.L., Ebert, M.H., Goyer, P.F., Jimerson, D.C., Klein, W.J., Bunney, W.E. Jr., and Goodwin, F.K. Aggression, suicide, and serotonin: Relationships to cerebrospinal fluid amine metabolites. Presented at the American Psychiatric Association Annual Meeting, New Orleans, Louisiana, 1981.

Brown, L.G., Goodwin, F.K. Ballenger, J.C., Goyer, P.F., and Major, L.F. Aggression in humans correlates with cerebrospinal fluid amine metabolites. *Psychiatry Res.*, 1: 131-139, 1979.

Carlsson, A., Corrodi, H., Fuxe, K., and Hökfelt, T. Effect of antidepressant drugs on the depletion of intraneuronal brain 5-hydroxytryptamine stores caused by 4-methyl-α-metatyramine. *Eur. J. Pharmacol.*, 5:357-366, 1969.

Carroll, B.J., Feinberg, M., Greden, J.F., Tarika, J., Albala, A.A., Haskett, R.F., James, N.M., Kronfol, Z., Lohr, N., Steiner, M., de Vigne, J.P., and Young, E. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry*, 38:15-22, 1981.

Coppen, A., Shaw, D.M., and Farrell, J.P. Potentiation of the antidepressive effect of a monoamine-oxidase inhibitor by tryptophan. *Lancet*, I:79-81, 1963.

d'Elia, G., Lehmann, J., and Raotma, H. Evaluation of the combination of tryptophan and ECT in the treatment of depression. I. Clinical analysis. *Acta Psychiatr. Scand.*, 56: 303-318, 1977.

Feighner, J.P., Robins, E., Guze, S.B., Woodruff, R.A. Jr., Winokur, G., and Munoz, R. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry*, 26:57-63, 1972.

Freed, A., Kerr, T.A., and Roth, M. The treatment of obsessional neurosis. *Br. J. Psychiatry*, 120:590-591, 1972.

Gadelius, B. *Om tvangstankar och dermed beslagtade* fenomen. (On compulsive thoughts and related phenomena.) Lund, Sweden: Malströms bokhandel, 1896.

Goodwin, D.W., Guze, S.B., and Robins, E. Follow-up studies in obsessional neurosis. *Arch. Gen. Psychiatry*, 20: 182-187, 1969.

Marks, I.M. New approaches to the treatment of obsessive-compulsive disorders. *J. Nerv. Ment. Dis.*, 156:420-426, 1973.

Marks, I.M., Stern, R.S., Mawson, D., Cobb, J. and McDonald, R. Clomipramine and exposure for obsessive-compulsive rituals. I. *Br. J. Psychiatry*, 136:1-25, 1980.

Montgomery, S.A. Clomipramine in obsessional neurosis: A placebo controlled trial. *Pharmaceutical Med.*, 1:189-192, 1980.

Montgomery, S.A., and Åsberg, M. A new depression scale designed to be sensitive to change. *Br. J. Psychiatry*, 134:382-389, 1979.

Rydin, E., Schalling, D., and Åsberg, M. Rorschach ratings in depressed and suicidal patients with low CSF 5-HIAA. *Psychiatry Res.* (In press)

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria. Rationale and reliability. *Arch. Gen. Psychiatry*, 35:773-782, 1978.

Stern, R.S., Marks, I.M., Mawson, D., and Luscombe, D.K. Clomipramine and exposure for compulsive rituals. II. Plasma levels, side effects, and outcome. *Br. J. Psychiatry*, 136:161-166, 1980

Thorén, P., Åsberg, M., Cronholm, B., Jörnestedt, L., and Träskman, L. Clomipramine treatment of obsessive-compulsive disorder. I. A controlled clinical trial. *Arch. Gen. Psychiatry*, 37:1281-1285, 1980a.

Thorén, P., Åsberg, M., Bertilsson, L., Mellström, B., Sjöqvist, F., and Träskman, L. Clomipramine treatment of obsessive compulsive disorder. II. Biochemical aspects. *Arch. Gen. Psychiatry*, 37:1289-1294, 1980b.

Träskman, L., Åsberg, M., Bertilsson, L., Cronholm, B., Mellström, B., Neckers, L.M., Sjöqvist, F., Thorén, P., and Tybring, G. Plasma levels of chlorimipramine and its demethyl-metabolite during treatment of depression. Differential biochemical and clinical effects of the two compounds. *Clin. Pharmacol. Ther.*, 26:600-610, 1979.

van Praag, H.M. Central monoamines and the pathogenesis of depression. In: van Praag, H.M., Lader, M.H., Rafaelsen, O.J., and Sachar, E.J. (eds.), *Handbook of Biological Psychiatry. Part IV. Brain Mechanisms and Abnormal Behavior. Chemistry.* New York: Marcel Dekker, 1981, pp. 159-205.

Wålinder, J., Skott, A., Nagy, A., Carlsson, A., and Roos, B.-E. Potentiation of antidepressant action of clomipramine by tryptophan. *Arch. Gen. Psychiatry*, 33: 1384-1389, 1976.

Yaryura-Tobias, J.A., and Bhagavan, H.N. L-tryptophan in obsessive-compulsive disorders. *Am. J. Psychiatry*, 134: 1298-1299, 1977.

Quo Vadis—Biology of Schizophrenia

Chair: **Edward Domino, M.D.**
University of Michigan
Ann Arbor, Michigan

Introductory Comments

Edward F. Domino, M.D.[1]

The pathogenesis of each of the schizophrenias is very poorly understood. It is becoming apparent that no single biological theory is adequate to explain the etiology of these diseases. The evidence that current antipsychotic drugs act primarily through blockade of dopamine receptors is most convincing. However, a significant proportion of schizophrenic patients are nonresponders to antipsychotic drugs, a fact well known since their introduction in the 1950s. Even in patients who are drug responders, it seems unlikely that their psychotic symptoms are caused by excessive levels of dopamine or its turnover in the central nervous system. In fact, the clinical biochemical evidence is to the contrary. There is evidence for both supersensitivity as well as subsensitivity of dopamine receptors in some schizophrenic patients. The fact that some dopamine agonists, like apomorphine, in low doses may also temporarily relieve some symptoms of schizophrenia suggests that the discovery of new selective presynaptic dopamine receptor agonists may be a useful therapeutic approach. There is considerable evidence for multiple dopamine receptors in the brain. Our present drugs tend to act on these multiple receptors both pre- and postsynaptically. This tends to blur our thinking regarding their mechanism of action. Obviously, there is a need to discover more specific dopamine agonists and antagonists that act selectively pre- or postsynaptically on each subtype of adenylate cyclase linked and nonlinked dopamine receptors. The delayed time course of therapeutic benefit of the antipsychotic drugs suggests that more complex biochemical changes are occurring that involve other neurotransmitter systems as well. It is well known that the increase in prolactin secretion (as an index of dopamine blockade) occurs far more rapidly than the delayed antipsychotic effects of dopamine antagonists. Other putative neurotransmitters and neuromodulators including the prostaglandins, γ-aminobutyric acid, histamine, acetylcholine, phenethylamines, indolealkylamines, opioid peptides, etc. have all been implicated in schizophrenia. The structural changes in schizophrenic brains, as measured via computerized axial tomography (CAT) scans, as well as the decrease in cerebral cortical glucose utilization, as measured via positron emission tomography (PET) scans, suggests a most complex biology of schizophrenia. Where do we go from here? That is the purpose of the present workshop in which various points of view were discussed by a distinguished panel of speakers who have made important contributions to our knowledge in this field. The workshop was specifically designed to be speculative and provocative, for hopefully it will lead to new directions of research.

---

[1] University of Michigan, Ann Arbor, MI 48109 and Lafayette Clinic, Detroit, MI 48201.

Two Dimensions of Pathology in Schizophrenia: Dopaminergic and Non-Dopaminergic

Timothy J. Crow, Ph.D., D.P.M., F.R.C.P., F.R.C. Psych.[1]

The belief that the primary disturbance in schizophrenia is chemical has long been plausible; that it is a disturbance of neurohumoural function is supported by observations that schizophrenic symptoms can be exacerbated in patients and provoked in nonpsychotic individuals by drugs that act on specific transmitters. The psychosis seen in some amphetamine abusers may be indistinguishable from acute paranoid schizophrenia (Connell 1958; Ellinwood 1967). The psychotic changes, like those in schizophrenia, occur in clear consciousness (that is, in the absence of disorientation) and can include first-rank symptoms (certain types of auditory hallucinations, delusions of passivity and interference, thought alienation, and delusional perception). In animals, many of the behavioral effects of the amphetamines have been shown to be due to increased dopamine release from the central dopamine pathways (Randrup & Munkvad 1967), and the psychotic changes in man seem likely also to be associated with increased dopaminergic transmission.

Mechanism of Antipsychotic Effects

Both schizophrenic symptoms and those of the amphetamine psychosis are reduced by neuroleptic drugs. Carlsson and Lindqvist (1963) found that these drugs increase dopamine turnover and suggested this was secondary to blockade of the dopamine receptor. Dopamine-induced activation of adenylate cyclase in the corpus striatum is inhibited by neuroleptic drugs; this inhibition correlates well with antipsychotic potency (Miller et al. 1974) for a range of drugs, though the butyrophenone compounds are somewhat less active than would be predicted from their clinical effects. Nevertheless, while blockade of the dopamine receptor is an obvious explanation of the extrapyramidal actions of neuroleptic drugs, some controversy exists about the extension of that mechanism to explain their antipsychotic effect. The principal argument to the contrary (Crow & Gillbe 1974) is that the correlation between extrapyramidal and therapeutic effects is not perfect. Some drugs (such as thioridazine) have fewer Parkinsonian effects than would be expected from their clinical efficacy. These same drugs, however, have high anticholinergic potency (Miller & Hiley 1974)—in other words, they have "inbuilt" anti-parkinsonian activity. When this is taken into account, the relation between dopamine antagonism and therapeutic effectiveness becomes more compelling. In the corpus striatum, where there is an interaction between acetylcholine and dopamine, drugs with a low incidence of side effects have relatively weak effects on dopaminergic transmission. This interaction may not occur in the mesolimbic dopamine system (the nucleus accumbens and related structures), and here dopamine blockade correlates better with therapeutic effectiveness (Anden 1972; Crow et al. 1977). Moreover, when dopamine antagonism is assessed not in the adenylate cyclase

---

[1] Division of Psychiatry, Clinical Research Centre, Harrow, England HA1 3UJ.

system but as inhibition of butyrophenone binding (as assay that probably identifies a second type of dopamine receptor) the relative lack of potency of the butyrophenones disappears (Creese et al. 1976; Seeman et al. 1976). A recent clinical study (Johnstone et al. 1978a) showed that only the cis- or α-isomer of the thiaxanthene flupenthixol, which blocks the dopamine receptor, is effective in treatment; the β-isomer, which is very much less potent as a dopamine antagonist, is no more active than placebo. This result is hard to explain except on the basis that dopamine antagonism is necessary for the therapeutic effects. The dopamine blockade theory of neuroleptic action has thus survived stringent tests; and antagonism of dopamine receptors, particularly those located within the mesolimbic system and the subset that is specifically labeled by butyrophenones, is most probably the critical element in diminishing schizophrenic symptoms.

Amine Theories

Is there, therefore, a primary disturbance of dopaminergic transmission in schizophrenia? Probenecid blocks the elimination of the dopamine metabolite homovanillic acid (HVA) from cerebrospinal fluid and can be used to obtain an estimate of dopamine turnover in the central nervous system. Use of this technique (Bowers 1974; Post et al. 1975) has produced no evidence of an increase in HVA that could be attributed to overactivity of dopamine neurons. Indeed, within the group of schizophrenic patients poor prognosis (Bowers 1974) and increasing severity of symptoms (Post et al. 1975) are associated with decreased concentrations of HVA in the cerebrospinal fluid. Postmortem studies (Owen et al. 1978) have also shown no evidence of increased dopamine turnover—a surprising finding, since many patients coming to necropsy have been on long-term medication. Presumably, as in animal experiments, the acute effects of neuroleptic drugs on dopamine turnover disappear with continued administration. These studies give no support to the view that dopamine neurons are overactive in schizophrenia.

By contrast, there is evidence (Owen et al. 1978; Lee et al. 1978) that the number of dopamine receptors is increased in the brains of a proportion (perhaps two-thirds) of patients with schizophrenia, as shown by receptor assay techniques. In experiments on animals, the number of receptors has been found to increase after administration of neuroleptics; but the size of the change (around 100%) in schizophrenic patients is relatively large, and there is an increase in some patients who had been free of medication for the year before death (Owen et al. 1978). Moreover, two types of dopamine receptor can be identified by ligand-binding techniques, and only that type of receptor labeled by the butyrophenone antagonist drugs is increased in schizophrenia (Owen et al. 1980; Cross et al. 1981), while receptors labeled by both antagonist and agonist compounds are increased after administration of neuroleptics (Muller & Seeman 1977).

Other neurohumoral theories have been tested in postmortem studies of the brains of schizophrenics. On the basis of the LSD psychosis and the pharmacological antagonism by LSD of some effects of serotonin, Gaddum (1954) suggested that serotonergic transmission might be deficient. Tryptophan metabolism (by way of the serotonin and other pathways), however, is not abnormal in the schizophrenic brain (Joseph et al. 1979), and serotonin receptors (assessed by binding of LSD and 5-hydroxytryptamine) are unchanged (Owen et al. 1980; Whitaker et al. 1981). There have been conflicting reports on possible changes in monoamine oxidase activity in platelets (Murphy & Wyatt, 1972) in schizophrenia, but interest in the question has been diminished by the finding (Crow et al. 1979a; 1981) that enzyme activity, assessed with several different substrates, is normal in the brains of schizophrenics. Finally, there is evidence (Crow et al. 1972) that certain noradrenergic pathways (such as the locus coeruleus innervation of the cerebral cortex) play a part in reward mechanisms; Stein and Wise (1971) suggested that these pathways degenerate in schizophrenia. A deficient response to rewarding stimuli is a plausible explanation for some features of the disease, but studies (Cross et al. 1978) of the enzyme dopamine-β-hydroxylase (a marker for noradrenergic neurons) have not shown a consistent reduction in the schizophrenic brain.

At present, therefore, the only change found consistently in the postmortem studies of the schizophrenic brain is an increase in the numbers

Table 1

Neurohumoural Hypotheses of Schizophrenia

Authors	Theory	Principal Arguments	Evidence from Postmortem Studies	
			For	Against
Gaddum 1954; Woolley and Shaw 1954	Serotonin deficiency	LSD psychosis resembles schizophrenia, LSD blocks serotonin receptors		Serotonin turnover not decreased (Joseph et al. 1979) Serotonin receptors unchanged (Owen et al. 1980; Whitaker et al. 1981)
Randrup and Munkvad 1965, 1967, 1972	Dopamine neurone overactivity	Amphetamine psychosis resembles acute paranoid schizophrenia. Amphetamines increase dopamine release. Antipsychotic drugs block dopamine receptors		Dopamine turnover not increased (Owen et al. 1978)
Bowers 1974; Crow et al. 1976	Dopamine receptor supersensitivity	As above	Dopamine receptors increased (Owen et al. 1978; Lee et al. 1978)	
Stein and Wise 1971	Noradrenaline neuron degeneration	Reward processes are mediated by central noradrenergic systems; anhedonia is a core feature of chronic schizophrenia		Dopamine-β-hydroxylase not reduced (Cross et al. 1978)
Murphy and Wyatt 1972	Monoamine oxidase deficiency	Platelet monoamine oxidase activity is reduced in some schizophrenic patients		Monoamine oxidase activity not reduced (Crow et al. 1979a)

of dopamine receptors. If this change is related to the disease process rather than to its treatment, it could explain the beneficial effects of dopamine receptor blockade.

Problems for the Dopamine Hypothesis

However, there are problems for this modification of the dopamine hypothesis.

1. It has long been recognized (e.g., Hughes & Little 1967; Letemendia & Harris 1967) that neuroleptic drugs are of limited value in many chronic patients. Moreover, Kornetsky (1976) found that such patients are sometimes resistant to the psychosis-exacerbating effects of dexamphetamine which are attributed to increased dopamine release.

2. The therapeutic effects of blockade of dopamine receptors, and possibly of neuroleptic drugs in general, are limited to "positive" symptoms (delusions, hallucinations, and thought disorder). Negative symptoms (flattening of affect, poverty of speech, loss of drive) which are more commonly seen in chronic schizophrenia, are much less affected (Johnstone et al. 1978a).

3. The fundamental defect in some chronic schizophrenic illnesses may be quite distinct from that underlying the acute disturbance. Thus, cognitive changes (e.g., disorientation in time) that resemble those seen in the organic states are seen in some institutionalized patients (Crow & Mitchell 1975; Crow & Stevens 1978). Further, several radiological studies (Haug 1962; Asano 1967; Johnstone et al. 1976, 1978b; Weinberger et al. 1979) have suggested that there is a group of chronic patients, probably including those with the greatest deterioration, who have structural changes, as reflected by increased ventricular size of the brain.

Table 2

Structural Changes in Schizophrenia—Association with Clinical State

Study	Test	N	Abnormality	Association
Holden et al. 1973	echo-ECG.	65	3rd vent.	Treatment resistance
Johnstone et al. 1976	CT scan	18	lat. vent.	Intellectual impairment (Withers & Hinton) ? negative symptoms
Rieder et al. 1979	CT scan	17	lat. vent.	Intellectual impairment (Halstead-Reitan)
Donnelly et al. 1980	CT scan	15	lat. vent.	Intellectual impairment (Halstead-Reitan)
Golden et al. 1980	CT scan	42	lat. vent.	Intellectual impairment (Luria-Nebraska)
Weinberger et al. 1980a	CT scan	51	lat. vent.	Poor pre-morbid adjustment
Weinberger et al. 1980b	CT scan	20	lat. vent.	Treatment resistance
Gross et al. 1981	CT scan	117	3rd vent.	"Pure defect" state
Andreasen 1981	CT scan	52	lat. vent.	Negative symptoms impaired sensorium
Takahashi et al. 1981	CT scan	169	3rd vent., lat. vent., cortex	Blunted affect uncooperativeness

Abbreviations: vent = ventricle
lat = lateral

A summary of the main findings of those studies (one echo-encephalographic and nine CT scans) which have related evidence of structural change to clinical features of the disease (Table 2) reveals that such changes are associated with treatment resistance (two studies), intellectual impairment (four studies), and the presence of negative symptoms (three studies). The most commonly reported abnormality is an increase in lateral ventricular area, but it may be, as suggested by Takahashi et al. (1981) that when third ventricular widening is sought, it is found to be a more consistent change.

4. It has recently become recognized that some symptoms (e.g., Schneider's first-rank symptoms) which have often been regarded as particularly characteristic of schizophrenia are relatively ineffective predictors of long-term outcome (Brockington et al. 1978; Bland & Orn 1980). This is significant in that poor outcome was the characteristic by which Kraepelin considered that dementia praecox could be distinguished from manic-depressive psychosis.

Two Syndromes

To account for these findings, it has been proposed that two syndromes can be distinguished in those diseases currently described as schizophrenic and that each may be associated with a specific pathological process (Table 3). The first (the Type I syndrome, approximating "acute schizophrenia," and characterized by the positive symptoms—delusions, hallucinations, and thought disorder) is in some way associated with a change in dopaminergic transmission; the second process (the Type II syndrome, approximating the "defect state," and characterized by the negative symptoms—affective flattening and poverty of speech) is unrelated to dopaminergic transmission but may be associated with intellectual impairment and, perhaps, structural changes in the brain. Type I symptoms are reversible; Type II symptoms, which are more difficult to define, may indicate a component of irreversibility. The former predict a potential response to neuroleptics; the latter are more closely associated with a poor

Table 3

Two Syndromes of Schizophrenia*

	Type I Syndrome	Type II Syndrome
Symptoms	Positive symptoms (delusions, hallucinations, thought disorder)	Negative symptoms (affective flattening, poverty of speech, loss of volition)
Type of illness in which most commonly seen	Acute schizophrenia	Chronic schizophrenia
Potential for response to neuroleptics	Good	Poor
Presence of intellectual impairment	Absent	Sometimes present
Outcome	Reversible	? Irreversible
Pathological process	Disturbance of dopaminergic transmission (? increased dopamine receptors)	Cell loss leading to structural changes in the brain

*Crow, T.J. *Br. Med. J.*,280-66-68, 1970.

long-term outcome.

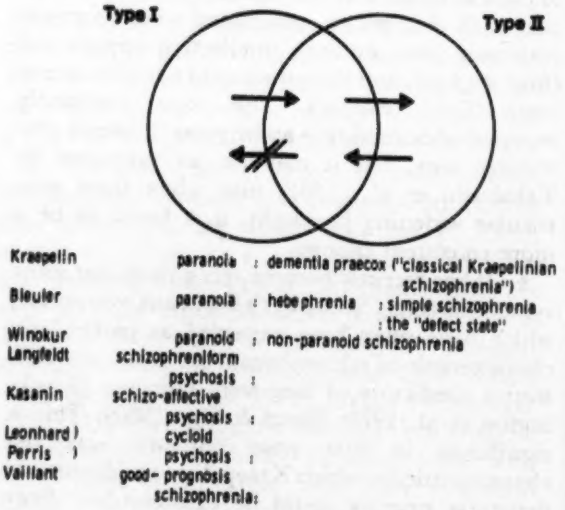
Even if the Type I and Type II syndromes represent different dimensions of pathology, it is apparent that they do not constitute separate diseases.

They are often associated together. For example, episodes of the Type I syndrome (positive symptoms) often progress into the Type II syndrome defect state with or without the persistence of positive symptoms; this might be described as classical Kraepelinian schizophrenia. On the other hand, either syndrome may occur alone. Thus, a pure Type I syndrome which remits may be described as a schizophreniform psychosis (Langfeldt 1960), or "psychogenic" or "reactive" schizophrenia (Faergeman 1963), a cycloid psychosis (Leonhard 1966; Perris 1974), schizo-affective psychosis (Kasanin 1933), or good-prognosis schizophrenia (Vaillant 1964).

The Type II syndrome may occur alone as in simple schizophrenia or in the defect state when positive symptoms have disappeared, and sometimes it may precede the onset of positive symptoms—as in the concept of childhood asociality propounded by Quitkin et al. (1976).

The paranoid/non-paranoid dichotomy can also be related to the concept, paranoid schizophrenia being equivalent to a chronic Type I syndrome, while non-paranoid schizophrenias (including the Bleulerian categories of hebephrenia and simple schizophrenia) are those which include a component of the Type II syndrome. A similar distinction is made by Winokur and Tsuang (1981). The relationship proposed between the two syndromes is indicated in the Figure, together with the correspondence of the three symptom constellations to various nosological terms of current or recent usage.

Of particular interest are the changes which occur with the passage of time. Thus, patients with the Type I syndrome may progress to acquire Type II symptoms, and in due course some of these will lose their positive symptoms. Some may re-acquire them, i.e., experience acute exacerbations of psychosis. What appears to be unusual, and if it does occur is worthy of note, is that patients with negative symptoms (Type II syndrome) should lose these symptoms once they are


Type I
Type II
Kraepelin
paranoia : dementia praecox ("classical Kraepelinian schizophrenia")
Bleuler
paranoia : hebephrenia : simple schizophrenia : the "defect state"
Winokur
paranoid : non-paranoid schizophrenia
Langfeldt
schizophreniform psychosis :
Kasanin
schizo-affective psychosis :
Leonhard
Perris
cycloid psychosis :
Vaillant
good- prognosis schizophrenia:

FIGURE

established. According to the hypothesis, this is because such symptoms are associated with a structural change in the brain.

The distinction between Type I and Type II syndromes explains a number of findings:

1. Angrist et al. (1980a) found that exacerbation of symptoms in individual patients by amphetamine predicted good response to neuroleptics, while absence of response to amphetamine predicted poor response. Re-analysis of individual Brief Psychiatric Rating Scale (BPRS) symptom scores (Angrist et al. 1980b) revealed that positive symptoms (the Type I syndrome) were exacerbated by amphetamine and improved by neuroleptics, while negative symptoms (the Type II syndrome) showed little change with either drug.

2. In a 30-year followup study, Tsuang (1980) found that disorientation at the time of first psychotic illness is a predictor of poor long-term outcome. Thus, disorientation in the acute illness may be a harbinger of the intellectual impairment of the Type II syndrome.

3. Recently, Owens and Johnstone (1980) have found that negative symptoms in long-stay patients are strongly correlated with intellectual impairment (the Type II syndrome) and also with neurological signs, but that none of these features is significantly related to positive symptoms (the Type I syndrome).

4. The prediction that increased dopamine receptors are related to positive symptoms has been tested in a study of 14 patients whose clinical state had been assessed before death on standardized rating scales. The number of dopamine receptors assessed as maximum spiroperidol binding was found to be significantly ($p < 0.01$) associated with positive but not negative symptoms (Crow et al. 1981).

Causation

The cause of schizophrenic illness remains obscure. A genetic influence is undoubted, but the facts that the onset of symptoms is often in adult life and that concordance in monozygotic twins (about 50%) falls short of 100 percent suggest that genes may be relevant only in predisposing to some other factor. Infection with slow virus may be relevant (Crow et al. 1979b; Crow 1978, 1980, 1981; Tyrell et al. 1979; Albrecht et al. 1980). Some neurotropic viruses (i.e., polio, herpes, simplex and zoster) are selective in the cells that attack. Conceivably a slow virus infection might be associated either with a primary chemical disturbance (i.e., through an affinity for a receptor site), as in the Type I syndrome, or with a more general disturbance of higher cognitive functions associated with structural changes in the brain, as in the Type II syndrome.

References

Albrecht, P., Torrey, E. F., Boone, P., Hicks, J.T., and Daniel, N. Elevation of cytomegalovirus antibody in the cerebrospinal fluid of schizophrenic patients. *Lancet*, ii:769-771, 1980.

Anden, N.E. Dopamine turnover in the corpus striatum and the limbic system after treatment with neuroleptic and anti-acetylcholine drugs. *J. Pharmacy Pharmacol.*, 24:905-906, 1972.

Andreasen, N. CT scan abnormalities in schizophrenia: Relationship to positive and negative symptoms. Paper presented to the Royal College of Psychiatrists Annual Meeting, London, July 1981.

Angrist, B., Rotrosen, J., and Gershon, S. Responses to apomorphine, amphetamine, and neuroleptics in schizophrenic subjects. *Psychopharmacology (Berlin)*, 67:31-38, 1980a.

Angrist, B., Rotrosen, J., and Gershon, S. Differential effects of amphetamine and neuroleptics on negative vs positive symptoms in schizophrenia. *Psychopharmacology (Berlin)*, 72:17-19, 1980b.

Asano, N. Pneumoencephalographic study of schizophrenia. In: Mitsuda, H., (ed.), *Clinical Genetics in Psychiatry, Problems in Nosological Classification*. Tokyo: Igaku-Shoin, 1967, pp. 209-219.

Bland, R.C., and Orn, H. Schizophrenia: Schneider's first rank symptoms and outcome. *Br. J. Psychiatry*, 137:63-68, 1980.

Bowers, M.B. Central dopamine in schizophrenic syndromes. *Arch. Gen. Psychiatry*, 31:50-54, 1974.

Brockington, I.F., Kendell, R.E., and Leff, J.P. Definitions of schizophrenia; concordance and prediction of outcome. *Psychol. Med.*, 8:387-398, 1978.

Carlsson, A., and Lindqvist, M. Effect of chlorpromazine and haloperidol on formation of 3-methoxy-tyramine and normetanephrine in mouse brain. *Acta Pharmacol. Toxicol.*, 20:140-144, 1963.

Connell, P.H. *Amphetamine Psychosis*. London: Oxford University Press, 1958.

Creese, I., Burt, D.R., and Snyder, S.H. Dopamine receptor binding predicts clinical and pharmacological potencies of antischizophrenic drugs. *Science*, 192:481-483, 1976.

Cross, A.J., Crow, T.J., Killpack, W.S., Longden, A., Owen, F., and Riley, G.J. The activities of brain dopamine-β-hydroxylase and catechol-o-methyl transferase in schizophrenics and controls. *Psychopharmacology (Berlin),* 59:117-121, 1978.

Cross, A.J., Crow, T.J., and Owen, F. [^{3}H]-flupenthixol binding in post-mortem brains of schizophrenics: Evidence for a selective increase in D2 receptors. *Psychopharmacology (Berlin),* 74:122-124, 1981.

Crow, T.J. (1978) Viral causes of psychiatric disease. *Postgrad. Med. J.,* 54:763-767, 1978.

Crow, T.J. The search for an environmental agent in schizophrenia. *Trends. Neurosci.,* July XIII-XIV, 1980.

Crow, T.J. Biological basis of mental disorders: The case for viral aetiology. In: Tognoni, G., Bellantuono, C., and Lader, M. (eds.), *Epidemiological Impact of Psychotropic Drugs.* Amsterdam: Elsevier-North Holland, 1981, pp. 33-51.

Crow, T.J. Baker, H.F., Cross, A.J., Joseph, M.H., Lofthouse, R., Longden, A., Owen, F., Riley, G.J., Glover, V., and Killpack, W.S. Monoamine mechanisms in chronic schizophrenia: Post-mortem neurochemical findings. *Br. J. Psychiatry,* 134:249-256, 1979a.

Crow, T.J., Deakin, J.F.W., Johnstone, E.C., and Longden, A. Dopamine and schizophrenia. *Lancet,* ii:565-566, 1976.

Crow, T.J., Deakin, J.F.W., and Longden, A. The nucleus accumbens—possible site of antipyschotic action of neuroleptic drugs? *Psychol. Med.,* 7:213-221, 1977.

Crow, T.J., Ferrier, I.N., Johnstone, E.C., Macmillan, J.F., Owens, D.G.C., Parry, R.P., and Tyrrell, D.A.J. Characteristics of patients with schizophrenia or neurological disorder and virus-like agent in cerebrospinal fluid. *Lancet,* i:842-844, 1979b.

Crow, T.J., and Gillbe, C. Brain dopamine and behaviour. A critical analysis of the relationship between dopamine antagonism and therapeutic efficacy of neuroleptic drugs. *J. Psychiatric Res.,* 11:163-172, 1974.

Crow, T.J., and Mitchell, W.S. Subjective age in chronic schizophrenia: Evidence for a sub-group of patients with defective learning capacity? *Br. J. Psychiatry,* 126:360-363, 1975.

Crow, T.J., Owen, F., Cross, A.J., Ferrier, I.N., Johnstone, E.C., McCreadie, R.G., Owens, D.G.C., and Poulter, M. Neurotransmitter enzymes and receptors in post-mortem brain in schizophrenia: Evidence that an increase in D2 receptors is associated with the Type I syndrome. In: Reiderer, P., and Usdin, E. (eds.), *Transmitter Biochemistry of Human Brain Tissue.* London: Macmillan, 1981, pp. 85-96.

Crow, T.J., Spear, P.J., and Arbuthnott, G.W. Intracranial self-stimulation with electrodes in the region of the locus coeruleus. *Brain Res.,* 36:275-287, 1972.

Crow, T.J., and Stevens, M. Age disorientation in chronic schizophrenia: The nature of the cognitive deficit. *Br. J. Psychiatry,* 133:137-142, 1978.

Donnelly, E.F., Weinberger, D.R., Waldman, I.N., and Wyatt, R.J. Cognitive abnormalities associated with morphological brain abnormalities on computed tomography in chronic schizophrenic patients. *J. Nerv. Ment. Dis.,* 168:305-308, 1980.

Ellinwood, E.H. Amphetamine psychosis: I. Description of the individuals and process. *J. Nerv. Ment. Dis.,* 144:274-283, 1967.

Faergeman, P.M. *Psychogenic Psychoses.* London: Butterworth, 1963.

Gaddum, J.H. Drugs antagonistic to 5-hydroxytryptamine. In: Wolstenholme, G.W. (ed.), *Ciba Foundation Symposium on Hypertension.* Boston: Little Brown, 1954, pp. 75-77.

Golden, C.J., Moses, J.A., Zelazowski, R., Graber, R., Zatz, L.M., Horvath, T.B., and Berger, P.A. Cerebral ventricular size and neuropsychological impairment in young chronic schizophrenics. *Arch. Gen. Psychiatry,* 37:619-623, 1980.

Gross, G., Huber, G., and Schuttler, R. Computerized tomography studies in schizophrenic disease. Presented at Third World Congress of Biological Psychiatry, Stockholm, June 28-July 3, 1981.

Haug, J.O. Pneumoencephalographic studies in mental disease. *Acta Psychiatr. Scand. (Suppl.),* 165:1-104, 1962.

Holden, J.M.C., Forno, G., Itil, T., and Hsu, W. Echoencephalographic patterns in chronic schizophrenia (relationship to therapy resistance). *Biol. Psychiatry,* 6:129-141, 1973.

Hughes, J.S., and Little, J.C. An appraisal of the continuing practice of prescribing tranquillizing drugs for long-stay psychiatric patients. *Br. J. Psychiatry,* 113:867-873, 1967.

Johnstone, E.C., Crow, T.J., Frith, C.D., Husband, J., and Kreel, L. Cerebral ventricular size and cognitive impairment in chronic schizophrenia. *Lancet,* ii:924-926, 1976.

Johnstone, E.C., Crow, T.J., Frith, C.D., Carney, M.W.P., and Price, J.S. Mechanism of the antipsychotic effect in the treatment of acute schizophrenia. *Lancet,* i:848-851, 1978a.

Johnstone, E.C., Crow, T.J., Frith, C.D., Stevens, M., Kreel, L., and Husband, J. The dementia of dementia praecox. *Acta Psychiatr. Scand.,* 57:305-324, 1978b.

Joseph, M.H., Baker, H.F., Crow, T.J., Riley, G.J., and Risby, D. Brain tryptophan metabolism in schizophrenia: A post-mortem study of metabolites on the serotonin and kynurenine pathways in schizophrenic and control subjects. *Psychopharmacology (Berlin),* 62:279-285, 1979.

Kasanin, J. The acute schizo-affective psychoses. *Am. J. Psychiatry,* 90:97-126, 1933.

Kornetsky, C. Hyporesponsivity of chronic schizophrenic patients to dextroamphetamine. *Arch. Gen. Psychiatry,* 33:1425-1428, 1976.

Langfeldt, G. Diagnosis and prognosis in schizophrenia. *Proc. R. Soc. Med.,* 53:1047-1052, 1960.

Lee, T., Seeman, P., Tourtellotte, W.W., Farley, I.J., and Hornykiewicz, O. Binding of ^{3}H-neuroleptics and ^{3}H-apomorphine in schizophrenic brains. *Nature,* 274:897-900, 1978.

Leonhard, K. *Aufteilung der endogenen Psychosen.* (The distribution of endogenous psychoses.) Berlin: Akademia-Verlag, 1966.

Letemendia, F.J.J., and Harris, A.D. Chlorpromazine and the untreated chronic schizophrenic: A long-term trial. *Br. J. Psychiatry,* 113:950-958, 1967.

Miller, R.J., and Hiley, C.R. Antimuscarinic properties of neuroleptics and drug-induced Parkinsonism. *Nature,* 248:596-597, 1974.

Miller, R.J., Horn, A.S., and Iversen, L.L. The action of neuroleptic drugs on dopamine-stimulated adenosine cyclic 3', 5'-monophosphate production in neostriatum and limbic forebrain. *Mol. Pharmacol.*, 10:759-766, 1974.

Muller, P., and Seeman, P. Brain neurotransmitter receptors after long-term haloperidol: Dopamine, acetylcholine, serotonin, α-noradrenergic, and naloxone receptors. *Life Sci.*, 21:1751-1758, 1977.

Murphy, D.L., and Wyatt, R.J. Reduced monoamine oxidase activity in blood platelets from schizophrenic patients. *Nature*, 238:225-226, 1972.

Owen, F., Cross, A.J., Crow, T.J. Longden, A., Poulter, M., and Riley, G.J. Increased dopamine receptor sensitivity in schizophrenia. *Lancet*, ii:223-225, 1978.

Owen, F., Cross, A.J., Crow, T.J., Lofthouse, R., and Poulter, M. Neurotransmitter receptors in brain in schizophrenia. *Acta Psychiatr. Scand (Suppl.)*, 291:20-26, 1980.

Owens, D.G.C., and Johnstone, E.C. The disabilities of chronic schizophrenia — Their nature and the factors contributing to their development. *Br. J. Psychiatry*, 136:384-395, 1980.

Perris, C., A study of cycloid psychoses. *Acta Psychiatr. Scand.* (*Suppl.*), 253:1-75, 1974.

Post, R.M., Fink, E., Carpenter, W.T., and Goodwin, F.K. Cerebro-spinal fluid amine metabolites in acute schizophrenia. *Arch. Gen. Psychiatry*, 32:1063-1069, 1975.

Quitkin, F., Rifkin, A., and Klein, D.F. Neurologic soft signs in schizophrenia and character disorder. *Arch. Gen. Psychiatry*, 33:845-853, 1976.

Randrup, A., and Munkvad, I. Special antagonism of amphetamine induced abnormal behaviour. Inhibition of stereotyped activity with increase of some normal activities. *Psychopharmacologia* (*Berlin*), 7:416-422, 1965.

Randrup, A., and Munkvad, I. Stereotyped activities produced by amphetamine in several animal species and man. *Psychopharmacologia* (*Berlin*), 11:300-310, 1967.

Randrup, A., and Munkvad, I. Evidence indicating an association between schizophrenia and dopaminergic hyperactivity in the brain. *Orthomol. Psychiatry*, 1:2-7, 1972.

Reider, R.O., Donnelly, E.F., Herdt, J.R., and Waldman, I.N. Sulcal prominence in young chronic schizophrenic patients: CT scan findings associated with impairment on neuropsychological tests. *Psychiatry Res.*, 1:1-8, 1979.

Seeman, P., Lee, T., Chau-Wong, M., and Wong, K. Antipsychotic drug doses and neuroleptic/dopamine receptors. *Nature*, 261:717-719, 1976.

Stein, L., and Wise, C.D. Possible etiology of schizophrenia: Progressive damage to the noradrenergic reward system by 6-hydroxy-dopamine. *Science*, 171:1032-1036, 1971.

Takahashi, R., Inaba, Y., Inanaga, K., Kato, N., Kumashiro, H., Nishimura, T., Okuma, T., Otsuki, S., Sakai, T., Sato, T., and Shimazono, Y. CT scanning and the investigation of schizophrenia. In: Perris, C., Struwe, G., and Jansson, B. (eds.), *Biological Psychiatry*. Amsterdam: Elsevier-North Holland, 1981, pp. 259-268.

Tsuang, M.T. Thirty to 40-year follow-up of schizophrenia: outcome and stability of diagnosis. Paper presented to the Schizophrenia Group. The Wellcome Trust, 22nd May 1980.

Tyrrell, D.A.J., Parry, R.P., Crow, T.J. Johnstone, E.C., and Ferrier, I.N. Possible virus in schizophrenia and some neurological disorders. *Lancet*, i:839-841, 1979.

Vaillant, G. Prospective prediction of schizophrenic remission. *Arch. Gen. Psychiatry*, 11:509-518, 1964.

Weinberger, D.R., Bigelow, L.B., Kleinman, J.E., Klein, S.T., Rosenblatt, J.E., and Wyatt, R.J. Cerebral ventricular enlargement in chronic schizophrenia associated with poor response to treatment. *Arch. Gen. Psychiatry*, 37:11-13, 1980a.

Weinberger, D.R., Cannon-Spoor, E., Potkin, S.G., and Wyatt, R.J. Poor premorbid adjustment and CT scan abnormalities in chronic schizophrenia. *Am. J. Psychiatry*, 137:1410-1413, 1980.

Weinberger, D.R., Torrey, E.F., Neophytides, A.N., and Wyatt, R.J. Lateral cerebral ventricular enlargement in chronic schizophrenia. *Arch. Gen. Psychiatry*, 36:735-739, 1979.

Whitaker, P.M., Crow, T.J., and Ferrier, I.N. Tritiated LSD binding in frontal cortex in schizophrenia. *Arch. Gen. Psychiatry*, 38:278-280, 1981.

Winokur, G., and Tsuang, M. Paranoid vs. non-paranoid schizophrenia: Definition and association. In: Perris, C., Struwe, G., and Jansson, B. (eds.), *Biological Psychiatry*. Amsterdam: Elsevier-North Holland, 1981, pp. 761-765.

Woolley, D.W., and Shaw, E. A biochemical and pharmacological suggestion about certain mental disorders. *Proc. Natl. Acad. Sci. USA*, 40:228-231, 1954.

Schizophrenia and Late Maturational Brain Changes in Man[1]

Irwin Feinberg, M.D.[2]

Recent findings in neurobiology suggest that maturational changes take place in the brain much later in life than had previously been thought. In this context, several lines of evidence suggest that a major reorganization of the human brain takes place in adolescence:

1. There is a marked decline in the abundance of deep (Stage 4) sleep and in the amplitude of the delta waves which characterize this stage. Between the ages of 10 and 16 years, these variables show as much change as they do over the next 30 years (Feinberg & Carlson 1968; Feinberg et al. 1977; Williams et al. 1974).

2. A marked diminution in neuroanatomical plasticity occurs. For example, a left hemisphere

---

[1] This work was supported by the Veterans Administration.

[2] Veterans Administration Medical Center and The University of California at San Francisco 94121.

lesion which causes aphasia in a 10-year-old child is usually followed by full recovery of speech if the right hemisphere is spared: the same lesion in a 20-year-old person results in a permanent aphasia.

3. The ability to carry out sustained logical thinking and to solve complex and abstract problems emerges in full flower toward the end of adolescence. While these skills surely depend upon continued learning, they may also require morphological changes in the neural substrate of thought.

4. The changes listed above are normal developmental phenomena. An abnormal developmental occurrence in adolescence is the emergence of schizophrenia. To be sure, some patients who develop this illness have a long history of behavioral disturbance so that one may question how important a role adolescence itself plays. However, one also finds patients whose psychosocial development was normal or outstanding prior to the onset of a schizophrenic illness. The abrupt change from a social, productive, and happy youngster to a delusional, withdrawn, and frightened schizophrenic is one of the most tragic events in medicine. The profound nature of this change suggests that the neural substrate of behavior has altered in some fundamental way.

Recently, Peter Huttenlocher (1979) of the University of Chicago described a late change in brain morphology which might underlie the striking behavioral and electrophysiological changes of adolescence. He observed a marked reduction in the density of synapses in postmortem specimens of human cortex between ages 2 and 16 years; most of this change seems to take place in late childhood and early adolescence. Huttenlocher's finding (as he himself suggested) could directly account for the reduction in neuroanatomical plasticity which occurs during adolescence. It could also underlie the decline in delta wave amplitude during sleep. The electroencephalogram (EEG) recorded at the scalp is the summation of slow, synchronous potential changes in large neuronal pools; a decrease in connectivity could reduce the size of the neuronal groups capable of synchronous discharge.

The author has commented on the fact that adolescence is characterized by the emergence of the ability to carry out sustained logical operations and solve complex and abstract problems. It might seem counter-intuitive to suggest that a neuronal change contributing to this cognitive development is an actual decline in neuronal connections. But this may well prove to be the case. One plausible model, consistent with Huttenlocher's data, is that shortly after birth all potentially useful interconnections develop. This extremely high density of synapses permits great plasticity but has a cost to information processing: too many neuronal connections may make it difficult to distinguish and organize functionally the particular neuronal chains required for sustained logical thought and problem solving. When, toward the end of adolescence, the connections needed for adaptation have been specified by the organism's interaction with the environment, unexploited connections are eliminated. The effect of this elimination is to reduce neuroanatomical plasticity but to increase certain information-processing capacities.

If synaptic pruning of this sort actually takes place, it would not be the first example of systematic creation and elimination of redundant neural elements in brain development. Programmed cell death (Cowan 1973) plays an important role in regulating the development of the nervous system. In the course of embryologic development, many excess neurons are regularly produced; at later and highly predictable stages, those neurons which have not achieved their appropriate connections die. This mechanism is so highly reproducible that it must be under precise genetic control; so also, one would postulate, is the elimination of redundant synapses much later in development. The mechanisms by which the synapses are eliminated is unknown, but it seems likely that neuroendocrine processes play an important role.

If a widespread, genetically programmed elimination of synapses occurs in adolescence, an error in this process may give rise to schizophrenia. The defect might result from the elimination of too many, too few, or the wrong connections. Elsewhere (Feinberg 1978), it was suggested that corollary discharge mechanisms (Evarts 1971) play an important role in the control of thinking, and that several cardinal symptoms of schizophrenia could be understood as resulting from failure of similar mechanisms in the "motor systems" of thinking.

We have already noted that the extent of neuronal interconnections might determine the size of the neuronal pools whose synchronous, slow potential change gives rise to delta waves. In this regard, it is of interest that the most firmly established brain abnormality in schizophrenia is a reduction in Stage 4 sleep (Feinberg & Hiatt 1978). This abnormality, although neither specific to, nor invariably present in, schizophrenia, has been found in 40-50 percent of the samples of schizophrenic patients investigated. Computer analysis suggests that it is largely due to reduced delta wave amplitude in the first period of non-REM sleep (Hiatt, Floyd, & Feinberg, submitted for publication).

The highly speculative nature of this discussion is obvious. But whether or not its neuroanatomic basis is the change in synaptic density described by Huttenlocher, there is compelling but as yet neglected evidence that a major reorganization of the brain takes place in adolescence. This reorganization is associated with striking changes in sleep EEG, brain plasticity, and problem-solving capacity. An error in so pervasive a developmental process may be responsible for some types of schizophrenia.

References

Cowan, W.M. Neuronal death as a regulative mechanism in the control of cell number in the nervous system. In: Rockstein, M. (ed.) *Development and Aging in the Nervous System.* New York: Academic Press, 1973.

Evarts, E.V. Feedback and corollary discharge: A merging of the concepts. *Neurosci. Res. Program Bull.*, 9:86-112, 1971.

Feinberg, I. Efference copy and corollary discharge: Implications for thinking and its disorders. *Schizophr. Bull.*, 4:636-640, 1978.

Feinberg, I., and Carlson, V.R. Sleep variables as a function of age in man. *Arch. Gen. Psychiatry*, 18:239-250, 1968.

Feinberg, I., Hibi, S., and Carlson, V.R. Changes in EEG amplitude during sleep with age. In: Nandy, K., and Sherwin, I. (eds.) *Aging Brain and Senile Dementia.* New York: Plenum Press, 1977, pp. 85-98.

Feinberg, I., and Hiatt, J.F. Sleep patterns in schizophrenia: A selective review. In: Williams, R.L., and Karacan, I. (eds.) *Sleep Disorders: Diagnosis and Treatment.* New York: Wiley & Sons, 1978, pp. 205-231.

Huttenlocher, P.R. Synaptic density in human frontal cortex—Developmental changes and effects of aging. *Brain Res.*, 163:195-205, 1979.

Williams, R.L., Karacan, I., and Hursch, C.J. *Electroencephalography (EEG) of Human Sleep: Clinical Applications.* New York: Wiley & Sons, 1974.

Dopamine and the Neural Substrates of Depression

Chair: Hans C. Fibiger, Ph.D.
University of British Columbia
Vancouver, B.C., Canada

Evidence in Support of a Role of Dopamine in Affective Illness

Angelos E. Halaris, M.D., Ph.D.[1]

The first indications of a link between dopamine (DA) and affective disorders appeared in the late sixties. It was not until recently, however, that serious consideration was given to DA in addition to other neurotransmitters commonly associated with the pathophysiology of manic-depressive illness. A growing body of evidence suggests that along with norepinephrine (NE) and 5-hydroxytryptamine (5-HT), DA plays a role in affective illness. Newer compounds with selective effects on DA receptors and specific DA agonist or antagonist activity are assisting in the characterization of various subtypes of depression. Correlations between forms of psychopathology and DA metabolism have clearly defined a group of depressives with diminished excretion of homovanillic acid (HVA) in cerebrospinal fluid (CSF). These studies have associated DA with retarded forms of depression and certain aspects of manic behavior.

Compared to the extensive literature on antidepressants and NE or 5-HT, animal studies seeking to establish dopaminergic involvement in antidepressant drug action are relatively sparse. There are two reasons for this disparity. First, DA was long held to be a precursor of NE, lacking any transmitter activity of its own. This assumption later proved to be erroneous. Second, research has focused heavily on NE as the transmitter primarily responsible for the pathogenesis and treatment of affective illness. Thus, the number of basic studies concerned with antidepressant action and dopaminergic transmission is small.

---

[1] Department of Psychiatry, UCLA School of Medicine, and Veterans Administration Medical Center Brentwood, Los Angeles, CA 90073.

Effect of Tricyclics on DA Metabolism

One of the earlier findings from this laboratory was that chlorimipramine and other tertiary drugs increased DA levels in rat whole brain. The increases were substantial (40-60%) and time-dependent. Since similar time-dependent changes had been obtained with brain levels of 5-HT after chlorimipramine, it was hypothesized that there may be a link between uptake inhibition and changes in amine metabolism, possibly via feedback mechanisms or a direct effect of tricyclics on neuronal firing. This hypothesis led to the detection of DA uptake inhibition by chlorimipramine and other psychotropic compounds. These findings were later confirmed by Ghosh and Hrdina (1977), who obtained marked increases in striatal DA (up to 140%) with imipramine, desmethylimipramine, and amitriptyline. The increase was time-dependent and biphasic. There were concomitant alterations in levels of HVA which were a mirror image of the changes in the concentration of DA. The authors hypothesized that the ability of tricyclic antidepressants to affect striatal concentrations of DA and HVA are relevant to the beneficial effects of these agents in the treatment of Parkinson's disease.

Antidepressant Drugs and Dopamine Uptake

Reuptake blockade of NE and 5-HT by antidepressants and a consequent shift in amine metabolites have been key findings for inferring the therapeutic mode of action of antidepressants and, by extension, the biochemical substrate of affective illness. The possibility that tricyclic antidepressants also inhibit DA uptake had been largely ignored or considered to be of little pharmacological and clinical significance. Using synaptosomal preparations from rat whole brain, it was demonstrated that a number of antidepressants block DA uptake (Halaris et al. 1975; Halaris & Freedman 1975). The degree of inhibition was variable and could not be systematically explained on the basis of molecular structure or side-chain substituents. In the group of antidepressants, it was not possible to detect differences in potency between secondary and tertiary drugs. Among those drugs tested, some secondary (nortriptyline and protriptyline) and some tertiary (chlorimipramine and amitriptyline) tricyclics were potent agents in inhibiting DA uptake. Desipramine, imipramine, and doxepin were weaker, as were iprindole and the tetracyclic maprotiline.

The tricyclic drug concentrations required to produce 50 percent inhibition of DA uptake (IC50 values) were initially considered to be high compared with IC50 values for NE and 5-HT uptake. However, IC50 values obtained in whole rat brain preparations can be misleading, since specific brain regions may exhibit selectivity for inhibition of DA uptake. When regional analysis of DA uptake was performed, the *hypothalamus* was the region in which tricyclic (and nontricyclic) antidepressants produced *in vitro* uptake inhibition in the micromolar range (Table 1). Kinetic analysis revealed that uptake inhibition was of the competitive type. It is noteworthy that iprindole—which has no effect on NE uptake—also inhibited DA uptake in the micromolar range.

In another study, selected tricyclics were injected into rats acutely or chronically. The uptake experiments were performed with synaptosomal preparations from whole brain of pretreated animals. Chlorimipramine, among the most potent antidepressants to inhibit DA uptake, produced significant inhibition, indicating that the drug reaches active sites in spite of the fact that preparations from whole brain rather than hypothalamus were used. Similar results were obtained when lower doses were given for 3 weeks.

Finally, the specificity of the accumulation of labeled amines when performing uptake experiments has often been questioned. It has been

Table 1

Dopamine Uptake in Hypothalamus

Drug	IC_{50} (M)
Desipramine	4.2×10^{-6}
Doxepin	4.4×10^{-6}
Clomipramine	6.3×10^{-6}
Imipramine	7.3×10^{-6}
Bupropion	2.0×10^{-6}
Iprindole	2.2×10^{-6}
Pridefine	2.5×10^{-6}

suggested that biogenic amines can be taken up by nerve-endings other than those of the transmitter used. This is likely to occur at high substrate concentrations. However, if the concentration of labeled amine is less than the Km for the high affinity uptake system, then the risk of nonspecific accumulation is minimized. To rule out that tritiated DA is partially taken up by noradrenergic terminals in hypothalamus, the freely cycling female rat was used as a test model. It was demonstrated that the cyclic and phase-dependent pattern of DA uptake by hypothalamic nerve-endings differs completely from that of NE in the course of a full estrous cycle (Davis et al. 1977, 1978). If tritiated DA were entering NE terminals, the resulting pattern of DA uptake during the various phases of the rat estrous cycle would be similar, if not identical, to that of NE.

Uptake inhibition of DA is not unique to tricyclic antidepressants. A number of newer compounds exhibit significant inhibitory activity. In a comparative study of such new antidepressants, Randrup and Braestrup (1977) investigated the potency of a number of conventional and newer drugs on the inhibition of NE, DA, and 5-HT uptake. Their results indicate that the newer antidepressants butriptyline, mianserin, and trimipramine are about equipotent with maprotiline, iprindole, and the classical tricyclics in inhibiting striatal DA uptake. Interestingly, nomifensine, a clinically efficacious antidepressant (Pecknold et al. 1975) is one of the most potent inhibitors of DA uptake; it is equally potent with benztropine and seven times more potent than cocaine.

The Case of Bupropion (Wellbutrin^{R})

Bupropion is a phenylethylamine derivative with clinically established antidepressant activity. Its chemical structure differs from that of conventional antidepressants, and the compound does not significantly affect norepinephrine or serotonin. A number of clinical studies have confirmed that bupropion is significantly better than placebo. Bupropion may exert its antidepressant effects via direct or indirect stimulation of DA receptors. To assess whether bupropion is a direct or indirect DA agonist, two types of experiments were performed. First, the effect of bupropion on DA uptake in striatal synaptosomal preparations was determined. Second, use was made of the stereotypy response believed to be mediated by striatal dopaminergic neurons. The uptake experiments revealed bupropion to be a moderately potent inhibitor of striatal DA uptake (Table 2). When injected into rats, it elicited stereotyped behavior in a dose-dependent manner. Since these experiments did not differentiate between a direct vs. indirect DA agonist activity of bupropion, an animal model for surgical induction of DA receptor supersensitivity was devised. This model will be discussed briefly.

By means of parasaggital knife cuts performed bilaterally, the ascending nigrostriatal fibers were transected prior to their entry into the striatum. The lesion resulted in a 96 percent depletion of striatal DA by the fourteenth day after surgery. Bupropion produced intense stereotyped behavior in lesioned animals on Days 3 and 7 after surgery

Table 2

Effect of Bupropion (Wellbutrin^{R}) on Biogenic Amine Uptake

Amine/Region	IC_{50} (μM)
DA - Striatum	1.5
DA - Hypothalamus	2.0
NE - Hypothalamus	2.6
5-HT - Cortex	154.5

at doses that did not induce stereotypy in sham-lesioned controls. Since DA depletion in striatum was not complete 1 week post-lesion, the appearance of intense stereotypy in lesioned animals was probably due to supersensitive DA receptors responding to enhanced dopaminergic transmission caused by reuptake blockade. However, on the fourteenth day post-lesion, when DA depletion was virtually complete, the stereotypy response of the lesioned animals was much weaker. Since presynaptic terminals have undergone degeneration by 14 days after axotomy, the ability of bupropion to elicit stereotyped behavior at this time is probably due to a direct effect on DA receptors. Therefore, it appears that bupropion is a mixed direct/indirect DA receptor agonist.

Bupropion had no significant effects on 5-HT uptake. While an effect of the drug on noradrenergic transmission has not been ruled out, bupropion appears to act primarily via a dopaminergic mechanism. Whether the results from the above animal experiments can explain bupropion's clinical antidepressant efficacy remains to be established.

Behavioral Effects and Conclusions

Two reports have described behavioral effects of tricyclic antidepressants mediated by dopaminergic mechanisms. Molander and Randrup (1976a,b) used gnawing behavior in mice as an index of dopaminergic activity. The antidepressants tested potentiated gnawing induced by levodopa in combination with a decarboxylase inhibitor. In a followup study, these drugs also potentiated the apomorphine-induced gnawing. The authors concluded that tricyclics enhance behaviors associated with brain DA.

Taken together, the above observations give strong support to the contention that tricyclic and non-tricyclic antidepressants affect dopaminergic transmission in the CNS. These drugs exert significant effects on the uptake and metabolism of brain DA and potentiate behavioral effects commonly attributed to dopaminergic mechanisms. However, the relevance of the animal studies to the clinical efficacy of tricyclic antidepressants, the induction of mania in susceptible manic-depressives, and the exacerbation of schizophrenia with these drugs remains to be established. Certainly, the clinical effects of the newer, non-tricyclic antidepressants, such as nomifensine and bupropion, compel attention to DA as a neurotransmitter involved in manic-depressive illness.

References

Davis, B.F., Davis, C.F., and Halaris, A.E. Variations in in the uptake of ^{3}H-dopamine during the rat estrous cycle. *Life Sci.*, 20:1319-1332, 1977.

Davis, C.F., Davis, B.F., and Halaris, A.E. Variations in the uptake of ^{3}H-norepinephrine during the rat estrous cycle. *Life Sci.*, 21:1387-1394, 1978.

Ghosh, P.K., and Hrdina, P.D. Effects of tricyclic antidepressants on the content and metabolism of dopamine in the rat striatum. *Can. J. Physiol. Pharmacol.*, 55:383-388, 1977.

Halaris, A.E., Belendiuk, K.T., and Freedman, D.X. Antidepressant drugs affect dopamine uptake. *Biochem. Pharmacol.*, 24:1896-1898, 1975.

Halaris, A.E., and Freedman, D.X. Psychotropic drugs and dopamine uptake inhibition. In: Freedman, D.X. (ed.), *Biology of the Major Psychoses.* New York: Raven Press, 1975, pp. 247-258.

Molander, L., and Randrup, A. Effects of thymoleptics on behavior associated with changes in brain dopamine. I. Potentiation of dopa-induced gnawing of mice. *Psychopharmacology (Berlin),* 45:261-265, 1976a.

Molander, L., and Randrup, A. Effects of thymoleptics on behavior associated with changes in brain dopamine. II. Modification and potentiation of apomorphine-induced stimulation of mice. *Psychopharmacology (Berlin),* 49:139-144, 1976b.

Pecknold, J.C., Ban, T.A., Lehmann, H.E., and Klingner, A. A clinical trial with nomifensine, a new antidepressant drug. *Int. J. Clin. Pharmacol.*, 11:304-308, 1975.

Randrup, A., and Braestrup, C. Uptake inhibition of biogenic amines by newer antidepressant drugs: Relevance to the dopamine hypothesis of depression. *Psychopharmacology (Berlin),* 53:309-314, 1977.

Mania, Depression, and Brain Dopamine: An Overview

Axel Randrup, Ph.D.,[1] Ib Munkvad, M.D.,[1] and Rasmus Fog, M.D.[1]

Dopaminergic mechanisms in the brain seem to be importantly related to the pathogenesis and treatment of several neuropsychiatric diseases, i.e., mania, depression, schizophrenia, Parkinson's disease, and Gilles de la Tourette's disease.

The relation with the affective disorders was suggested in the early 1970s by the following: antimanic, antidepressive, and depressogenic effects of neuroleptic drugs (dopamine blockers); effects of amphetamines, apomorphine, and L-DOPA (dopamine agonists) on mood and affective diseases; correlation of Parkinsonism and other disorders of the basal ganglia with depression; effects of thymoleptics on animal behavior believed to be associated with changes in brain dopamine, etc. (Randrup et al. 1973a, 1973b, 1975). In the years following, this body of evidence was strengthened by new findings: Involvement of dopamine in an interesting monkey model of depression and in reward mechanisms; marked effects on lithium on supersensitive postsynaptic dopamine receptors and on the turnover of dopamine; effects of tricyclic thymoleptics and electrostimulation (both after repeated application) on dopamine receptors; dopaminergic effects of second generation antidepressive drugs, particularly nomifensine, bupropion, and amoxapine) Harrison-Read 1981; Randrup et al. 1979, 1981a; Serra et al. 1980, 1981; present study group).

The dopaminergic effects of chronic thymoleptics seems to be associated with mild excitatory effects on behavior, but these drugs can also be sedative and exert stress-protecting effects somewhat similar to the "neuroleptic indifference." The mechanisms of these effects are yet largely unknown, although there is evidence indicating dopaminergic involvement. But animal experiments are possible here, and this appears to be a particularly interesting area for future research (Pekkarinen, 1970; Garzon & Del Rio 1981).

Amphetamines produce abnormal behavior in animals and humans, which has been studied as a model psychosis. Stereotypy is a prominent feature of the abnormality, and this feature has a particularly strong correlation with brain dopamine. Many types of behavior can become stereotyped e.g., sniffing, biting, locomotion, aggressive-defensive posture and, in humans, also mental activities such as thinking. Stereotyped thinking can, for example, consist in rumination on one or a few paranoid ideas. Behavioral and mental stereotypies are also common in endogenous psychoses, and the present investigators have pointed out that constant or long-lasting affects (e.g., melancholic mood) might be regarded as an analogy, in the affective area, of stereotyped thinking and behavior (Randrup et al. 1981a, 1981b).

The hypothesis that brain dopamine is importantly related to mood and affective disorders has been strengthened by recent evidence, but it has also become increasingly clear that the relation is not a simple one, and more is known now about the interaction of dopaminergic and nondopaminergic systems in the brain.

References

Garzon, J., and Del Rio, J. Hyperactivity induced in rats by long-term isolation: Further studies on a new animal model for the detection of antidepressants. *Eur. J. Pharmacol.*, 74:287-294, 1981.

Harrison-Read, P.E. Behavioural studies with lithium in rats: Implications for animal models of mania and depression. In: Hrdina, P.D., and Singhal, R.L. (eds.), *Neuroendocrine Regulation and Altered Behaviour*. London: Croom Helm, 1981, pp. 224-262.

Pekkarinen, A. The inhibiting effect of thymoleptic antidepressants on the neurogenic increase of the corticosteroid content of the rat plasma. *Acta Pharmacol. Toxicol.* (*Copenh.*), 28:71, 1970.

Randrup, A., Munkvad, I., and Scheel-Krüger, J. Mechanisms by which amphetamines produce stereotypy, aggression, and other behavioural effects. In: Ban, T.A., Boissier, J.R., Gessa, G.J., et al. (eds.), *Psychopharmacology, Sexual Disorders, and Drug Abuse*. Amsterdam: North-Holland Publishing Company, Prague: Avicenum, Czechoslovak Medical Press, 1973a.

---

[1] St. Hans Mental Hospital, Dept. E., DK-4000 Roskilde, Denmark.

Randrup, A., Munkvad, I., Fog, R., Gerlach, Y., and Molander, L. Possible role of brain dopamine in mania and depression. In: Mazur, M. (ed.), *IV Congress of the Polish Pharmacological Society*. Lodz, Poland, 1973b, p. 35.

Randrup, A., Munkvad, I., Fog, R., Gerlach, Y., Molander, L., Kjellberg, B., and Scheel-Krüger, J. Mania, depression, and brain dopamine. In: Essmann, W., and Valzelli, L. (eds.), *Current Developments in Psychopharmacology*. Vol. 2. New York: Spectrum Publications, Inc., 1975, pp. 205-248.

Randrup, A., Munkvad, I., Fog, R., Braestrup, C., and Molander, L. The case for involvement of dopamine in depression and mania. In: Saletu, B., Berner, P., and Hollister, L. (eds.), *Neuropsychopharmacology*. New York: Pergamon Press, 1979, pp. 139-150.

Randrup, A., Munkvad, I., and Fog, R. Mental and behavioural stereotypies elicited by stimulant drugs. Relation to the dopamine hypothesis of schizophrenia, mania, and depression. In: Angrist, B., Burrows, G.D., Lader, M., et al. (eds.), *Recent Advances in Neuropsychopharmacology*. New York: Pergamon Press, 1981a, pp. 63-74.

Randrup, A., Munkvad, I., and Fog, R. Formulations of the dopamine hypothesis for affective disorders following the accumulation of new evidence. In: Perris, C., Struwe, G., and Jansson, B. (eds.), *Biological Psychiatry, 1981*. Amsterdam: Elsevier, 1981b, pp. 732-737.

Serra, G., Argiolas, A., and Gessa, G.L. Apomorphine-induced sedation: An animal model of mental depression. In: Brambilla, F., Racagni, G., and de Wied, D. (eds.), *Progress in Psychoneuroendocrinology*. Amsterdam: Elsevier, 1980, pp. 135-143.

Serra, G., Argiolas, A., and Gessa, G.L. Opposite changes in DA autoreceptors sensitivity induced by chronic antidepressants and neuroleptics. In: Gessa, G.L., and Corsini, G.U. (eds.), *Apomorphine and Other Dopaminomimetics*. Vol. 1. New York: Raven Press, 1981, pp. 133-141.

Nonlinear Dynamics in Brain Processes

Chair: **Arnold J. Mandell, M.D.**
Department of Psychiatry
University of California
La Jolla, California

A Mathematical Model for the Effect of Tetrahydrobiopterin Level on Tyrosine Hydroxylase Kinetic Fluctuations[1]

Patrick V. Russo, B.S.[2]

For twelve years Mandell's group, among others, has been studying the regulation of brain tyrosine hydroxylase and tryptophan hydroxylase and using in traditional kinetics experiments the saturating conditions prescribed by the Michaelis-Menten approach (Mandell 1978). However, during the last several years it has become clear that physiological concentrations of the substrates tyrosine and tryptophan and their cofactor tetrahydrobiopterin (BH_4) in brain are well below saturation; they are, in fact, below their K_m for their respective enzymes (Friedman et al. 1972; Wurtman et al. 1974; Bullard et al. 1978; Mandell et al. 1980; Lovenberg et al. 1982). Therefore, the group has undertaken kinetic experiments in which assay concentrations of coreactants are brought as near as possible to physiological levels, and the enzyme activities are sampled at fine-grained intervals of observation across time or across increasing reactant concentration.

Figure 1 is a schematic comparison of results obtained with saturating vs. non-saturating substrates. Observe the reiterative multiple velocity plateaus generated by the non-saturating condition for both time courses and substrate kinetics. What at first appeared to be noise was shown eventually to be small but reproducible

---

[1] This work is supported by USPHS Grant DA-00265 from the National Institute on Drug Abuse.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

variance which required for its quantification a fresh analytical approach.

Time series analysis was found to be a useful descriptive tool. Time courses and substrate kinetics are detrended by linear regression with subsequent normalization to remove the slope and intercept. The raw data are thus transformed to a zero-mean time series of A values, allowing analysis of both its amplitude and frequency components.

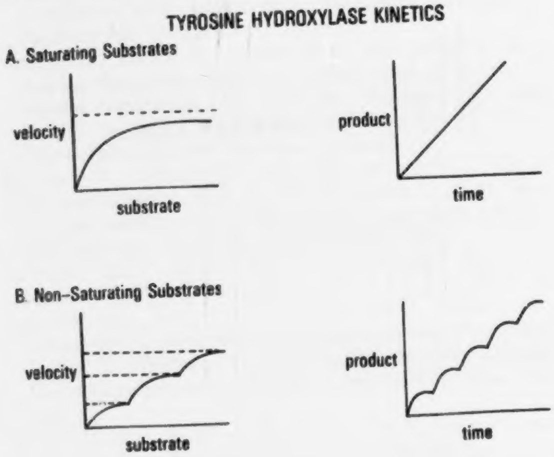


FIGURE 1

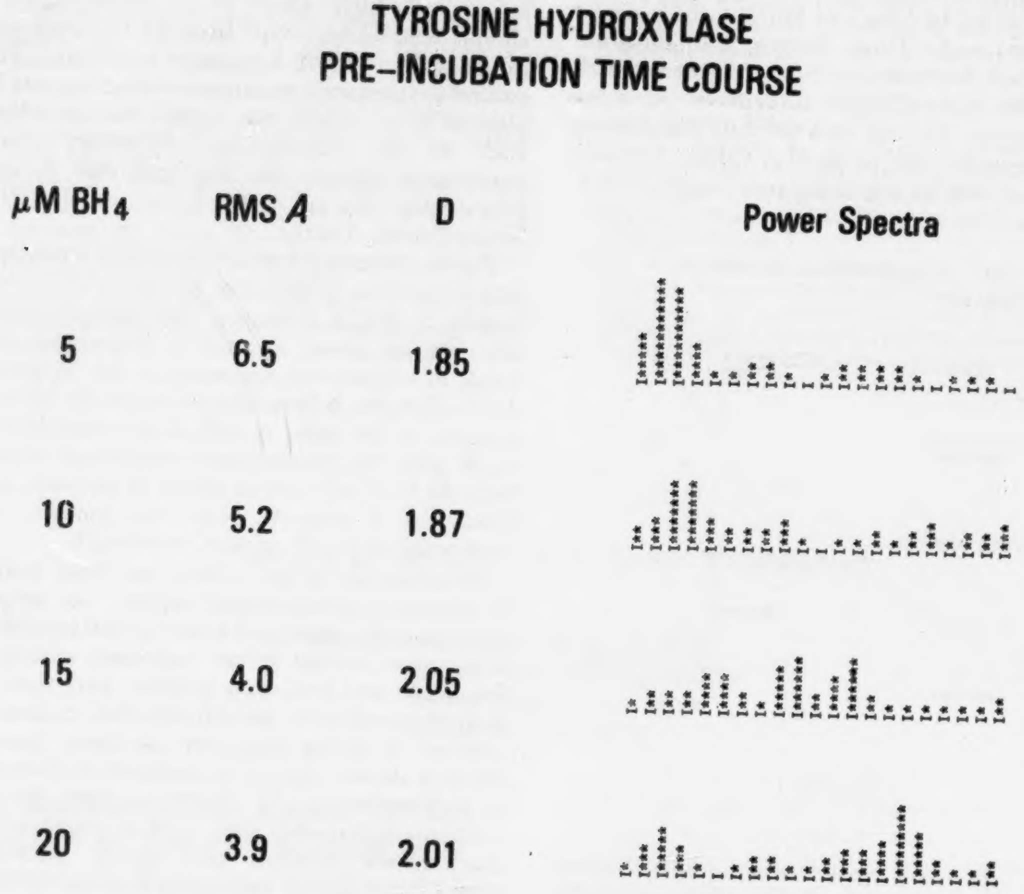
One measure of amplitude is root mean square (RMS) of A, defined as $\sqrt{\Sigma A^2/t}$. Squaring the individual values removes the negative ones, so the greater the amplitude or energy of the fluctuations, the higher the average RMS_A. To characterize its frequency or periodic nature, the series is subjected to Fourier analysis, and the resulting power spectrum reveals the relative amounts of power occurring across a range of frequencies. In addition, the Hausdorff-Besicovitch dimension D (Mandelbrot 1977) has provided an index of composite frequency or the dimensionality of the system. These qualitative metrics and their derivation appear in detail in several publications (Knapp et al. 1981, 1982; Knapp & Mandell 1982; Mandell & Russo 1981; Mandell et al. 1982).

In many systems there is a negative correlation between frequency and amplitude, for example, in the electroencephalograph (EEG) where fast waves are typically low voltage and slow waves are generally high voltage. In the present studies a similar relationship exists between D (composite frequency) and RMS (composite amplitude). For control preparations the negative slope appears in plots of D vs. RMS, but certain manipulations such as the introduction of certain pharmacological ligands can uncouple that inverse relationship (Knapp 1982; Knapp et al. 1982; Mandell et al. 1982).

Figure 2 shows the usual D vs. RMS relationship in tyrosine hydroxylase as well as the power spectra as BH_4 is increased. The asterisks represent relative power at various frequencies; the range of frequencies, expressed in the reciprocal as wavelengths, is from 80 minutes on the left to 2 minutes on the right. As BH_4 is increased from 2 to 20 μM, the predominant wavelength moves from 40 to 20 minutes to about 10 minutes, and finally to 4 minutes, with the possible reemergence of the 40-minute wavelength.

Examination of the effects on these indices of various pharmacological agents (i.e. propranolol, amphetamine) and experimental conditions shows that instead of an unlimited variety of amplitude and frequency profiles, only three or four are possible for the reproducible variance to inscribe. A strong frequency can form, become faster or slower, change in amplitude or dampen, or randomize into a chaotic regime. Several mathematical models were tried in searching for characteristic profiles, and several nonlinear dynamical systems suggested that the profiles could be simulated mathematically (Lorenz 1963; May 1976, 1980; Rössler 1976).

Mathematically, the simplest example is from an equation used in population dynamics and reviewed by May (1980). The limited range of possible profiles is shown in Figure 3. The reiterative equation contains only one parameter, the force term r, which is increased to the values shown in the respective panels with the following results. The system moves from equilibrium at $r = 1$ to a damped oscillator around $r = 2$, to a fast limit cycle around $r = 2.5$. At $r = 3.92$ a slower limit cycle is apparent; at $r = 4.0$ a chaotic regime is seen; finally at $r = 6$ the system is at equilibrium or death. The force term r is reminiscent of changing BH_4 cofactor level in the enzyme assays. At very high levels of BH_4 no fluctuations



TYROSINE HYDROXYLASE
PRE–INCUBATION TIME COURSE

μM BH_4	RMS *A*	D	Power Spectra
5	6.5	1.85	
10	5.2	1.87	
15	4.0	2.05	
20	3.9	2.01	

FIGURE 2

are observed (not unlike the equilibrium "death" at a very high *r* value, Figure 3). At low or intermediate levels of BH_4 or substrate, long or short wavelengths predominate, with "chaotic" regimes interspersed.

In sum, because endogenous levels of substrate and cofactor in brain as well below saturation, valuable new information may be obtained with subsaturating, more nearly physiological assay constituents, and the subsequent application of appropriate mathematical descriptors of the dynamical character of the resulting data.

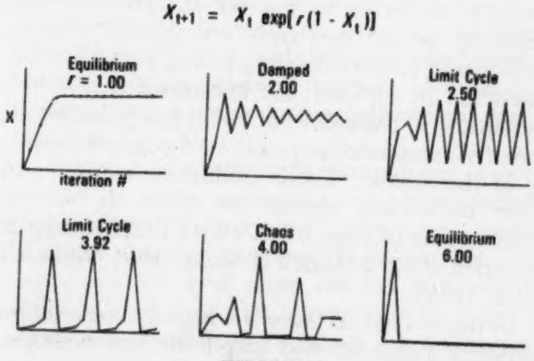


FIGURE 3

References

Bullard, W.P., Guthrie, P.B., Russo, P.V., and Mandell, A. Regional and subcellular distribution and some factors in the regulation of reduced pterins in rat brain. *J. Pharmacol. Exp. Ther.*, 206:4-20, 1978.

Friedman, P.A., Kappelman, A.H., and Kaufman, S. Partial purification and characterization of tryptophan hydroxylase from rabbit hindbrain. *J. Biol. Chem.*, 247:4165-4173, 1972.

Knapp, S., and Mandell, A.J. Lithium, brain tryptophan hydroxylase, and hemispheric asymmetry. *Psychiatry Res.* (In press)

Knapp, S., Ehlers, C., Russo, P.V., and Mandell, A.J. A cross-disciplinary approach to the action of lithium: A vertical integration. In: Lux, H., Aldenhoff, J., and Emrich, H. (eds.), *Basic Mechanisms in the Action of Lithium.* Amsterdam: Excerpta Medica. (In press)

Knapp, S., Mandell, A.J., Russo, P.V., Vitto, A., and Stewart, K.D. Strain differences in kinetic and thermal stability of two mouse brain tryptophan hydroxylase activities. *Brain Res.*, 230:317-336, 1981.

Lorenz, E.N. Deterministic nonperiodic flow. *J. Atmos. Sci.*, 20:130-140, 1963.

Lovenberg, W., Levine, R., and Miller, L. Catecholamine synthesis and the hydroxylase cofactor. In: Usdin, E., Weiner, N., and Youdim, M. (eds.), *Second Conference on Monoamine Enzymes.* London:Macmillan. (In press)

Mandelbrot, B.B. *Fractals: Form, Chance, and Dimension.* San Francisco: W.H. Freeman, 1977.

Mandell, A.J. Redundant mechanisms regulating brain tyrosine and tryptophan hydroxylases. *Ann. Rev. Pharmacol. Toxicol.*, 18:461-493, 1978.

Mandell, A.J., and Russo, P.V. Striatal tyrosine hydroxylase activity: Multiple conformational kinetic oscillators and product concentration frequencies. *J. Neurosci.*, 1:380-389, 1981.

Mandell, A.J., Bullard, W.P., Yellin, J.B., and Russo, P.V. The influence of *d*-amphetamine on rat brain striatal reduced biopterin concentration. *J. Pharmacol. Exp. Ther.*, 213:569-574, 1980.

Mandell, A.J., Knapp, S., Ehlers, C.L., and Russo, P.V. The stability of constrained randomness: Lithium prophylaxis at several neurobiological levels. In: Post, R.M., and Ballenger, J.C. (eds.), *The Neurobiology of the Mood Disorders.* Baltimore: Williams & Wilkins. (In press)

May, R.M. Simple mathematical models with very complicated dynamics. *Nature*, 261:459-467, 1976.

May, R.M. Nonlinear phenomena in ecology and epidemiology. *Ann. NY Acad. Sci.*, 357:267-281, 1980.

Rössler, O.E. An equation for continuous chaos. *Phys. Lett.*, 57A:397-398, 1976.

Wurtman, R.J., Larin, F., Mostafapour, S., and Fernstrom, J.D. Brain catechol synthesis: Control by brain tryosine concentration. *Science*, 185:183-184, 1974.

Ordering the Fluctuations of Tryptophan Hydroxylase: Lithium and Chlorimipramine[1]

Suzanne Knapp, Ph.D.[2]

Tryptophan hydroxylase (TPOH; E.C.1.14.16.4) demonstrates stable hyperbolic kinetic functions under equilibrium assay conditions, i.e., when concentrations of substrate (tryptophan) and cofactor (tetrahydrobiopterin, BH_4) are saturating. However, as the concentration ratio of cosubstrates and enzyme approaches unity the system becomes unstable, manifesting kinetic functions with reiterative plateaus across increasing cofactor concentration (Knapp & Mandell 1979). Measures of TPOH activity under non-equilibrium conditions across small increments of cofactor concentration or time have shown velocity fluctuations characterized by multiple saturation plateaus over cofactor and multiple power (frequency) spectral peaks over time, suggesting that the population dynamics of a complex system of dissipative oscillators may be reflected in the enzyme's kinetic processes (Knapp & Mandell 1982; Knapp et al. 1981).

In clinical studies, lithium slows the frequency and reduces the amplitude of the recurring mood cycles characteristic of manic-depressive disease (Schou 1973). Likewise, at the macromolecular level, lithium slows the frequency of Purkinje cell discharge rate (Schultz et al. 1981), of neurotransmitter receptor rhythms in the central nervous system (CNS) (Kafka et al. 1982), and of electroencephalograph (EEG) (Itil & Akpinar 1971), and reduces the amplitude of evoked field potentials of dentate granule cells in rat hippocampal slices (MacVicar et al. 1981). Tricyclic drugs, which share with lithium clincial antidepressant properties, also slow the frequencies of Purkinje cell discharge rates (Schultz et al. 1981) and CNS receptor rhythms (Kafka et al. 1982). This report describes the effects of lithium and the tricyclic antidepressant chlorimipramine (CMI) on the frequency and amplitude components of rat raphé TPOH velocity fluctuations

---

[1] This work is supported by USPHS Grant DA-00265.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

observed in both short and long residence time kinetics.

In variational kinetic studies, the fundamental unit of data is the amplitude of deviation (A) of each averaged product concentration point at a given coreactant concentration or time from the mean velocity function as determined by linear regression analysis, normalized for slope and intercept. Computer routines are available from the International Mathematics and Statistics Library with which to perform time series analysis on the A values. The average amplitude or energy of the process is calculated as the root mean square (RMS) of A. The "frequency morphology" of the enzyme population of dissipative oscillators is determined using autocorrelation functions, power spectra, and an independent descriptor, the Hausdorff-Besicovitch dimension D (Mandelbrot 1977), a scale-invariant exponent reflecting the complexity of the perimeter of the one-dimensional A map of the complex function. The rougher the surface of the A function, the more often it changes direction, the longer the perimeter, and the higher the value of D, indicating an increase in degrees of freedom, fluctuation frequency, and the dimensionality of the system. Changes in D of 0.04 to 0.06 are replicable. The analytic methods used are further

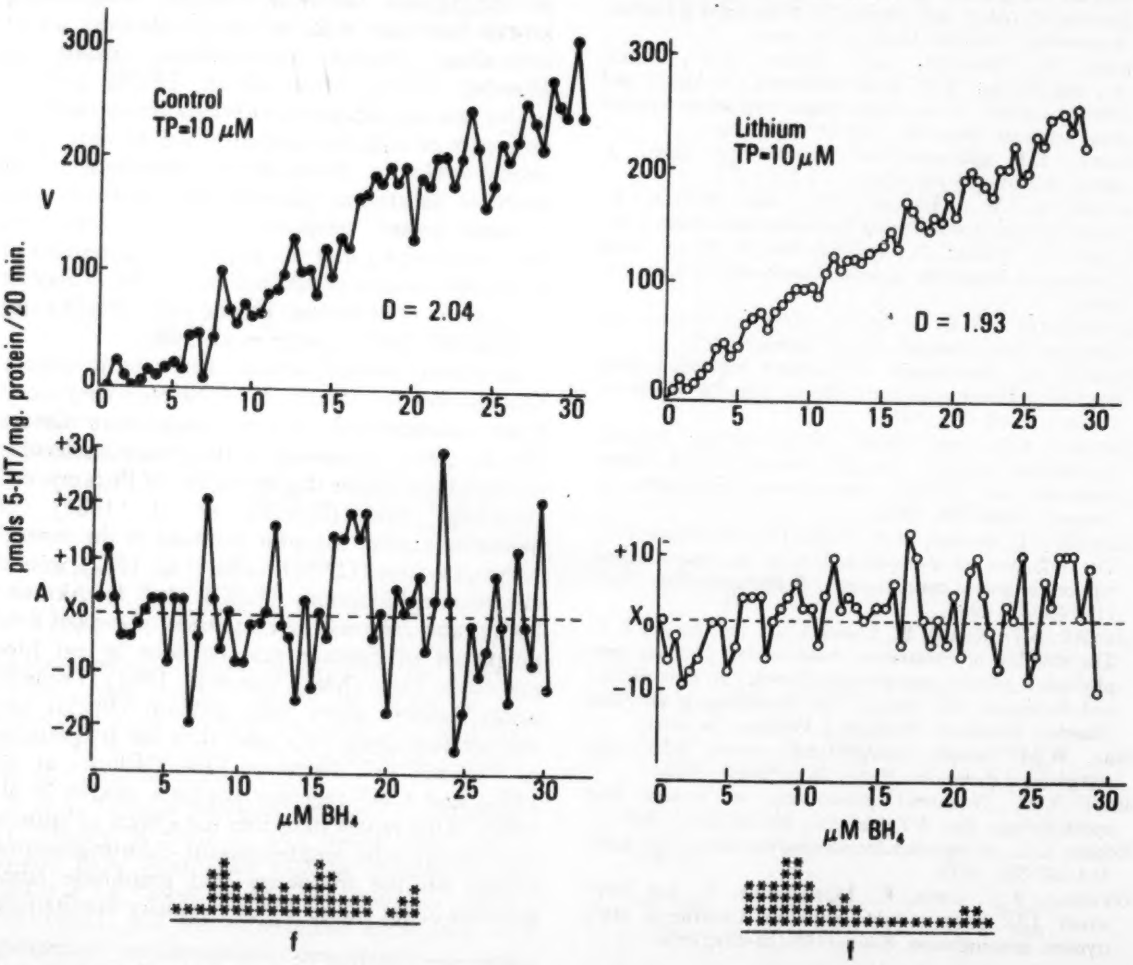


FIGURE 1. Cofactor-velocity functions, A-value transforms, and power (frequency) spectra of TPOH kinetic behavior in the absence and presence of 3 μM lithium.

detailed elsewhere (Mandell & Russo 1981).

Figure 1 presents the results from typical fluctuation experiments in which average product concentrations were determined from 60 duplicate assays across cofactor concentration at intervals of 0.5 μM BH_4. The upper portion of the figure shows the velocity functions obtained in the absence and presence of 3 μM lithium. Below them are shown the A value transforms, which clearly illustrate a lithium-induced reduction in the amplitude of variation. Fourier transformation of the A values from each experiment yielded the power spectra shown, in which the abscissa represents frequency in intervals of cofactor concentration, and the ordinate represents the distribution of power. The diffuse distribution of peaks across the control spectrum suggests multiple subpopulations of phase; in the presence of lithium a single broad peak is observed in the range of increasing cofactor concentrations, consistent with the ion reducing the heterogeneity of the enzyme population. The lower D value also reflects the slower fluctuation frequency in the presence of lithium (1.93 vs. 2.04 for the control sample).

Figure 2 demonstrates the relationship between the average frequency (D_A) and amplitude log (RMS_A) of TPOH when assayed across time in the absence and presence of lithium or CMI. Each point represents the average frequency and amplitude values from one independent experiment; each experiment consisted of 60 duplicate assays performed across time at concentrations of tryptophan and BH_4 that were held near physiological levels, 10 μM and 20 μM, respectively. On the left, the diffuse scatter of points around a negative slope is consistent with the unstable, variably coupled subpopulations postulated for the control population of enzyme oscillators in the absence of a stabilizing ligand. The negative slope reflects the inverse relationship usually observed between frequency and amplitude. The presence of lithium changes that relationship, as is indicated by the positive slope and the relatively tight distribution of points around it (correlation coefficient $r = 0.765$). CMI

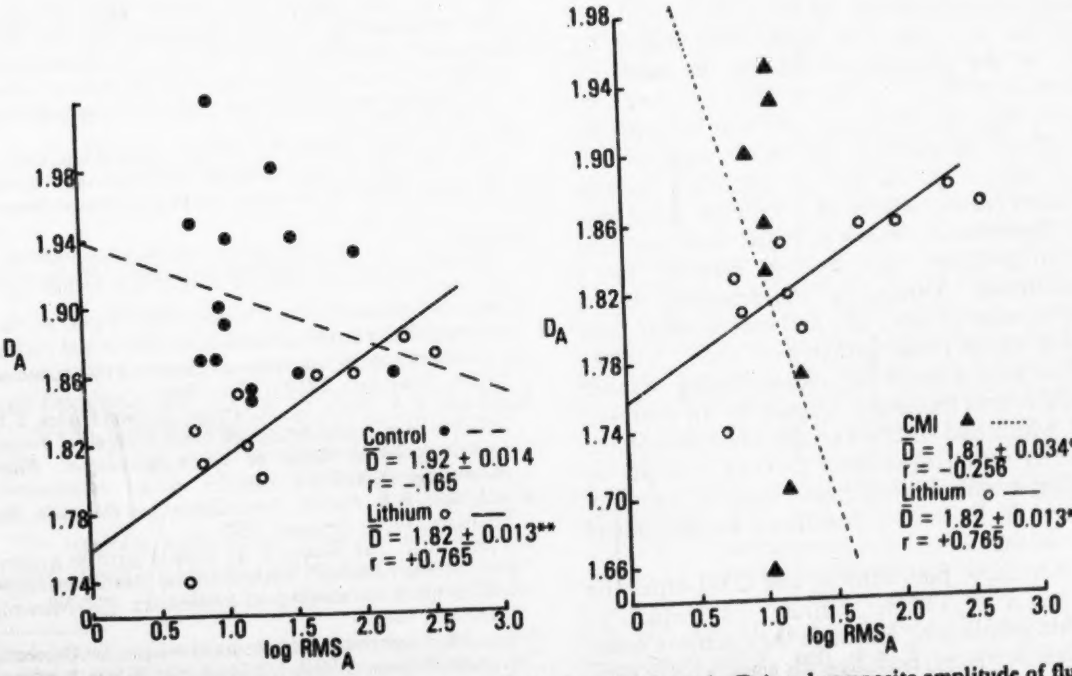


FIGURE 2. Plots showing relationship between composite frequency metric (D_A) and composite amplitude of fluctuations (log RMS_A) in control TPOH preparations and in the presence of lithium or CMI.

also changes the relationship between frequency and amplitude, as is indicated by the almost vertical regression slope. Whereas the ensemble of control points demonstrates a relatively wide range of both average frequencies and average amplitudes, lithium restricts the fluctuation frequency (most D_A values occur between 1.82 and 1.86), but CMI restricts the fluctuation amplitude across a wide range of frequency values. The mean D values, averaged for each group of experiments, indicate that both lithium and CMI significantly slow the fluctuation frequency of TPOH below the control D values of 1.92 ± 0.014.

Alternative to the long residence time TPOH assays across cofactor concentration and time (Figures 1 and 2), short residence time (initial rate) measures were performed in which the enzyme-enriched supernatant containing lithium, CMI, or neither was maintained on ice separate from the assay reactants. At 1.5-minute intervals, duplicate enzyme aliquots were removed and incubated with complete reaction mixtures for 2 minutes, yielding a series of 40 short residence determinations. The Table compares the average D_A values for TPOH activities determined in 25 separate experiments in the absence and presence of lithium or CMI. The significantly higher D_A value in the presence of lithium in these experiments (2.08 ± 0.016 vs. 2.01 ± 0.021 for control) supports the hypothesis that lithium's initial effect is to uncouple the loosely and variable phase control population of nonlinear protein oscillators (demonstrable only with the small temporal observation window of initial rates) and that macromolecular uncoupling results in a Gaussian-like population characterized by a larger number of more like and independent components which phase-gather over time (Winfree 1980) to yield a single population having reduced amplitude and frequency (Figure 2). In contrast, CMI, which had no effect on the mean fluctuation frequency of short residence kinetics, may act by inducing a more homogeneous state of coupling, reducing the variability postulated for the control preparation.

In summary, both lithium and CMI order the fluctuations of TPOH: lithium via frequency, CMI via amplitude. Although they achieve order by different routes, both ligands significantly slow the mean fluctuation frequency of the enzyme activity, altering the inverse relationship usually observed between frequency and amplitude. Short and long residence time studies suggest that different statistical mechanisms of organization of the population of nonlinear enzyme oscillators may underlie the shared and disparate effects of these two classes of drugs.

Table

Estimates of Mean TPOH Product Concentration Frequencies in the Absence and Presence of Lithium or CMI

Condition	*N* (40-Point Assays)	D_A ± S.E.M.
Control	10	2.01 ± 0.021
Lithium	8	2.08 ± 0.016*
CMI	4	1.99 ± 0.007

*$p < 0.05$ vs. Control; 0.002 vs.CMI

References

Itil, T.M., and Akpinar, S. Lithium effect on human electroencephalogram. *Clin. Encephalogr.*, 2:89-102, 1971.

Kafka, M.S., Wirz-Justice, A., Naber, D., Marango, P.J., O'Donohue, R.L., and Wehr, T.A. The effect of lithium on circadian neurotransmitter rhythms. *Neuropsychobiology*, 8:41-50, 1982.

Knapp, S., and Mandell, A.J. Conformational influences on brain tryptophan hydroxylase by submicromolar calcium: Opposite effects of equimolar lithium. *J. Neural Transm.*, 415:1-15, 1979.

Knapp, S., and Mandell, A.J. Lithium, brain tryptophan hydroxylase, and hemispheric asymmetry. *Psychiatry Res.* (In press)

Knapp, S., Mandell, A.J., Russo, P.V., Vitto, A., and Stewart, K.D. Strain differences in kinetic and thermal stability of two mouse brain tryptophan hydroxylase activities. *Brain Res.*, 230:317-336, 1981.

MacVicar, B.A., Weir, G., Riexinger, K., and Dudek, F.E. Paradoxical effects of lithium on field potentials of dentate granule cells in striae of rat hippocampus. *Neuropharmacology*, 20:489-496, 1981.

Mandelbrot, B.B. *Fractals: Form, Chance, and Dimension.* San Francisco: W.H. Freeman, 1977.

Mandell, A.J., and Russo, P.V. Striatal tyrosine hydroxylase activity: Multiple conformational kinetic oscillators and product concentration frequencies. *J. Neurosci.*, 1:380-389, 1981.

Schou, M. Prophylactic lithium maintenance. In: Gershon, S., and Shopsin, B. (eds.), *Lithium—Its Role in Psychiatric Research and Treatment.* New York: Plenum Press, 1973, pp. 169-294.

Schultz, J.E., Siggins, G.R., Schocher, F.W., Türck, M., and Bloom, F.E. Effects of prolonged treatment with lithium and tricyclic antidepressant drugs on discharge frequency, norepinephrine responses, and beta-receptor binding on rat cerebellum: Electrophysiological and biochemical comparison. *J. Pharmacol. Exp. Ther.*, 216:28-38, 1981.

Winfree, A.T. *The Geometry of Biological Time.* New York: Springer-Verlag, 1980.

Characterization of Drug Effects on the EEG by Power Spectral Band Time Series Analysis[1]

Cindy L. Ehlers, Ph.D.,[2] and James W. Havstad, Ph.D.[2]

A method for quantification of the electroencephalogram (EEG) that could be used to characterize drug-influenced states in order to link them to the expression of behavior on one hand, and to underlying biochemical mechanisms on the other, has long been sought. It has been suggested that a language for coherent explanation of specific drug effects at different levels of observation (i.e., from biochemistry to behavior) may lie in the descriptions of drug-induced changes in the distribution of values around mean functions across time or across samples (Mandell 1980).

In the present investigation, the ability of five drugs that are active in the central nervous system to alter the distribution of power in discrete frequency bands of the EEG (a first-order function) was studied. In addition, fluctuations in power in those frequency bands as a function of time, i.e., the power spectral band time series (a second-order function) were evaluated in order to characterize drug effects and correlations to behavior.

The subjects were three adult male Guyanan squirrel monkeys (*Saimiri sciureus*) weighing 835 to 993 grams. Under pentobarbital anesthesia (Nembutal, 35 mg/kg) screw electrodes had been implanted previously in their calvaria in a modified 10-20 array to approximate homotopic locations over frontal and parietal cortices similar to human sites. After at least 2 weeks' recovery from surgery, the monkeys were adapted to a loosely restraining Plexiglas chair for 2 hours, two times a week for 3 months, before the drug studies were begun. The psychoactive compounds studied and their doses were: amphetamine, 0.25 mg/kg; diazepam, 2.5 and 5.0 mg/kg; phenobarbital, 15 and 30 mg/kg; chlorpromazine, 5 and 10 mg/kg; and morphine, 2.5 and 5.0 mg/kg. All were administered orally, by gastric lavage. The order and dose of each drug were randomized for each animal, and at least 5 days elapsed between drug administrations.

On a test day, a monkey is chaired briefly and administered drug or vehicle and then returned to the home cage. Approximately 40 minutes later the animal is returned to the chair and placed in the recording chamber. EEG is recorded for 20 minutes on paper (Grass Model 7D polygraph) and on magnetic tape (Vetter Model D FM recorder) for later computer analysis. The present data were analyzed from artifact-free 15-minute segments of tape from the left fronto-parietal lead (F3-C3). The processing is done by a MINC LSI-11, which digitizes and calculates the power spectra of four-second epochs in 1/4-Hz increments over a range of 0.25 to 64 Hz, a procedure similar to that first described by Joy et al. (1971) and modified by Gehrmann and Killam (1976). The transformed data are then further compressed into eight frequency bands (0.5-1.0 Hz; 1-2 Hz; 2-4 Hz; 4-8 Hz; 16-32 Hz; 32-64 Hz; and 0.5-64 Hz). Mean power density of each frequency band over the entire recording period can then be calculated. In addition, as a function of time, the fluctuations in power density in each frequency band can be displayed as a time series. The calculation of the power spectral band time series is similar to that described by Gehrmann and Killam (1978) and Gehrmann et al. (1977).

The five drugs studied were differentiated from vehicle by various distributions of mean spectral power density in the four bands: 2-4 Hz; 4-8 Hz; 8-16 Hz; and 16-32 Hz (Figure 1). In the lower frequencies (2-4 and 4-8 Hz) amphetamine caused a small increase in power, whereas diazepam caused a dose-dependent decrease.

---

[1] This study was supported by the Esther A. and Joseph Klingenstein Foundation and USPHS Grant DA-01785 from the National Institute on Drug Abuse.

[2] Arthur V. Davis Center for Behavioral Neurobiology, The Salk Institute, San Diego, CA 92138.

Phenobarbital had little effect on power density in the lower frequencies. However, both morphine and chlorpromazine caused dose-dependent increases.

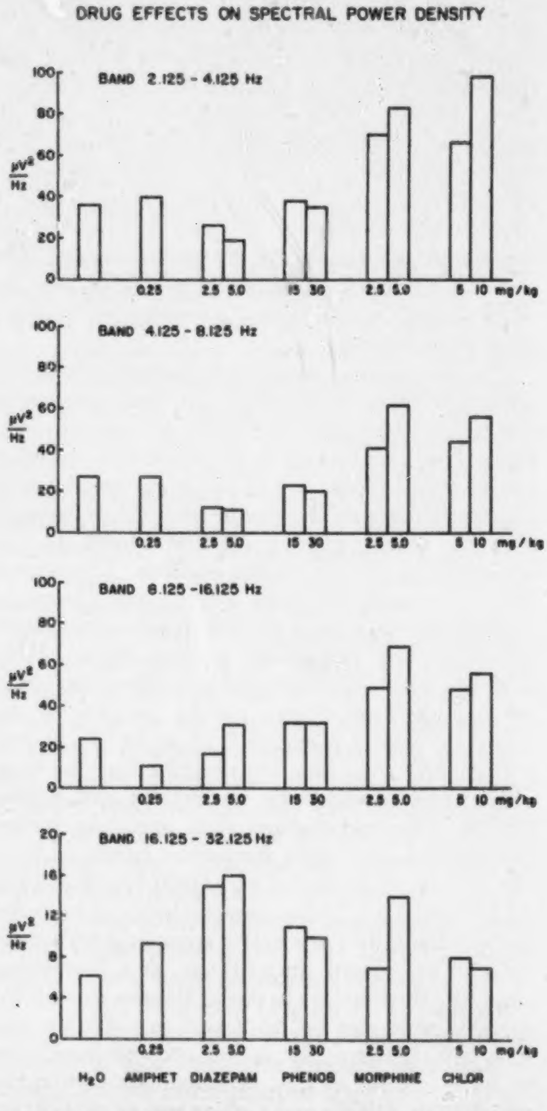


FIGURE 1. EEG mean spectral power density, μV^2/Hz, in four different frequency bands (2.125-4.125 Hz; 4.125-8.125 Hz; 8.125-16.125 Hz; 16.125-32.125 Hz) recorded from F3-C3 for 15 min in a typical monkey after oral administration of: water; amphetamine, 0.25 mg/kg; diazepam, 2.5 and 5.0 mg/kg; phenobarbital, 15 and 30 mg/kg; chlorpromazine, 5 and 10 mg/kg; and morphine, 2.5 and 5.0 mg/kg.

In the higher frequency band (8-16 Hz), which contains the posterior dominant rhythm, amphetamine caused a decrease in power. A decrease in power density following 2.5 mg/kg diazepam was noted, whereas the higher dose (5.0 mg/kg) caused a smaller increase in power in the 8-16 Hz band. A small increase in power, not dose-related, was also seen following administration of phenobarbital. Morphine and chlorpromazine both caused dose-related increases in power density. A different distribution of power was revealed in the high frequency band (16-32 Hz). Amphetamine and phenobarbital induced small increases in this band, whereas diazepam produced a dramatic dose-dependent increase. Neither chlorpromazine nor the low dose of morphine (2.5 mg/kg) caused any change in power density, but the higher morphine dose (5.0 mg/kg) caused an increase.

Analysis by power spectral band time series provided even better discrimination of drug effects which correlated well with the ongoing behavioral state of the animal. The bands that provided the best discrimination were the two representing frequencies of 8-16 Hz and 16-32 Hz. Under baseline conditions following water gavage or gavage of diazepam vehicle, all the monkeys fluctuated between a "vigilant" state associated with mild motor movement and visual scanning and a quiescent state associated with little visual scanning. This fluctuation in behavioral state was associated with distinct oscillations in the power spectra. During the more vigilant state the EEG was relatively desynchronized, concomitant with an increase in power density in the 16-32 Hz band. When an animal's behavior was quiescent, the EEG was relatively more synchronized, and power increased in the 8-16 Hz band. The oscillation in power spectral density and behavior was very stable under control conditions and was reproducibly altered by drug treatment.

In Figure 2, a distinct difference in the power spectral band time series is obvious after 2.5 mg/kg diazepam. A decrease in the dominant frequency of oscillation and the appearance of a higher frequency fluctuation are associated with a more quiescent behavioral state. A more random pattern of high and low frequency components is seen after 5.0 mg/kg diazepam and associated with mild sedation. A behavioral state and time

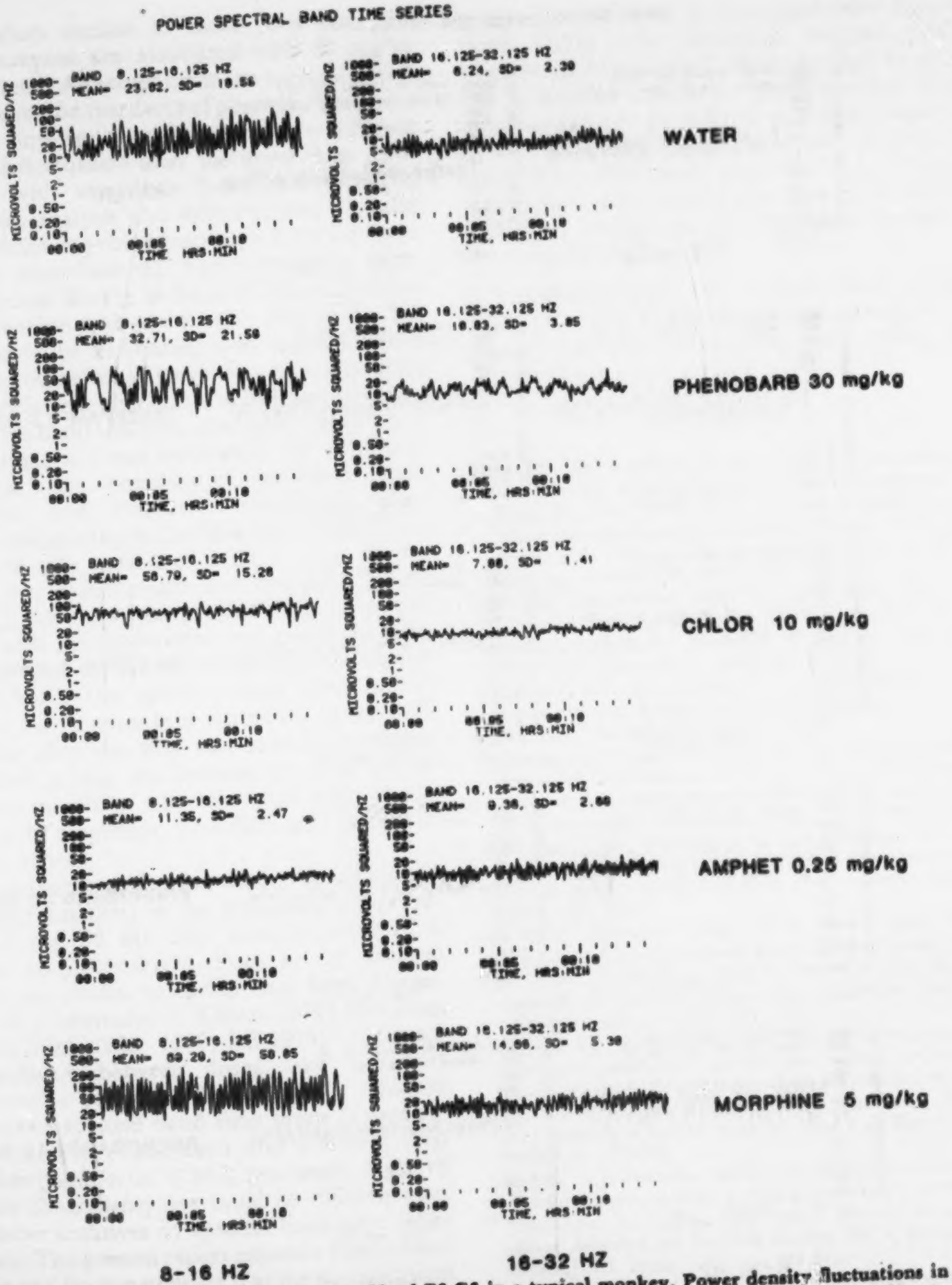


FIGURE 2. Power spectral band time series of lead F3-C3 in a typical monkey. Power density fluctuations in bands 8.125-16.125 and 16.125-32.125 Hz are presented from EEG recorded after oral administration of: water; diazepam, 2.5 and 5.0 mg/kg; and phenobarbital, 15 and 30 mg/kg. For each time series, power density ($\mu V^2/Hz$) is represented on the ordinate, and time (minutes) is represented on the abscissa.

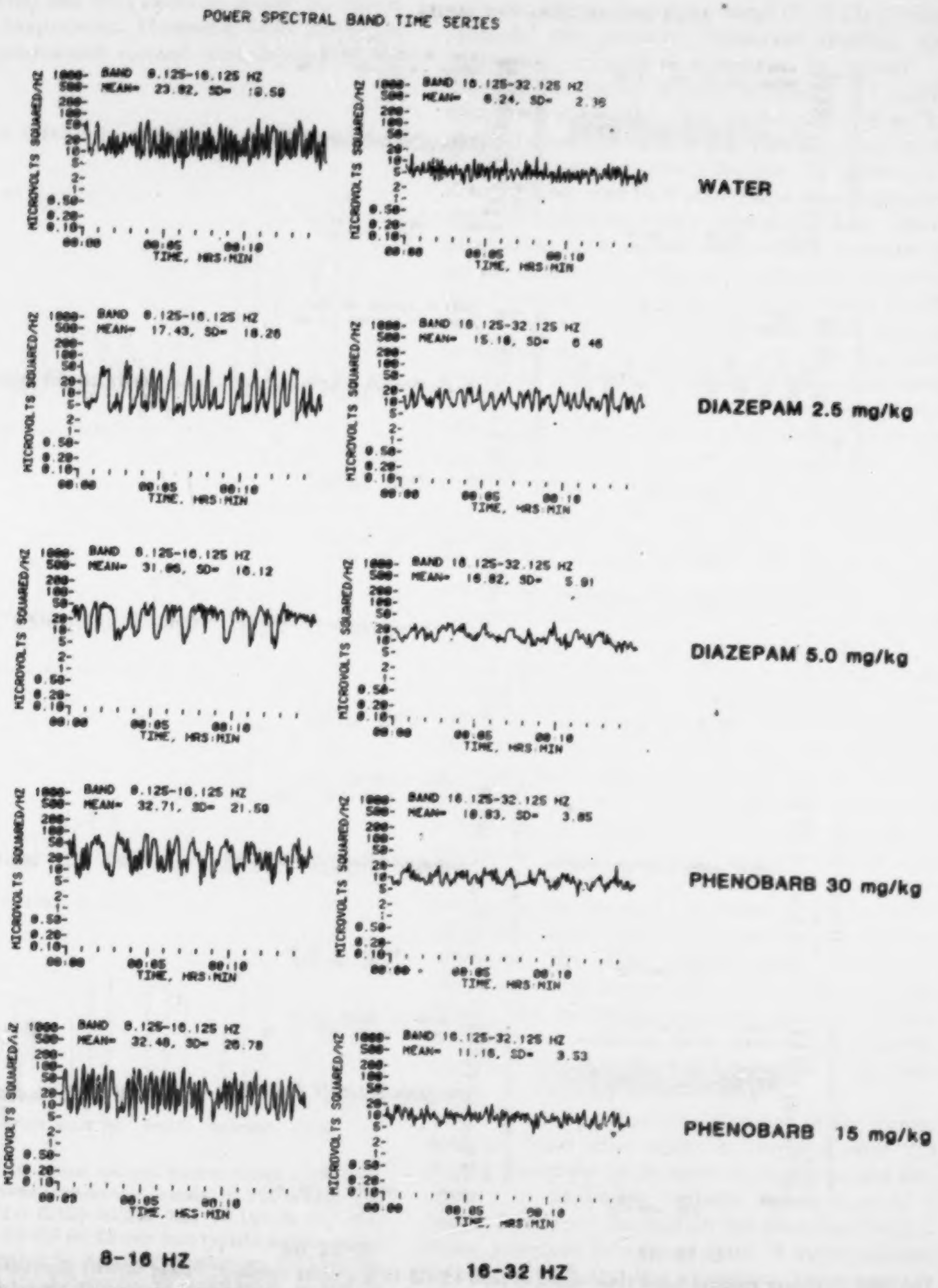


FIGURE 3. Power spectral band time series of lead F3-C3 in a typical monkey from EEG recorder after oral administration of: water; phenobarbital, 30 mg/kg; chlorpromazine, 10 mg/kg; amphetamine, 0.25 mg/kg; and morphine, 5.0 mg/kg. Coordinates are the same as in Figure 2.

series pattern similar to those seen after 5.0 mg/kg diazepam are associated with 30 mg/kg phenobarbital. Although the mean spectral power densities after the two doses of phenobarbital were identical, time series analysis reveals a different pattern of fluctuation after the lower dose, concomitant with very little behavioral sedation. Time series analysis also differentiated the mild sedation following chlorpromazine from that produced by phenobarbital. The increase in mean power spectral density in the 8-16 Hz range from chlorpromazine produced a stable time series that contrasted to the less stable, more random signal after phenobarbital (Figure 3). A stable time series associated with a decrease in mean power in the 8-16 Hz band was seen after administration of amphetamine and was associated with a vigilant behavioral state consisting of decreased motor movement and increased visual scanning, whereas the stability in the time series after chlorpromazine was associated with a state of decreased motor movement and decreased visual scanning. Although the profiles of mean power density with chlorpromazine and morphine were similar (Figure 1), the two drugs were clearly differentiable in the spectral band time series. Whereas the increase in mean power in the 8-16 Hz band after the first was associated with a stable time series, the increase in mean power following morphine was associated with an increase in the amplitude of the dominant rhythm in the time series.

Differentiable profiles in mean power density (a first-order function) in the frequency bands between 2 and 32 Hz after administration of a number of psychoactive drugs in the squirrel monkey are similar to earlier data from Rhesus monkeys (Gehrmann & Killam 1976) and from humans (Fink 1968, 1978; Itil 1974). A clearer differentiation between drugs, and one that relates well to ongoing behavior, can be achieved with power spectral band time series (a second-order function). Gehrmann and Killam (1978) and Gehrmann et al. (1977) previously reported that the benzodiazepines could be differentiated from other sedatives by spectral band time series analysis. The present report expands those observations and further suggests that the spectral band time series may be used to characterize drug-influenced behavioral states. Prigogine and Nicolis (1973) have suggested that the stability of a system is reflected in its second-order fluctuations. Using those principles, Mandell (1981) hypothesized that drug preference might be an effort to stabilize a person's "periodic order" (e.g., amphetamine) or to shift the statistical properties of one's system to a more random, less reactive state (e.g., diazepam, phenobarbital). Further studies may provide evidence to suggest that the EEG can provide an electrographic marker of such cognitive processes.

Acknowledgments: The authors thank Christi Franklin for her excellent technical assistance and Nancy Callahan for editing and typing the manuscript.

References

Fink, M. EEG classification of psychoactive compounds in man: Review and theory of behavioral associations. In: Efron, D., Cole, J.O., Levine, J., and Wittenborn, J.R. (eds.), *Psychopharmacology—A Review of Progress, 1957-1967.* Washington D.C.: U.S. Government Printing Office, 1968, pp. 497-507.

Fink, M. Psychoactive drugs and the waking EEG. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology—A Generation of Progress, 1966-1976.* New York: Raven Press, 1978, pp. 691-698.

Gehrmann, J.E., and Killam, K.F., Jr. Assessment of CNS drug activity in Rhesus monkeys by analysis of the EEG. *Fed. Proc.*, 35:2258-2263, 1976.

Gehrmann, J.E., and Killam, K.F., Jr. Studies of central functional equivalents I. Time-varying distribution of power in discrete frequency bands of the EEG as a function of drug exposure. *Neuropharmacology*, 17:747-759, 1978.

Gehrmann, J.E., Havstad, J.W., and Killam, K.F., Jr. Differentiation between CNS drugs in Macacca mulatta on the basis of stability of EEG power spectra. *Neurosci. Abstr.*, 392, 1977.

Itil, T.M. *Psychotropic Drugs and the Human EEG, Vol. 8 (Modern Problems of Pharmacopsychiatry.)* Basel:Karger, 1974.

Joy, R.M., Hance, A.J., and Killam, K.F., Jr. Spectral analysis of long EEG samples for comparative purposes. *Neuropharmacology*, 10:471-481, 1971.

Mandell, A.J. Vertical integration of levels of brain function through parametric symmetries within self-similar stochastic fields: From brain enzyme polymers to delusion. In: Pinsker, H.M., and Willis, W.D., Jr. (eds.), *Information Processing in the Nervous System.* New York:Raven Press, 1980, pp. 177-197.

Mandell, A.J. Statistical stability in random brain systems: Possible implications for polydrug abuse in the borderline syndrome. In: Mello, N.K. (eds.), *Advances in Substance Abuse: Behavioral and Biological Research, Vol. 2.* Greenwich, Conn:J.A.I. Press, 1981, pp. 299-341.

Priogogine, I., and Nicolis, G. Fluctuations and the mechanisms of instabilities. In: Marois, E. (ed.), *From Theoretical Physics to Biology.* New York:Karger, 1973, pp. 89-111.

Variational and Probabilistic Aspects of Exploratory Behavior in Space: Four Stimulant Styles

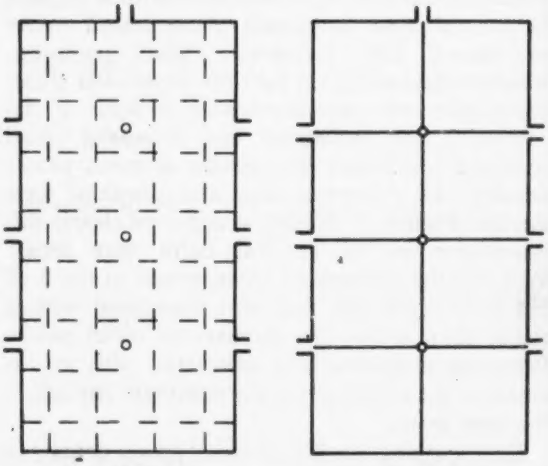
Mark A. Geyer, Ph.D.[1]

One of the primary goals of the science of Psychopharmacology is to understand and predict the effects of drugs on the molar behavior of the organism. In animal research, one of the most common behaviors of interest is spontaneous locomotor activity. This presentation describes an unusually detailed approach to the characterization of drug effects on the behavioral activity of rats in a novel environment.

While most activity measures assess only the quantity of activity—that is, activity goes up, goes down, or stays the same in response to a drug—the approach illustrated here provides both graphic and quantitative descriptions of *qualitative* differences in the locomotor activation elicited by stimulant drugs. Qualitative differences in the effects of drugs on activity are readily apparent by observation; but they may be assessed more precisely by examining variability in both the spatial and temporal domains. To illustrate the utility of measures of spatial variability, this report compares the effects of several drugs which, according to measures of the quantity of behavioral activity, are considered to be "stimulants."

Method

Male Sprague-Dawley rats (300-325 gms) were injected intraperitoneally (1 ml/kg) with either saline or the appropriate dose of one of the test drugs, as listed in the Table, 10 minutes before being placed in one of four holeboard/activity chambers for a 1-hour test session. The chamber, diagrammed in Figure 1, is a 12 X 2 inch black Plexiglas box with three floor holes and seven wall holes which serve as specific stimuli for the animal to investigate. As detailed elsewhere (Flicker & Geyer 1982), a Cartesian coordinate system of infrared beams is used to detect the position of the animal within the chamber. Each hole is also equipped with an infrared beam to detect holepokes, and a touchplate on the wall 5 inches above the floor is used to detect rearings. A microcomputer samples these circuits 10 times per second and permanently records all changes. Thus, the exact sequence of locomotor movements, holepokes, and rearings can be reproduced by the computer with a resolution of a tenth of a second in time and an inch and a half in space. The amount of activity can then be calculated as the total number of photobeam interruptions, as is done with several common activity monitors, or as crossovers from one 6-inch sector to another (Figure 1) Crossovers also measure locomotor activity.



A. PHOTOBEAMS B. SECTORS

FIGURE 1. Diagram of the holeboard box showing the ten holes in the walls and floor. (A) Dashed lines represent the 8 X 4 perpendicular array of photobeams. (B) Sectors divide the holeboard into eight 6-inch square areas. Crossovers were defined as the number of sector entries and were used as a measure of the amount of locomotor activity.

Standard Measures

The Table summarizes the basic results as hourly means for deltas (total number of photobeam breaks), crossovers, rearings, and both varied and repeated holepokes for the stimulant drugs tested. At the doses used, the various stimulants produced comparable in-

---

[1] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

creases in the amount of locomotor activity, as reflected by the deltas and crossovers. Indeed, if these were the only measures examined, one might conclude that these drugs produce similar effects. However, even the simplest of multivariate analyses quickly dispels that notion. In contrast to the other drugs, apomorphine is unusual in that the hyperactivity it produces is accompanied by a decrease rather than an increase in both rearing and holepoking. Furthermore, amphetamine differs from the other drugs in its preferential increase in repeated holepokes into the same hole. Makanjuola et al. (1977) have referred to repeated holepokes as stereotyped as opposed to exploratory holepokes, and have also found them to be preferentially increased by amphetamine.

Table

				Holepokes	
	Deltas	Crossovers	Rearings	Repeated	Varied
Saline 1 ml/kg	1802	1289	72	44	39
Amphetamine 1 mg/kg	4706	956	138	144	95
Caffeine 6 mg/kg	4428	776	153	101	123
Apomorphine 1 mg/kg	3974	921	28	11	20
Scopolamine 1 mg/kg	4237	1001	161	54	117

1. DELTAS is the sum of all photobeam interruptions.
2. CROSSOVERS are defined as movements from one 6-inch square sector to another.
3. HOLEPOKES were divided depending on whether or not there had been an intervening rearing or poke into a different hole between two pokes into the same hole.

Spatial Patterns of Locomotion

In order to characterize the effects of the stimulants on the patterns of locomotion, one must first understand some aspects of the spatial structure of the locomotor behavior of control animals exploring a novel chamber. When the computer reconstructions of each animal's locomotor patterns are displayed on a video terminal at ten times normal speed, it is evident that each control animal is remarkably consistent in terms of the patterns of locomotion across time and that each animal exhibits a preference for one end or corner, referred to as the home area. The behavior is generally organized as excursions from the home area in which the outward path is typically more varied than the rapid and direct return path.

At the relatively low dose of 1.0 mg/kg amphetamine sulfate, the normal pattern of locomotion is disrupted. The animals rarely exhibit a home area preference and make many seemingly random changes of direction. As demonstrated by Lat (1965) and Schiorring (1979), higher doses of amphetamine produce highly stereotyped, repetitive patterns of ambulation. In contrast, a comparable dose of caffeine produces hyperactivity without altering the normal structure. Caffeine-treated rats consistently exhibit a preference for one end of the chamber, and their behavior is constructed of excursions from this end along reasonably predictable paths. Thus, hyperactivity per se need not disrupt the typical spatial structure of exploratory locomotion. Both apomorphine and scopolamine produce dramatic alterations in the locomotor patterns. Many animals treated with apomorphine persistently and rapidly circle the chamber in a consistent direction for at least 40 minutes, without rearing or investigating the holes. While other apomorphine-treated rats do not rotate, each still exhibits an individualized perseverative pattern that is maintained for an extended period. Scopolamine-treated animals also rotate around the perimeter of the chamber, rarely entering the center. However, virtually all animals given scopolamine rotate one direction several times and then reverse their direction. This characteristic pattern is maintained throughout the session, with the frequency of reversals in direction decreasing with time. Unlike apomorphine, scopolamine-treated animals frequently pause enroute to rear and/or investigate the holes in the wall.

For a variety of reasons, it was important to develop descriptive statistics with which to summarize and quantify these stylistic differences in the effects of drugs on the patterns of locomotion. To condense the data, the chamber is divided into five regions: the two ends; the center; and the two long walls. The number of each of the 16 possible transitions from one region to another is then cumulated and displayed in a two-step transition matrix as if for a Markov Chain analysis. The coefficient of variation (CV) of this set of 16 values is then calculated as an indicator of the degree to which each animal's locomotor behavior is stereotyped or perseverative in the spatial domain. For example, if an animal's locomotion were uniformly distributed about the chamber, all the numbers in the matrix would be similar and the CV would be small. Conversely, if an animal predominantly repeats the same transitions—that is, he exhibits a stereotyped pattern—the CV would be correspondingly high. Figure 2 displays 40-minute plots of the locomotor patterns of three untreated rats, together with the CVs and the total number of transitions entered into the matrix. It is important to note that, both in Figure 2 and in larger groups of animals, there is no significant correlation between the amount of activity and the degree of its spatial variability.

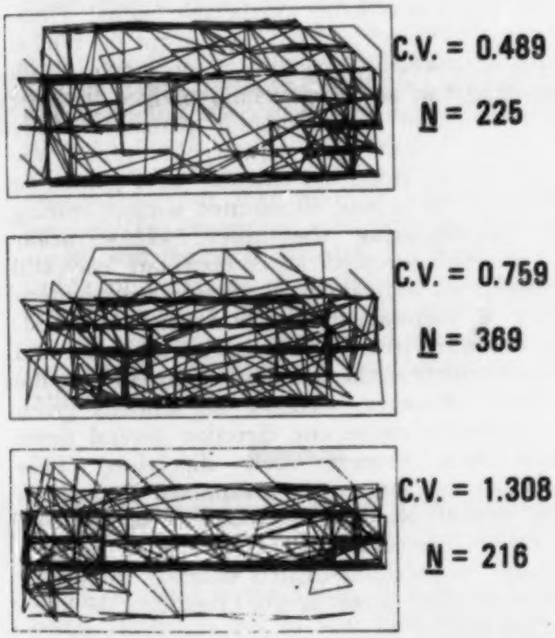


FIGURE 2. Computer reconstructions of the locomotor patterns exhibited by three untreated rats during a 40-minute session are shown together with the Coefficient of Variation (CV) and the number of transitions (*N*), as described in the text.

Figure 3 displays the group means (+/−SEM) for the CVs calculated for the hour of activity following treatment with either saline or one of the stimulant drugs. As suggested in the description of the computer reconstructions of the locomotor patterns, caffeine-treated animals are virtually identical to controls on this measure of variability, while the low dose of amphetamine produced significantly more random patterns. Conversely, both apomorphine and scopolamine significantly increased the CV, reflecting the highly stereotyped locomotor patterns induced by these drugs.

Despite the common characteristic of these stimulants in terms of their effect on the quantity of locomotor activity, each of them produces qualitatively different styles of behavioral activation which can be readily noted by observation and quantified by simple measures of spatial variability. During caffeine-elicited hyperactivity, the normal structure of the locomotor, rearing, and holepoking behaviors are maintained. With low doses of *d*-amphetamine, the spatial pattern of locomotion is randomized and repeated pokes into the same hole predominate. Apomorphine hyperactivity is unique in that rearing and investigatory holepoking are suppressed and the pattern of each animal's locomotion is highly stereotyped. Scopolamine-treated rats also exhibit a stereotyped pattern of locomotion, but one that is clearly distinguishable from that typical of apomorphine. In other studies, it has been

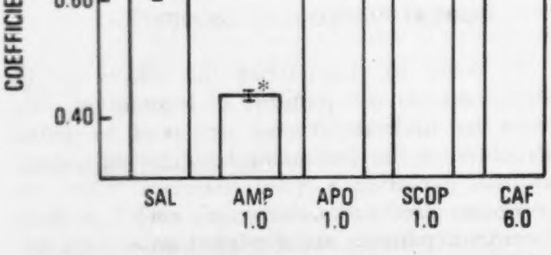


FIGURE 3. Group means (+/−SEM) are shown for the CVs (*see* text) calculated for the entire hour test session. An elevated CV reflects a repetitive spatial pattern of locomotion.

observed that significant changes in the pattern of locomotion can be detected with no change in the amount of activity (Flicker & Geyer 1982).

In the past 10 years, the field of Psychopharmacology has seen remarkable advances in the precision and sophistication of its anatomical, chemical, and physiological measures. It is clear that a similar increase in the sophistication of behavioral assessment techniques is warranted. It is hoped that the methods illustrated in this report will help to meet this need.

References

Flicker, C., and Geyer, M.A. Behavior during hippocampal microinfusions: I. Norepinephrine and diversive exploration. *Brain Res. Rev.*, 4:79-103, 1982.

Lat, J. The spontaneous exploratory reactions as a tool for pharmacological studies: A contribution towards a theory of contradictory results in psychopharmacology. In: Mikhelson, M.Y., Longo, V.G., and Votava, Z. (eds.), *Pharmacology of Conditioning, Learning, and Retention*. Oxford: Pergamon Press, 1965, pp. 47-66.

Makanjuola, R.O.A., Hill G., Dow, R.C., Campbell, G., and Ashcroft, G.W. The effects of psychotropic drugs on exploratory and stereotyped behavior of rats studied on a holeboard. *Psychopharmacology* (*Berlin*), 55:67-74, 1977.

Schiorring, E. An open field study of stereotyped locomotor activity in amphetamine-treated rats. *Psychopharmacology* (*Berlin*), 66:281-287, 1979.

Heart Rate Variational Characteristics in Psychopathology: A Pilot Study[1]

Michael R. Blackburn, Ph.D.[2]

Heart rate variational characteristics in a mixed group of psychiatric patients and the changes in those characteristics accompanying pharmacotherapy were examined. The variational characteristics of heart rate may be described in terms of the magnitude of change (variance) and the temporal pattern of change (periodicity). Variance represents the responsivity or instability in a system and is calculated by taking the average of squared deviations from the mean. Periodicity as used here represents order as detected through time series analyses involving auto correlations over incremented time intervals and their Fourier transformations to the frequency domain (Jenkins & Watts 1968). A relationship may exist between magnitude and the temporal pattern of change characteristic of the system's organization. For example, Zweiner (1978) noted the general positive relationship between period length and amplitude in both heart rate and blood pressure spectra. Because the regulation of heart rate as seen in the dynamics of the interbeat interval (IBI) is, through vagal and sympathetic mediation, normally sensitive to central nervous system events, the variational characteristics of this measure may be a peripheral reflection of central processes in psychopathology. The IBI measure was chosen for study because electrocardiogram recordings are convenient, noninvasive, and generally available.

Two Holter-monitor electrocardiograms (ECG) were obtained on each of 15 psychiatric inpatients of the San Diego Veterans Administration Medical Center. The first was a baseline record taken after 1 drug-free week on the ward. The second followed from 2 to 4 weeks after appropriate pharmacotherapy. Day (between 15:00 and 18:00 hours) and night (between 02:00 and 04:00 hours) ECG samples were transcribed from magnetic to paper tapes using an Avionics electrocardioscanner. Each sample was 24 minutes in length, but was divided into three sequential 8-minute segments for analysis. Thus, each patient was represented by a total of 12 8-minute segments of ECG data. The patient's data were grouped for statistical comparisons on the basis of medication received during therapy. Five patients received the tricyclic antidepressant imipramine; five, the butyrophenone antipsychotic haloperidol; and five, lithium carbonate. Their medical and psychiatric histories were not tabulated until after the ECG data analyses were complete (*see* Table 3). The rationale for grouping patients on the basis of drug assignment was based on the assumption that the clinical psychiatrists provided the most appropriate

---

[1] The author holds a traineeship from the USPHS under Grant MH-16109.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

therapeutic agents for their patients at the time. Furthermore, it was assumed that patients within a group shared factors that differed in degree from patients in other groups and that those factors were related to the reasons they received a particular drug. These expectations are somewhat justified by previous reports of factorial symptom profiles between groups of psychiatric patients receiving different psychotropic drugs (Overall et al. 1972; Overall & Henry 1973).

A time series of heart IBIs was produced from each 8-minute segment by dividing the segment into 40 consecutive 12-second epochs, then the distance between extreme beats of an epoch divided by the number of beats contained within the extremes was used to describe the average IBI for that epoch. A representative IBI was calculated for each of the 40 epochs per 8-minute segment. The means and coefficients of variation of the segment average IBIs were computed and translated to beats per minute. For spectral analysis, the time series were first detrended by least squares linear transformation. The transformed time series were then analyzed by Fast Fourier Transform (FFT) to generate a frequency-power spectrum reflecting the relative amplitude of heart IBI periodicities in frequencies from .04 to .002 Hz (in periods from 24 to 480 seconds, respectively). The spectral peak was identified from the FFT spectrogram as the frequency (period length) with the greatest associated power. Spectral peak power was expressed as a percentage of the total variance of the underlying time series. Results from the spectral analyses of the three 8-minute segments per subject within a condition (for example, baseline day) were averaged to increase within-subject reliability. Analyses of variance were performed on these averaged values. Within-subject correlations of spectral peak period and spectral peak power were computed with the results from analyses of the 8-minute (unaveraged) segments over all conditions (N = 12 per subject). Fisher's Z transformations of the correlation coefficients (Zar 1974) were tested by analysis of variance for group differences. The 5 percent level of statistical significance was tested throughout. All calculations except the analyses of variance were performed on a Burroughs 7800 computer using the International Mathematics and Statistical Library program packages in Fortran.

The three groups differed over all conditions on the measures of heart rate and its coefficient of variation (Table 1A). Heart rate was lower in the haloperidol group than in the other two groups, and the coefficient of variation was lowest in the lithium group. With the groups combined, heart rate was reduced at night, and the spectral peak power decreased at night (Table 1B). The only difference between baseline and drug conditions was a decrease in spectral peak power in the drug condition (Table 1C). Thus, both night and drug therapy conditions were accompanied by reductions in periodicity of heart rate change defined by reduced peak power. There were no interactions between the conditions or between the conditions and the groups. All three groups responded similarly to any change in the condition.

The measures of spectral peak period and spectral peak power were generally correlated in the imipramine and lithium groups, but not in the haloperidol group (Table 2). The positive correlation indicated that there was a linear relationship between period length and the signal-to-noise ratio of the periodicity; that is, when the spectral peak was located at the slow end of the spectrum, it tended to have a higher amplitude relative to the sum of the other variations in the record than a spectral peak located at the fast end of a spectrum derived from other data. In the haloperidol group, periodicity could not be predicted from the location of the period with the greatest amplitude in the spectrum.

Table 1

Average Values of Dependent Measures by Group and Condition

Comparisons	Heart Rate		Spectral Peak	
	Level	Variation[a]	Period Length	Power
A) Imipramine	84.3 bpm	0.052	195 sec	17.4%
Haloperidol	71.3*	0.061	199	16.5
Lithium	84.3	0.035*	162	16.7
B) Day	89.6	0.050	202	17.9
Night	70.2*	0.048	169	15.7*
C) Baseline	79.5	0.054	195	18.1
Drug	80.4	0.045	175	15.5*

[a] Coefficient of variation of heart rates within subjects

*$p < .05$

Table 2

Within-Subject Correlations of Spectral Peak Period and Power

Imipramine		Haloperidol		Lithium	
Subject	Correlation	Subject	Correlation	Subject	Correlation
1	0.20	1	0.01	1	0.83*
2	0.76*	2	0.28	2	0.78*
3	0.80*	3	0.12	3	0.60*
4	0.62*	4	0.42	4	0.09
5	0.95*	5	−0.14	5	0.28

*$p < .05$

The reduction in spectral peak power with pharmacotherapy is interesting because periodicity has often been associated with pathology (Glass & Mackey 1979). For example, in fetal monitoring during labor and delivery, a sinusoidal heart rate pattern was indicative of fetal distress (Rochard et al. 1976). A similar heart rate pattern was seen in neonatal hypoxia (Reid et al. 1979). Adult obstructive sleep apnea with periodic hypoxia was also accompanied by heart rate periodicity (Tilkian et al. 1977), as are other cardio-respiratory disorders such as Cheyne-Stokes respiration (Dowell et al. 1971) and chronic heart failure (Mantle et al. 1978). Examples of increased periodicity in heart rate were found for psychosomatic disorders (Zweiner 1978) and in oxygen saturation for schizophrenia (Lovett Doust 1980).

In both normal and abnormal cases, heart rate periodicity is usually related to respiration. The respiratory sinus arrhythmia accounts for a large part of the heart rate variation in periods less than 12 seconds in length (Luczak & Laurig 1973; Penaz et al. 1978). The contribution of respiratory sinus arrhythmia was eliminated in the present study by averaging IBIs over 12-second epochs to define each datum point. Sleep apnea could have contributed to the spectral peaks in the 24- to 480-second range, but probably did not because periodicity was reduced at night. Thus the periodicity in this group of psychiatric patients may be unrelated to respiration in the reported range, but reflect disturbances in other central systems. The interpretation of periodicity as abnormal depends, however, on its inappropriateness for the organism's adaptation. Periodicity may be considered pathological to the extent that it reduces the range of potentially adaptive variations. For example, autonomously periodic behavior captured by internal rhythmic mechanisms may become dissociated from environmental events and appear as stereotypy, compulsions, or paranoia. Halberg (1969) suggested that the alteration of periodic processes or the occurrence of periodicity in aperiodic processes may accompany or contribute to disease. If that is so, the restoration of original system variational characteristics may be a requirement for the return to health. This study has not directly demonstrated a change in variational characteristics with disease states, but it has indicated that periodicity may be reduced if the disease signs are ameliorated. Thus the normal condition can be predicted to be one of sensitive instability that allows the organism to respond adaptively to environmental change.

The positive relationship between period length and amplitude is commonly found in many measures, most notably the electroencephalogram, but the haloperidol group is noteworthy here in its failure to develop reliable correlations on these two heart rate variables. The certainty of the uniqueness of the haloperidol patients is reinforced by an examination of the patients' psychiatric classifications in Table 3. Of seven cases with research diagnostic criteria (RDC) indicative of schizophrenia, four were given haloperidol; two received lithium; and one received imipramine. Six of those seven had insignificant correlations of peak period and peak power. Thus the pathology of schizophrenia may involve mechanisms that disrupt the organization of central periodic processes. Neither the average peak location nor the average peak power were different between the haloperidol group and the other two groups. Therefore the distribution of power was no more random within individual spectra, but power did tend to be randomly distributed among the peak frequencies between spectra. This suggests that the haloperidol patients experienced not only periodic central disturbances but that there were inconsistencies in the contributions of these periodic processes. The inconsistency may result in a cognitive and emotional confusion characteristic of schizophrenia. The major psychoses may share the tendency for the central nervous system to become trapped in

Table 3

Characteristics of Sample

Medication Group	Subject	Age	Sex	Race	RDC*	Psychiatric and Medical Notes
Imipramine	1	44	M	W	Major depressive	Pulmonary disease
	2	33	M	W	Major depressive	
	3	46	M	W	Major depressive	Alcoholism
	4	52	M	W	Major depressive	Alcoholism; Bipolar I
	5	23	F	W	Schizoaffective	
Haloperidol	1	36	M	W	Schizoaffective	Bipolar I
	2	25	M	B	Schizoaffective	Alcoholism; cardiac disease
	3	30	M	W	Schizophrenia, paranoid	Alcoholism
	4	52	M	W	Major depressive	Cardiac disease
	5	18	M	B	Schizoaffective	
Lithium	1	57	M	W	Bipolar I	
	2	52	M	W	Bipolar II	Alcoholism
	3	22	M	?	Bipolar II	Records not available
	4	45	M	W	Schizoaffective	Alcoholism; pulmonary disease
	5	25	M	?	Schizophrenia, paranoid	Records not available

*Research Diagnostic Criteria (Spitzer, Endicott, and Robins)

limited modes of function, which modes could differ among the psychoses. Schizophrenia could then be further compounded by an instability between modes, differing from normal in the duration of their fluctuations and consequent inappropriateness to the environment.

Summary

Periodicity of heart rate change in a mixed group of psychiatric patients was found to decrease both at night and subsequent to pharmacotherapy. This finding is consistent with an interpretation of emergent periodicity as a sign of disease and could represent a brain state with limited capacity for adaptation. A subgroup of patients who received haloperidol as part of their indicated treatment during hospitalization was characterized by instability in a function governing rate changes. This instability could represent chaotic central nervous system processes that are manifested in confused cognition and inappropriate affect.

Acknowledgments: The author wishes to thank Dr. Leighton Huey for providing patient data, Patrick Russo for assistance in data analysis, and Dr. Arnold Mandell for direction and discussion.

References

Dowell, A.R., Buckley, C.E., Cohen, R., Whelan, R.E., and Sieker, H.O. Cheyne-Stokes respiration: A review of clinical manifestations and critique of physiological mechanisms. *Arch. Intern. Med.*, 127:712-726, 1971.

Glass, L., and Mackey, M.C. Pathological conditions resulting from instabilities in physiological control systems. *Ann. NY Acad. Sci.*, 316:214-235, 1979.

Halberg, F. Chronobiology. *Ann. Rev. Physiol.*, 31:675-725, 1969.

Jenkins, G.M., and Watts, D.G. *Spectral Analysis and Its Applications.* San Francisco: Holden-Day, 1968.

Lovett Doust, J.W. Sinus tachycardia and abnormal cardiac rate variation in schizophrenia. *Neuropsychobiology*, 6:305-312, 1980.

Luczak, H., and Laurig, W. An analysis of heart rate variability. *Ergonomics*, 16:85-97, 1973.

Mantle, J.A., Strand, E.M., Smith, L.R., James, and Rackley. Quantitative assessment of the autonomic control of the sinus node in man. In: Ripley, K.E., and Ostrow, H.G. (eds.), *Computers in Cardiology.* New York:IEEE, 1978, pp. 407-408.

Overall, J.E., and Henry, B.W. Decisions about drug therapy. III. Selection of treatment for psychiatric inpatients. *Arch. Gen. Psychiatry*, 28:81-89, 1973.

Overall, J.E., Henry, B.W., Markett, J.R., and Emken, R.L. Decisions about drug therapy. I. Prescriptions for adult psychiatric outpatients. *Arch. Gen. Psychiatry*, 26:140-145, 1972.

Penaz, J., Honzikova, N., and Fiser, B. Spectral analysis of resting variability in some circulatory parameters in man. *Physiol. Bohemoslovaca*, 27:349-357, 1978.

Reid, M.M., Jenkins, J., and McClure, G. Sinusoidal heart rate rhythms in severe neonatal hypoxia. *Arch. Dis. Child.*, 54:432-435, 1979.

Rochard, F., Schifrin, B.S., Goupil, F., Legrand, H., Blottiere, J., and Sureau, C. Nonstressed fetal heart rate monitoring in the antepartum period. *Am. J. Obstet. Gynecol.*, 126:699-706, 1976.

Spitzer, R.L., Endicott, J., and Robins, E. *Research Diagnostic Criteria*, 3d ed. New York: Biometrics Research, NY State Psychiatric Institute, 1977.

Tilkian, A.G., Guilleminault, C., Schroeder, J.S., Lehrman, K.L., Simmons, F.B., and Dement, W.C. Sleep-induced apnea syndrome, prevalence of cardiac arrhythmias and their reversal after tracheostomy. *Am. J. Med.*, 63:348-358, 1977.

Zar, J.H. *Biostatistical Analysis*. Englewood Cliffs, NJ: Prentice-Hall, 1974.

Zweiner, U. Physiological interpretation of autospectra, coherence and phase spectra of blood pressure, heart rate, and respiration waves in man. *Automedica*, 2:161-169, 1978.

Attending or Discriminating 40 Hz Modulated Tones Induces Phase-Locked Subharmonic Resonances in EEG

Scott D. Makeig, M.A.,[1] and Robert Galambos, M.D.[2]

Introduction

Recently, Galambos et al. (1981) published a study of brain potentials evoked by trains of tones or clicks at high rates, reporting that the human auditory evoked potential response shows a resonance near 40 Hz. The amplitude of this 40 Hz driven response decreases markedly in sleep. This fact, and the body of experiments linking spontaneous and evoked 40 Hz activity to cognition (Sheer 1970; Spydell 1979), suggested to the authors that the 40 Hz response might be usable to probe level of arousal. What follows is a preliminary report of an experiment designed to explore the effects of attention on the 40 Hz response.

Method

The stimuli consisted of trains of low (800 Hz), middle (1000 Hz), and high (1200 Hz) tonebursts, modulated at 40 Hz, and presented to six subjects under four task conditions — "count the low tones," "count the middle tones," "count the high tones," and "don't count."

The low and high tonebursts were relatively rare (each 12-20% of the total), and the middle tonebursts relatively frequent (60-84%). Four to eight blocks of data were collected from each subject, each block consisting of one run in each of the four conditions. Order of runs within blocks and order of tones within runs were randomized under direct computer control.

Each run lasted about 100 seconds and consisted of 96 tonebursts. Each toneburst consisted of ten tone pips (duration 5 msec), with an interpip interval of 25 msec (onset-to-onset). Each tonepip was composed of four, five, or six half-sinewave clicks. The interval between tonebursts was approximately one second (onset-to-onset), with 200 msec of random jitter introduced in inter-burst intervals to avoid phase-locking to ongoing electroencephalograph (EEG) rhythms.

Subjects were seated with eyes closed in a quiet room. Stimuli were delivered to the right ear at 30 dB above threshold. Subjects reported the task to be difficult, owing to the low level of the signal, the small differences between frequencies, and the necessity of sustaining attention throughout the 2-minute runs. Four channels of evoked responses were collected using Grass EEG amplifiers (bandpass 3-300 Hz) and a Nicolet averaging computer. Results from the bipolar derivation (Cz-Oz) are reported here.

Results

The top two traces of Figure 1 show the averaged (Cz-Oz) responses of one subject to the same

---

[1] Department of Music, University of California at San Diego, La Jolla, CA 92093.

[2] Children's Hospital and Health Center, San Diego, CA 92123.

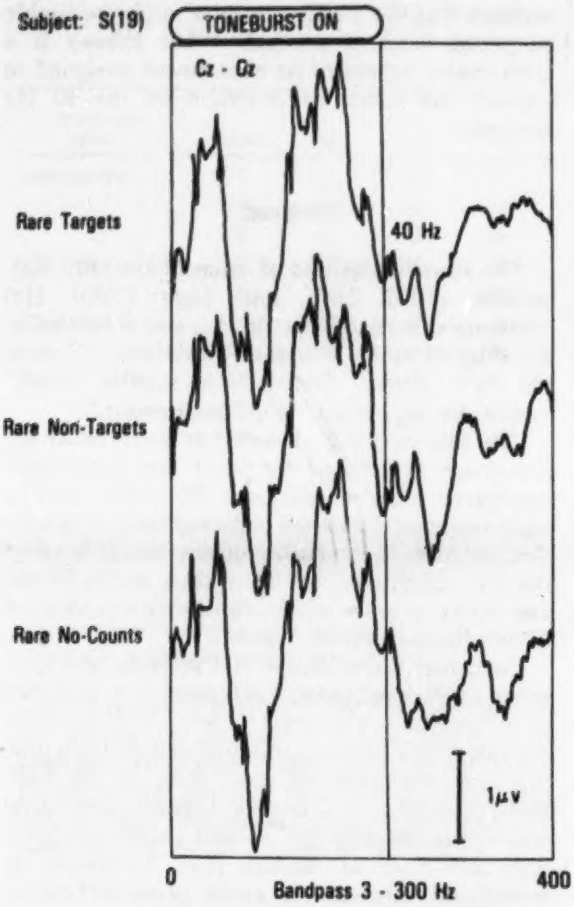


FIGURE 1. Average responses to rare targets (top trace), and rare non-targets in the "count high tones" and "count low tones" conditions (middle trace). Bottom trace is the response to the rare tones in the "don't count" condition. Each response is the sum of responses to about 200 tonebursts, in a total of eight blocks of trials over 80 minutes. The thin downward spikes in the responses during the time the toneburst is on are stimulus artifacts. (In these figures Cz positive is upward.)

stimuli (high and low tonebursts in the "count highs" and "count lows" conditions), segregated into "rare target" and "rare nontarget" responses. ("Rare nontargets" are the high tones in the "count lows" condition plus the low tones in the "count highs" condition.) The bottom trace is the responses to these same stimuli in the "don't count" condition (the "rare no counts"). Note in each of these traces the circa 1 μv 40 Hz modulation superimposed on the slower evoked response by the 40 Hz modulation of the toneburst.

The differences between pairs of the three responses shown in Figure 1 are seen in Figure 2. The (target-nontarget) and (nontarget-no count) difference waves each show a regular oscillation at circa 20 Hz which becomes locked in both frequency and phase to the moments of occurrence of tone pips within the toneburst (i.e., to multiples of 25 msec), and continues to at least the end of the sweep (400 msec after onset). A similar 20 Hz characteristic may be seen, less distinctly, in the (target-no count) comparison (Figure 2, bottom trace).

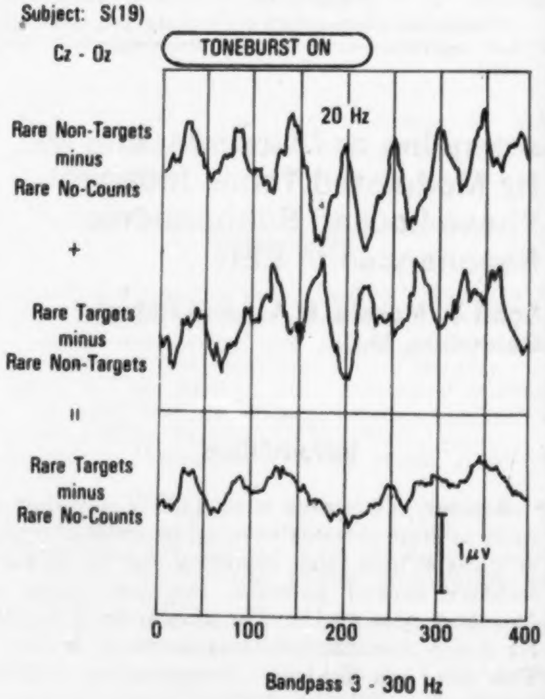


FIGURE 2. Difference waves between pairs of the three responses shown in Figure 1. Vertical lines are drawn every 50 msec. Note the progressive frequency and phase-locking of the difference waves and the stability of this phase-locking after offset of the toneburst.

Figure 3 shows the same difference wave comparisons for a second subject. Here frequency-and phase-locked rhythmic difference waves are also evident—but for this subject they are locked predominantly to about 10 Hz.

The (target-nontarget) comparisons for two other subjects are shown in Figure 4. Rhythmicities at about 13 Hz are evident (i.e., at about 1/3 of 40 Hz). In further experiments, evoked rhythmicities at 26 and at 32 Hz (2/3 and 4/5 of 40 Hz) have also been seen. However, rhythms evoked at frequencies other than 10 and 20 Hz have not been seen to "ring" on after toneburst offset, as do difference waves at 10 and 20 Hz (*see* Figure 4).

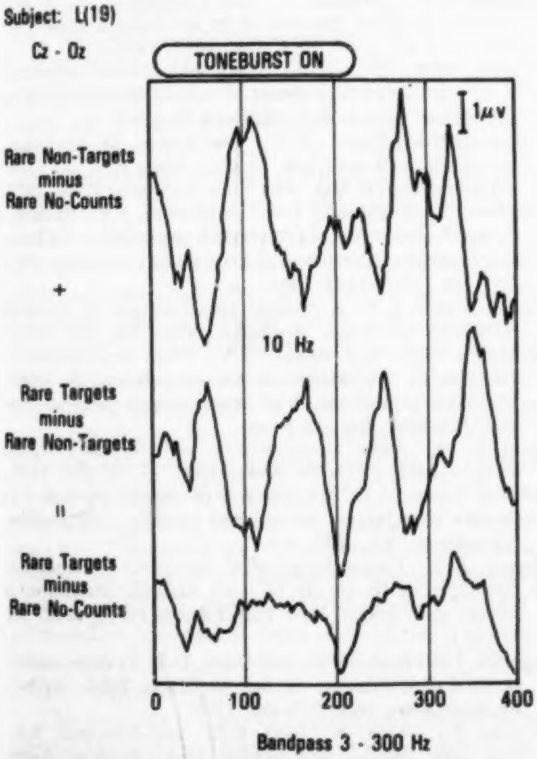


FIGURE 3. The same difference waves as shown in Figure 2 for another subject. Note again the progressive frequency- and phase-locking of the difference waves and their amplitude stability, in this case showing a 10 Hz characteristic.

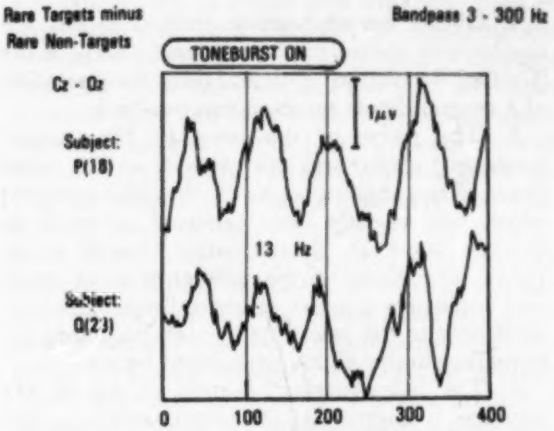


FIGURE 4. The target-nontarget comparisons for two other subjects who show a circa 13 Hz characteristic during the toneburst.

Tentative Conclusions

Results of these first experiments suggest:

1. Difference waves between responses evoked by target and nontarget 40 Hz-modulated tonebursts reveal differences in amount of nonlinear brain resonance to the modulating frequency of the bursts. These rhythmic difference waves reflect differences in task-relevance of the stimuli, and thus are a new class of endogenous cognitive evoked response, possibly related to the event-related rhythmicities (ERR) discussed by John (*see* Galambos & Hillyard 1981).

2. The rhythmic character of the difference responses seems to be most pronounced in comparisons involving *non*-targets in the "count" conditions. The authors note that similar stimulus-evoked "alpha-like" EEG activity has previously been associated with nontarget stimuli and "inhibitory" cognitive processes (*see* Morrell 1966).

3. The remarkable phase-locking and amplitude stability of the circa 20 and 10 Hz subharmonic difference waves (*see* Figure 2) may be related to the theorized relative stability of successive bifurcations in a variety of physical dynamic systems (Feigenbaum 1979), as well as to bifurcations at these same (40 Hz, 20 Hz, 10 Hz) frequencies reported in various psychophysical (Kristofferson 1980; Augenstein 1955) and electrophysiological (Barnett et al. 1971; Freeman 1961, 1962) experiments.

4. Of the few derivations studied so far, the rhythmic characteristic is seen most clearly in the (Cz-Oz) derivation. This suggests the operation of a central dipole oriented front-to-back.

5. The phase of the circa 10 Hz (target-nontarget) differences corresponds to the same phase of the ongoing alpha rhythm (Oz-positive) which has recently been reported to result in quickest two-flash discrimination (Varelo et al. 1981). The phase of the difference wave could thus indicate a process of central modulation of sensitivity to the intermittent high-frequency information in the 40 Hz modulated bursts.

6. The "after-ringing" portion of the 40 Hz response is augmented for targets and attended tones in some subjects, but not augmented in others.

7. While the degree of stability of these responses within subjects has not been fully assessed, within the sessions reported here these responses seem to be remarkably stable, save perhaps in the "don't count" condition.

Discussion

The authors plan systematic investigations of the range and stability of the responses, and on the effects of changing modulating frequency and modality of the stimuli. They also intend to explore the relation of these phenomena to the endogenous responses (N1, P3, N4, etc.) seen in experiments using unmodulated stimuli (Hillyard et al. 1978).

The present evoked rhythmicities may bear some relation to the harmonic nonlinear phenomena seen in transition to turbulence of driven responses in physical (Feigenbaum 1979; Keolian et al. 1981) and biological (Mandell & Russo 1982) systems. Their range is similar to the variety of harmonic responses to photic driving seen in the raw EEG by Mundy-Castle (1953) and Fukushima (1975). They may also relate to the body of psychophysical theory and experiment relating to "perceptual moments" and "excitability cycles" (reviewed in Harter 1966). While these results are not yet thoroughly tested, they renew interest in exploring the role of nonlinear resonant brain dynamics in cognition.

References

Augenstein, L.G. Evidences of periodicities in human ta performance. In: Quastler (ed.), *Information Theory i Psychology: Problems and Methods.* Glencoe, Ill:The Fre Press, 1955.

Barnett, T.P., Johnson, L.C., Nautall, P., Hicks, N., and Nute, C. Bispectrum analysis of electroencephalographi responses during waking. *Science,* 172:401-402, 1971.

Feigenbaum, M.J. The onset of turbulence. *Phys. Let.,* 74A:375, 1979.

Freeman, W.J. Phase and long-term excitability changes i prepyriform cortex of cats. *Exp. Neurol.*, 5:505-518, 1961.

Freeman, W.J. Linear approximation of prepyriform evoke potentials in cats. *Exp. Neurol.*, 5:477, 1962.

Fukushima, T. Application of EEG-Interval-Spectrum Analysis (EISA) to the study of photic driving responses *Arch. Psychiatry,* 220:99, 1975.

Galambos, R., and Hillyard, S.A. Electrophysiologic approaches to human cognitive processing. *Neurosci. Re Prog. Bull.*, 20(2), 1981.

Galambos, R., Makeig, S., and Talmachoff, P. A new auditory potential recorded from the human scalp. *Pro Natl. Acad. Sci. USA,* 78(4):2643-2647, 1981.

Harter, M.R. Excitability cycles and cortical scanning A review of two hypotheses of central intermittency i perception. *Psychol. Bull.*, 68(1):47-58, 1967.

Hillyard, S.A., Picton, T.W., and Regan, D. Sensation, perception, and attention: Analysis using EPs. In: *Event-Related Potentials in Man.* New York: Academic Press, 1978.

Keolian, R., Turkevich, L.A.; Putterman, S.J., Rudnick, I., and Rudnick, J.A. Subharmonic sequences in the Fara-day experiment: Departures from period doubling. *Phys Rev. Lett.*, 47(6):1133, 1981.

Kristofferson, A.B. A quantal step function in duratio discrimination. *Percept. Psychophys.*, 27(4):300-306, 1980.

Mandell, A.J., and Russo, P.V. From equilibrium t autonomous rhythmicity across neurobiological levels Toward a general theory of desensitization and habitua-tion. *Pharmacol. Rev.* (In press)

Morrell, F. Some characteristics of stimulus-provoked alpha activity. *EEG Clin. Neurophysiol.*, 21:552-556, 1966.

Mundy-Castle, A.C. An analysis of central responses to photic stimulation in normal adults. *EEG Clin Neurophysiol.*, 5:1, 1953.

Sheer, D.E. Electrophysiological correlates of memory consolidation. In: Ungar, G. (ed.), *Molecular Mechanisms in Memory and Learning.* New York:Plenum Press, 1980, pp. 177-211.

Spydell, J.D., Ford, M.R., and Sheer, D.E. Task dependent cerebral lateralization of the 40 Hertz EEG rhythm *Psychophysiology,* 16(4):347-350, 1979.

Varela, F.J., Toro, A., John, E.R., and Schwartz, E.L. Perceptual framing and cortical alpha rhythm. *Neuro-psychologia,* 19(5):675-686, 1981.

Vol. 18, No. 3, July 1982

Nonlinear Dynamics in Brain Processes[1]

Arnold J. Mandell, M.D.[2]

Universal patterns of behavior, often claimed for human personality syndromes described in the psychoanalytic language of instinct and defense, may be defined and explored more rigorously using global properties of the structure of solutions to N-dimensional nonlinear differential equation sets representative of the behavior of an open, complex interactive system, i.e., the brain. Two conceptual approaches, irreversible thermodynamics and dynamical control theory, make different assumptions concerning the critical determinants of these emergent forms.

Freud lived at 19 Berggasse, "half way up the street" between the homes of the poor below and those of the independently wealthy with higher house numbers (Engelman 1976). The new machines of the Industrial Revolution running on the closed system thermodynamics of Carnot cycles and the Darwinian survival theme of private entrepreneurship were certainly consistent with an energy-dependent psychoanalytic ordering principle of "needs" and their fulfillment. Structure emerged from this dissipation. Energy also drove the fluctuations of the linear, time-dependent diffusivities of Brownian motion (Einstein 1905) that brought an unexpected degree of predictability to randomness for Freud's contemporary Einstein who, working for barely adequate wages at a patent office was, in a way, also "half way up." The need was for survival, and it was attended by a fear of nonlinear unpredictability. Heroic attempts were made to derive N-particle probability densities from functionals of one-particle systems in moderately dense gases—without success.

The dominant turn-of-the-century theme of required energy might explain why the work of two contemporaries of Freud and Einstein, Jung in psychoanalysis, and Poincaré in mathematical physics, was relatively ignored. Jung's message came not from the brainstem but from the upper shakras: myth and form better represented man's supramolecular order that (once fed) organized all the rest (Jung 1956). Poincaré said that given the fact that things were moving already, the constraints (laws) of nature derived not from limitations on activation energy required to get out of a potential well, but restrictive features of interaction; for example, a thing cannot stand on a place that is already occupied. When more than two things are closely engaged, it is difficult to know what comes next with respect to specific predictive parameter values; yet topological dynamics have revealed that there are definite limitations on the number of possibilities (Poincaré 1957). When Boltzmann's dense gas became non-independent particles, even at long times, "slaving" social organization and its measurement via order parameters crept quietly into what is now an exploding physics of complex systems (Haken 1978).

Recent research confirms Kety's findings in the late 1940s that the whole brains of wild psychotic patients and normal sleeping people burn the same mean number of calories per minute (Kety et al. 1948) but are vastly different with respect to the temporal and spatial arrangements of "hot" spots (Sokoloff et al. 1981). A surface on which a multiplicity of topographies can add up to the same mean energy utilization is consistent with the statistical thermodynamics of an ensemble of systems with a variety of entropic "styles" of information transport whose phase relations, couplings, not available fuel, are deterministic with respect to measures of thought, feelings, and action. These ruling dynamical forms appear to lie somewhere between cause and effect.

At the molecular level, a similar isoenergy surface has been portrayed for the multiplicity of hydrogen (proton) configurations on protein macromolecules which determine their electromagnetic moments and therefore their pattern of interactional cooperativity (Kirkwood & Shumaker 1952). Genetic differences in an enzyme can be expressed in altered amino acid sequences away from the active site, leading to no loss of catalytic activity but alterations in the structural stability of the protein associated with changes in its regulatory properties and time-dependent patterns of variation in biosynthetic activity (Knapp et al. 1981). These characterizations are not about *what* or *how much*, but about style.

---

[1] This study is supported by USPHS Grant DA-00265 from the National Institute on Drug Abuse and a grant from the John D. and Catherine T. MacArthur Foundation.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

Poincaré's global, geometric, qualitative approach to dynamical systems offers no natural system of coordinates. The portrait of the equation set fills the entire phase space, changing with every turn of the parameter knob; an evolutionary scenario which itself becomes the mathematical object of interest. Surprisingly, qualitative aspects of local, parametized vector space, for example, the stability of the motions of a regional flow near a critical point, may generalize to the entire system (Abraham & Marsden 1967). Psychiatrists knew this already: the obsessional reveals the characteristics of his dynamical brain system in all that he does—from choosing what color socks to wear in the morning to eating each vegetable separately on his dinner plate—all preserving the characteristic symplectic structure of his manifold. The tails of the distribution of values around the mean for any measure reveal a mix of expanding (hysterical) and contracting (obsessional) motions leading to individually unique routes of convergence to invariant measures. Perhaps this reveals the same entropic property seen in statistical physics as characteristic relaxation times or wavelengths of the complex system's spontaneous fluctuations.

Looking through time down the manifold of the mean, attention is paid to the quality of the dynamical activity around it. The Reynolds decomposition of flow separates the average velocity from its varying part. When the graph of a deterministic two-dimensional graph of x causing f(x) is cut transversely, there are distinctive patterns in the surrounding foliage made of what used to be called error. Those in psychiatry are interested in such things: the *hows* that ride on the *whats*, the patterns of variation around the mean, the hetero- and homoclinic orbits that develop around saddle nodes seen in transverse sections, distinctive personality styles that reveal themselves in doing routine things, the process not the content of what goes on in psychotherapy hours.

Quantitative study of these qualities has evolved a variety of useful and closely related abstract metrics: eigenvalue indices of stability; critical exponents describing expansions and contractions of flows; Lyapounov characteristic exponents; geometric and topologic dimensionality; rate of information change; autocorrelation and correlation lengths; probability density distributions, especially the higher moments; phase space topology and geometry; the morphology of transverse sections; and frequency (power) spectra. Symbolic dynamics describe pattern generation and recognition beyond the state space specifics. Those in psychiatry are in search of just such schemes.

The following is a brief example of a characteristic style of evolution by several complex brain systems under repeated perturbation; the transition from a quasi-stable equilibrium to autonomous, limit cycle rhythmicity that might loosely be called a Hopf bifurcation.

Data from a study of single frog muscle endplate potentials before and after prolonged nerve stimulation (del Castillo & Katz 1954) were digitized and the values expressed as deviations from the mean voltage level (Figure 1). Spectral analysis of the frequency of variation around the mean in these intracellular recordings of random activity shows that the unimodal population, manifesting a single prominent spectral density (top graph and spectrum), split into two subpopulations with the development of response inhibition (bottom graph and spectrum). See Mandell and Russo (1981) for the statistical methods used.

The local anesthetic quinacrine which, like prolonged nerve stimulation or contact with cholinergic agonists, induces a desensitized state [as procaine does Marty (1978)] also binds cholinergic receptors and emits fluorescent noise. Analysis of these receptor fluctuations from the data of Grünhagen and Changeux (1976) reveals a similar dynamical progression (Figure 2). The control at a low drug level shows a single statistical (not limit cycle) spectral peak and associated autocorrelation length. As the system lost its response to the cholinergic agonist—an increase in sodium conductance by a *Torpedo marmorata* electric organ microsac—the spectrum reflected a change from equilibrium behavior to rhythmic "bursting" of a subpopulation observable in the undamped periodicity of the graph of the autocorrelation function. Figures 1 and 2 demonstrate the similarity in statistical manifestations of desensitization in membrane-conductance and receptor motional processes: the birth from a single population in an (average) equilibrium state of a subpopulation in a limit cycle associated with habituation of the response. After bifurcation there is fast, spontaneous rhythmic activity in a coherent subpopulation, a speculation confirmed by a recent report of the "burst" kinetics of desensitized cholinergic membrane preparations (Sakmann et al. 1980).

At the next level of neurobiological complexity, polysynaptic spinal cord flexor reflexes, an examination of the distributions of interspike intervals in spinal cord interneurons during response habituation, from the work of Groves and Thompson (1973), shows that the interneurons that were capable of a progression from sensitization to an inhibited response after repeated stimulation manifested an initial single population distribution (Figure 3, S), but those that only habituated (Figure 3, H) manifested a multiplicity of frequency-labeled populations (or the phase-locked spontaneous activity of a subharmonically bifurcating chaotic attractor).

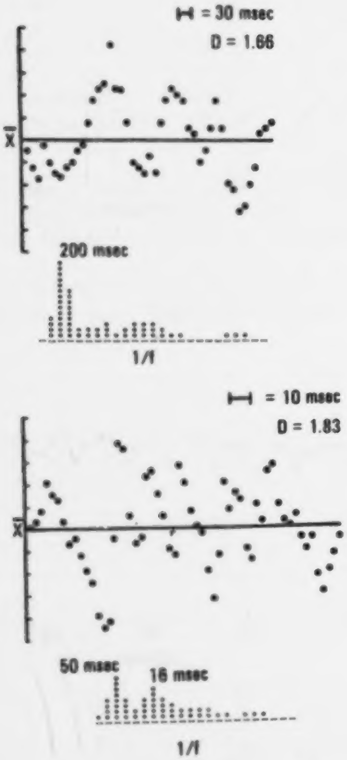


FIGURE 1. Spectral analysis of frequency of variation around mean intracellular recording of "random" endplate potentials before and after prolonged nerve stimulation, showing population bifurcation associated with response inhibition. *See* text.

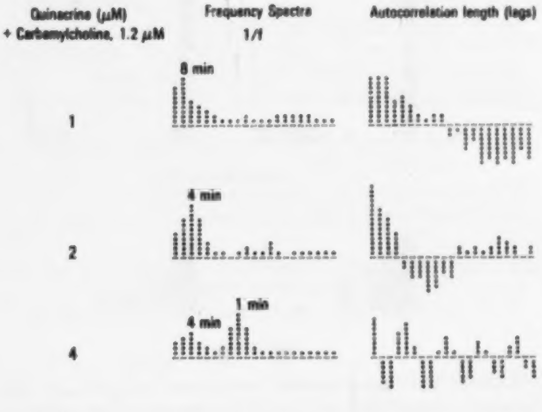


FIGURE 2. Spectra and autocorrelation functions showing shift from equilibrium behavior to subpopulation "bursting" associated with loss of response to cholinergic agonist in a population of cholinergic receptors. *See* text.

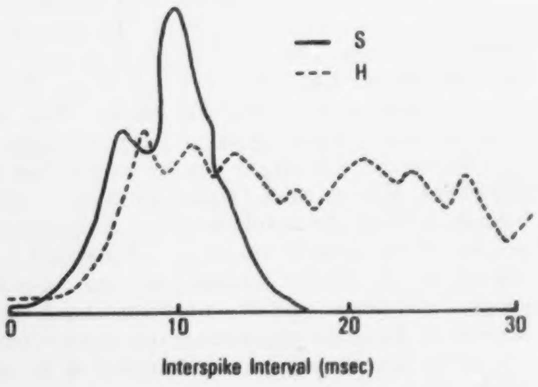


FIGURE 3. Distributions of interspike intervals in spinal cord interneurons during response habituation, showing distinction between those that manifested a single population distribution and those that contained a multiplicity of frequency-labeled populations. *See* text.

pages tightly bound

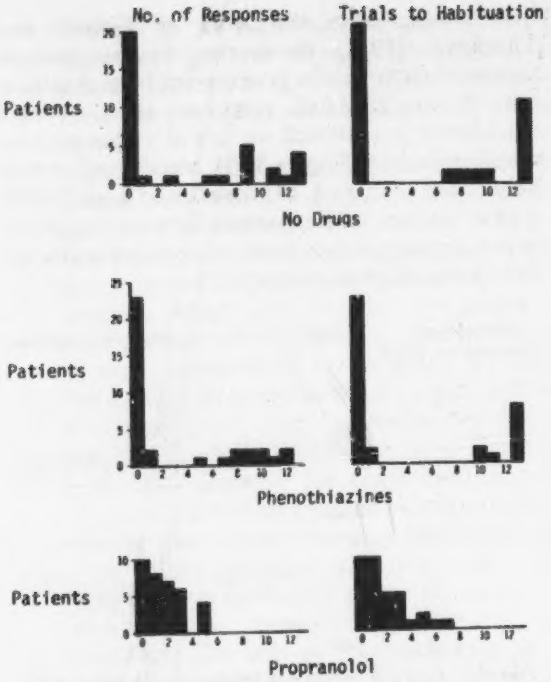


FIGURE 4. Characteristic response irregularity and failure of some schizophrenic patients to habituate an autonomically mediated skin conductance response to tones (Gruzelier 1978), showing the contrasting effects of phenothiazines and propranolol on those responses.

In Figure 4, data from Gruzelier (1978) show the characteristic response irregularity and failure of some schizophrenic patients to habituate an autonomically mediated skin conductance response to tones. The defect was not corrected by phenothiazines, but was normalized by either d- or l-propranolol (Gruzelier 1979). That the d-isomer was as effective as the l-isomer suggests that β-receptor blocking is not the mechanism of this effect. Recent work (Figure 5) suggests that both d- and l-propranolol can phase a significant portion of the kinetic variations of nigrostriatal dopaminergic tyrosine hydroxylase into a strong single rhythmic peak—perhaps coupling previously disparate populations into a more harmonically functioning whole (Mandell & Russo 1981).

It would be interesting indeed if the split-mind implied by the name of the schizophrenic syndrome were, in some cases, from a dynamical systems point of view, literally correct. It was Pavlov (1928) who first saw the deep relationships among the post-habituated state of "internal inhibition," the chronic "inhibitory condition" of schizophrenic patients, the functional cortical hemispheric splitting involved in dissociative phenomena, and the schizophrenic syndrome as resulting from the "destruction of the normal unification of the activity of the whole cortex."

It is hoped that this example suggests that the present era of qualitative mathematical description of the behavior of complex and dense systems promises a language for a scientifically based attempt at the fusion of clinical psychiatric phenomenology and neurobiological mechanism. Especially exciting is the possibility that infinite dimensional control and state spaces may be characterized by measures of low dimensional dynamical structure.

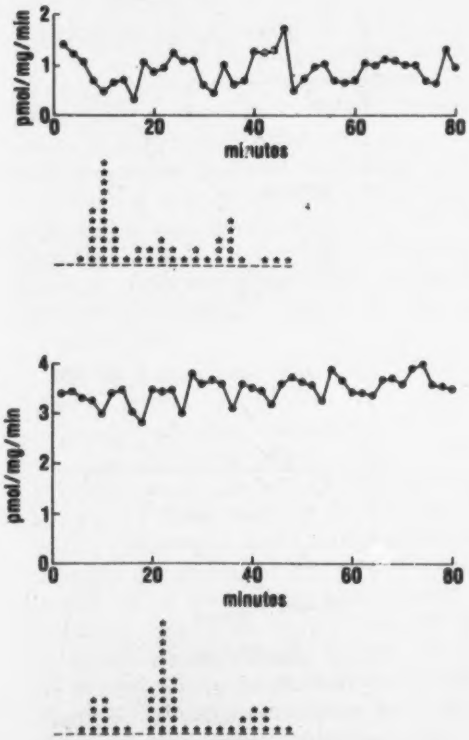


FIGURE 5. Time series containing median values from 80-minute time courses of tyrosine hydroxylase kinetic behavior. The top graph shows a typical control; the bottom graph reflects the faster, more regular periods induced by 5 μM propranolol.

References

Abraham, R., and Marsden, J.E. *Foundations of Mechanics*. New York:Benjamin, 1975.

del Castillo, J., and Katz, B. Statistical factors involved in neuromuscular facilitation and depression. *J. Physiol.*, 123:574-585, 1954.

Einstein, A. On the movement of small particles suspended in a stationary liquid demanded by the molecular-kinetic theory of heat. *Am. d. Physik,* 17:549-560, 1905.

Engelman, E. *Berggasse 19; Sigmund Freud's Home and Office, Vienna, 1938.* New York:Basic Books, 1976.

Groves, P.M., and Thompson, R.F. A dual-process theory of habituation: Neural mechanisms. In: Peeke, H.V.S., and Herz, M.J. (eds.), *Habituation, Vol. II.* New York: Academic Press, 1973, pp. 175-206.

Grünhagen, H.H., and Changeux, J.-P. Studies on the electrogenic action of acetylcholine with *Torpedo marmorata* electric organ. *J. Mol. Biol.*, 106:517-535, 1976.

Gruzelier, J.H. Propranolol acts to modulate autonomic orienting and habituation processes in schizophrenia. In: Roberts, E., and Amacher, P. (eds.), *Propranolo and Schizophrenia.* New York:Liss, 1978, pp. 99-118.

Gruzelier, J.H. Lateral asymmetries in electrodermal activity and psychosis. In: Gruzelier, J.H., and Flor-Henry, P. (eds.), *Hemisphere Asymmetries of Function in Psychopathology.* New York:Elsevier/North-Holland, 1979, pp. 149-187.

Haken, H. *Synergetics.* New York:Springer-Verlag, 1978.

Jung, C.G. *Symbols of Transformation.* Princeton N.J.:Princeton University Press, 1956 (Bollingen Series XX).

Kety, S.S., Woodford, B.B., Harmel, M.H., Freyhan, F.A., Appel, K.E., and Schmidt, C.F. Cerebral blood flow and metabolism in schizophrenia. *Am. J. Psychiatry,* 104:765-770, 1948.

Kirkwood, J.G., and Shumaker, J.B. Forces between protein molecules in solution arising from fluctuations in proton charge and configuration. *Proc. Natl. Acad. Sci. USA,* 38:863-871, 1952.

Knapp, S., Mandell, A.J., Russo, P.V., Vitto, A., and Stewart, K.D. Strain differences in kinetic and thermal stability of two mouse brain tryptophan hydroxylase activities. *Brain Res.*, 230:317-336, 1981.

Mandell, A.J., and Russo, P.V. Striatal tyrosine hydroxylase activity: Multiple conformational kinetic oscillators and product concentration frequencies. *J. Neurosci.*, 1:380-389, 1981.

Marsden, J.E., and McCracken, M. *The Hopf Bifurcation and Its Applications.* New York:Springer-Verlag, 1976.

Marty, A. Noise and relaxation studies of acetylcholine induced currents in the presence of procaine. *J. Physiol.*, 278:237-250, 1978.

Pavlov, I.P. *Lectures on Conditioned Reflexes, Vol. I.* New York: International University Press, 1928, pp. 363-380.

Poincaré, H. *Les Méthod's Nouvelles de la Mécanique Celesté.* (The New Methods of Celestial Mechanics.) New York:Dover, 1957.

Sakmann, B., Patlak, J., and Neher, E. Single acetylcholine-activated channels show burst-kinetics in presence of desensitizing concentrations of agonist. *Nature,* 286:71-73, 1980.

Sokoloff, L., Bunney, W.E., Jr., Kuhl, D., Buchsbaum, M., Chase, T., Rapoport, S., Rush, A.J., and Farkas, T. Positron emission tomography and cortical localization: Clinical studies in psychiatry and neurology. Paper presented at the American College of Neuropsychopharmacology meeting, Coronado, California, 1981.

Interaction Among Government, Industry, and Extramural Investigators: New Developments and Problems

Co-Chair **Arthur Rifkin, M.D.**
The Mount Sinai School of Medicine
New York, N.Y.

and

Barrett Scoville, M.D.
National Institute of Neurological Disease and Strokes
Bethesda, Md.

An Investigator's View

Arthur Rifkin, M.D.

The purpose of this study group was to discuss problems and solutions in the interaction among government, industry, and investigators in the development and clinical testing of new drugs, and in the evaluation of the results of drug research. Different opinions exist among these groups about the balance between scientific purity and clinical exigencies, the government's role in promoting or directing the development of drugs, and other issues involved in characterizing new therapies.

The aim was not merely to air dissatisfaction, but to state what the problem was and what should be done about it. The most optimistic expectation was that a consensus on some issues which may influence the future policy would be reached.

In recent years the protocols coming from the drug companies have been much more sophisticated in methodology, an improvement investigators welcome. This results from the growing recognition that approval of new drugs or new indications for old drugs should hew to a higher standard than before. One can usually date a clinical trials paper by its methodology alone as optimum technique changes. For example, the need to define diagnosis by atheoretical operational criteria, and to define relapse and remission in equally empirically operational terms, methodology absent in the most elegant of early studies, are now accepted as necessary. The usual competitive drives of the three players in this field—industry, government, and investigators—have combined to pursue excellence. The investigator wants his work to be believed and to be influential. To accomplish this, he must impress his peers with the adequacy of his methodology and the data analysis. How discouraging it is to be faced with a challenge to data and conclusions after months to years of work because of what others consider flaws in design or analysis. It is clear that the investigator has an interest in the tightest methodology and data analysis.

The drug company's interest, let us assume nothing more than unbridled capitalism, is to sell its product. To do this it needs a good drug to sell, it must convince the FDA of its safety and efficacy, and it must persuade the physician to prescribe it. The cost of developing and promoting a drug is enormous. It must be in the interest of the company to assure itself that its new drug or new indication is really going to work. Too often persons outside of the industry focus on its marketing aspect, which is far removed from scientific issues and easy to ridicule. They wonder if the rose of Ludiomil will sell better than the butterfly of Sinequan. Marketing aside, however, the first question facing those in the corporate boardrooms is whether the drug really works and is reasonably safe. Only if that question is answered affirmatively can they go forward and consider questions of marketing. Therefore, it is in industry's self-interest to encourage the use of the most accurate methodology and data analysis.

The third leg of this tripod, the FDA, also has its vested interest in clinical accuracy. So then, if everyone is interested in the best methodology, where is the problem?

There are some divergent interests among these groups. On the industry's side, they want as smooth sailing as possible once they are convinced that the drug works and that it is marketable, and they chafe at bureaucratic restrictions. They pressure investigators to live up to FDA standards even if they think them excessive in order to facilitate approval. The FDA is not interested in the drug company's profit, but only in protecting the public from ineffective or unsafe drugs, so they are interested in the most pure methodology.

The investigator has a responsibility shared by none of the other two partners in bringing new drugs out: he must take care of a sick person. Most improvements in methodology have been at the expense of the ease of following usual clinical procedures. In "the bad old days," making a diagnosis did not require laboriously completing scales such as the Schedule for Affective Disorders and Schizophrenia (SADS), and counting off symptoms, and making sure that all raters understood clearly and equally the distinction between thought insertion and delusions of reference. The rating scales are longer and are used more often. Diagnostic distinctions are much more careful. We are much more likely to bother the patient with requests for body fluids. All these techniques cost something that is often not apparent to those not on the firing line of obtaining data. They cost the acceptance and compliance of the patient. Without research subjects, this whole enterprise founders, so the investigator is in the position of fighting back against the FDA and the drug company, who want more purity, because the investigator fears he will lose his subjects by annoying them too much. In these days of declining interest in psychiatry by medical students, and in declining availability of money for training and research, the clinical investigator may be an endangered species. It somehow seems easier to do things in studies the further away you get from the patient.

Two issues have come up recently to make life difficult for the investigator.

It is becoming customary to insist that the blind psychiatrist treating the patient and obtaining the research data not learn which treatment his patient received until the entire study is completed. The reason is that if he learns, for example, that patients on Treatment A do better than those on Treatment B, that may bias his future ratings, especially if he thinks he can, or actually can, distinguish the treatments by their adverse reactions. There is some face validity to this, but consider the clinical consequences. If we are comparing an antidepressant to placebo, what does the clinical investigator do with the patient when he completes the trial? If he responded and received placebo, the clinician would not want to continue drug treatment. If he responded and received the active drug, the best clinical treatment would be to continue the drug openly and not risk relapse by switching to another drug. If the patient did not respond and received placebo, we might choose a different drug for followup care than if he did not respond to an active drug—or a supposedly active one. For example, if the experimental drug is a new tricyclic antidepressant (TCA), we might not wish to try another TCA, but switch to a monoamine oxidase inhibitor or electroconvulsive treatment.

When confronted with this problem, the investigator asks the drug company what it expected him to do with the patient who completed. The answer usually is to put completers on a moderate dose of another antidepressant. This is unreasonable. The patient who had responded to the experimental tricyclic, who gets a lower dose, might relapse; the patient who had not responded to the experimental drug would continue to get a possibly ineffective treatment. The placebo patient who did respond would get a moderate dose of an antidepressant abruptly—unnecessary treatment.

A more common situation would be a comparison of a new antidepressant with a standard one. Similar problems arise if the investigator tries to keep the treating psychiatrist blind and yet able to continue to treat his patient. If the investigator switches everyone who finished the study to a moderate dose of the standard antidepressant, the following would occur:

1. The patient who responded to the experimental drug would be abruptly switched to another;
2. The patient who responded to full dosage of the standard drug would be switched abruptly to a lower dose;
3. The patient who did not respond to the ex-

perimental drug would be switched abruptly to another perhaps similar drug;

4. And, worst of all, the patient who did not respond to full dosage of the standard drug would be switched to a lower dose and face another 6 weeks of ineffective treatment.

Similar unpleasant scenarios could be given for other types of drug trials.

The only way out that this writer could devise was to abruptly switch psychiatrists when the subject finished the study, keeping the first psychiatrist blind and free to continue to treat other patients in the study, while the second psychiatrist broke the blind and received other patients as they finished the study, i.e., a two-platoon system of psychiatrists.

To do all this maneuvering for the sake of the possibility of bias, if the treating psychiatrist breaks the blind as each patient completes, seems to be an example of methodological purity exceeding its bounds.

Another way of avoiding this conflict of interest is to use blind clinical raters and unblind psychiatrists. This is possible, but not perfect: the unblind psychiatrist may adjust dosage differently if he knows he is prescribing an experimental or standard drug, i.e., he may tolerate more adverse reactions of the standard drug. It is more expensive to use clinical raters if the research must pay for both the clinical rater and the psychiatrist.

Another area of difficulty is the use in some recent protocols of the provision that if the dose is lowered, it cannot again be raised because the change in adverse reactions may tip off the blind psychiatrist to whether the drug is active or placebo, or even which of two active drugs is being taken according to differential adverse reactions. This restriction will lead to two results: the blind psychiatrist will be loath to reduce dosage knowing he can not go up again, and be left giving an inadequate dose so that the subject will perhaps suffer needlessly or drop out; or the blind psychiatrist will lower the dose and threaten the accuracy of the study's attempt to answer a clinical question because of insufficient exposure to drugs.

This is another example of trying to restrict the freedom of the investigator for the sake of purer science, but actually losing more than gaining, because the impact on the clinical situation was not adequately considered.

Industry's Response to New Drug Developments

Victor B. Slotnick, Ph.D., M.D.[1]

The pharmaceutical industry maintains an ongoing interaction with the Food and Drug Administration (FDA), clinical investigators, and academia. The following are some examples of interactions that have involved the FDA.

About 5 years ago, the company was planning to initiate a 400-patient program to assess the long-term safety and efficacy of a neuroleptic in chronic schizophrenic outpatients. The patients in this program were to be treated in double-blind fashion for 12 months. During the year of treatment, each patient was to have 10 psychometric assessments. The paperwork involved in collecting efficacy data for each patient consisted of the following: Twenty Brief Psychiatric Rating Scale (BPRS) sheets (10 assessments x 2 sheets per assessment), 10 sheets of outpatient functioning assessments, and 10 sheets of Clinical Global Impressions (CGI) assessments. The total was 40 sheets of paper for each patient.

In discussing the potential paper load with the FDA, company representatives suggested supplying one summary sheet with raw efficacy data for each patient. The FDA agreed with the proposal; however, they recommended the following: 1) that the raw data for each patient be transcribed to the summary sheet after each patient completed treatment; 2) that the senior investigator sign the raw data summary sheets after transcription; and 3) that the investigator keep the original psychometric assessments for the appropriate period of time. The volume of paperwork for each patient's case report form was thus reduced by about 80 percent.

Turnaround Time of Submission to the FDA

Over the last year or so, the company's experience with regard to the amount of time the

---

[1] Clinical Investigation, McNeil Pharmaceutical, Spring House, PA 19477.

FDA has taken to respond to submissions has been encouraging.

In October 1980, a New Drug Application (NDA) for a neuroleptic with data for about 800 patients was submitted. In January 1981 the company received a written request for additional information and a request to meet with the FDA. Company representatives met with the FDA to discuss the NDA and requested that the NDA be presented to the FDA and its Advisory Committee in April. Although there was no definitive outcome from presentation to the Advisory Committee, it was heartening to experience a review of an NDA with an Advisory Committee presentation in a period of slightly less then 6 months.

In late October of this year, the company submitted a supplemental NDA to the Division. About *10 days later,* the company received a letter from the FDA indicating that the supplemental NDA had been reviewed to a limited extent and the Division felt that the submission should be transferred from supplemental NDA status to NDA status. Although the review of the NDA is still in progress, information apprising us of the status of our submission was obtained from the FDA in a relatively short period of time.

About 6 weeks ago, the company submitted a special clinical safety report for an investigational neuroleptic to the FDA. A copy of the report was hand-carried to the FDA the morning of the day of submission. That afternoon, the FDA contacted our Regulatory Affairs personnel with questions and comments concerning that submission—a same-day response.

Requests from Investigators for Clinical Supplies

During the past several years, the company has received many requests from physicians for clinical supplies. Most of these requests have been for placebos to match oral or injectable dosage forms of the company's commercially available drugs. About 1 1/2 years ago, the company implemented a policy about such placebos: they are considered to be investigational drugs. In order to obtain placebos to match marketed drugs, an investigator is required by the company to file with the FDA and obtain an individual investigational new drug (IND) number. In general, the investigators requesting placebos have cooperated with this policy.

Compassionate INDs

A working definition of a "compassionate IND" is as follows: A request by a physician to the FDA to treat a patient who has a specific life-threatening or non-life-threatening clinical condition with an investigational drug. It should be noted that the current FDA regulations make no mention of compassionate INDs. It is a fairly safe assumption that most pharmaceutical companies represented in the audience receive a fair number of requests for their investigational drugs to be used in compassionate clinical situations.

About a year ago, McNeil received a special request from one division of the FDA concerning compassionate INDs. It appeared that this division had received many requests from individual physicians requesting to study a McNeil investigational drug in two non-life-threatening compassionate clinical conditions. Because of the increased workload for the FDA, they requested that McNeil file the paperwork for those individual physicians under the company's IND for that drug.

However, an informal survey of medical colleagues revealed that other divisions of the FDA permit physicians to file directly with the FDA in order to obtain a compassionate IND.

Although McNeil was not averse to working with the Neuropharmacology Division, the problem could have been handled satisfactorily with less burden placed upon the sponsor if the Division had given McNeil a special IND number for those compassionate studies with the provision that the IND be supplemented with those physicians wishing to use the investigational drug. In all fairness, it must be added that the Division did bend a bit. At McNeil's request they allowed a reduction of the frequency of monitoring visits by the company's clinical research support staff.

Physician-Investigator Without an Institutional Review Board (IRB)

In July of 1981, the FDA published a new regulation to the effect that physicians treating patients with investigational drugs outside an institutional setting are required to have IRB approval for their studies. Most of the clinical investigators in the audience probably do not fall into this category because of their institutional setting. However, and perhaps more commonly in areas other than psychopharmacology, many private practice physicians interested in conducting investigational drug studies do not now have IRBs available to review their protocols.

In anticipation of the above regulations, and prior to their publication in the *Federal Register,* McNeil Pharmaceutical set up and organized an independent IRB in the area near McNeil. The Spring House IRB became operational in September 1981.

The Spring House IRB, in addition to protecting the patient, serves the following purposes:

1. to make an IRB available to any private practice physician interested in conducting a study with an investigational drug protocol for McNeil Pharmaceutical;
2. to reduce the cost for the approval of an investigational drug protocol; and
3. to reduce the time required for review and approval of an investigational drug protocol.

The Balance Sheet (The Other Side of the Ledger)

Paul Leber, M.D.[1]

Alistair Cooke, the noted TV essayist, once asked a bootblack, who was on the eve of his retirement, what he had learned about life in America during the many years he had shined shoes in the corridors of New York's Grand Central Station. The man, who had immigrated from Europe as a child some 70 years earlier, said without a moment's hesitation "In America, there is no free lunch!"

The bootblack clearly understood a basic principle, not, of course, unique to American soil, that you rarely get something for nothing. It is interesting to examine how this "natural" law applies to our attempts to respond to the perceived public demand for less costly and more efficient new drug development and approval.

In general, costs are conceived in terms of either time or money. In the course of clinical drug development, costs are obviously affected by the number of subjects studied, the complexity of clinical trial design, and the task and cost of data analysis. For example, increasing the complexity of the clinical trials (i.e., adding more kinds of observations and having them made more often by several independent raters) will obviously increase costs. Moreover, the subsequent analysis of data collected from large and complicated trials will also be more difficult, more expensive, and more time consuming. Sheer numbers count, too! While it is conceivable that the cost per subject or cost per individual study may fall as the absolute numbers of patients and studies increase, it is safe to assume that, other factors held constant, a new drug application (NDA) based on 20 Phase III studies enrolling 1,000 subjects will cost more than one with 10 studies enrolling 500 patients.

Given these facts, it is not surprising that, in the face of a public mandate to reduce cost, both the Agency and commercial sponsors will consider the feasibility of reducing (1) trial design complexity, (2) the number of subjects studied, and (3) the cost of data analysis in the preapproval/premarketing phase of new drug development.

This is all well and good, but recall that there is no free lunch! Pay less; get less!

It is the author's purpose to focus your attention on the other side of the balance sheet not pass judgment on the specific items involved nor judge the relative merits of the assets and debits entered. He wishes only point out that changes in one side of the ledger require changes in another part.

First the obvious. If fewer subjects are studied during the premarketing phase of new drug evaluation, our ability to detect relatively low frequency adverse or untoward drug effects will be decreased. A quick calculation illustrates any point. To be 95 percent certain of detecting at least one example of an event which occurs at an incidence of 1 per 100 patients treated for 1 month at some effective dose level of a drug, 300 patients must be observed at that dose (or a higher one) for the month. This figure is derived assuming a Poisson distribution of rare events. For general use, a good rule of thumb is that the number of subjects studied must be equal to three times the

---

[1] Food and Drug Administration, Rockville, MD 20857.

reciprocal of the estimated event rate (i.e., 300 for an incidence of 1 per 100, 1500 for an incidence of 1 per 500).

Again, the author is not passing judgment; he is merely emphasizing that if we elect to study fewer patients before a drug is approved, one should not be surprised if a relatively common adverse event is reported during postmarketing experience which was not detected during premarketing drug trials. *Parenthetically, the FDA is well aware of this problem and is actively expanding existing and developing new postmarketing surveillance strategies and programs.*

In contrast to safety, drug efficacy is determined in an absolute sense and is thus less likely to be affected by current trends toward smaller sample sizes. Thus, sample size can only be reduced to the point that the potency of the drug (that is, its efficacy) will allow.

Experts today are, in the author's opinion, even more exacting than in the past about what kind and quality of evidence collected from controlled clinical investigations is persuasive and substantial (i.e., evidence sufficient for drug approval). Thus, a modest drug, which is only slightly more effective than placebo, may require that many more subjects be studied to establish its efficacy than a potent drug would. One caveat, the author is not speaking to the issue of the magnitude of clinical effectiveness declared clinically meaningful. Rather, his comments assume that a small mean difference observed or produced by a modest drug is clinically meaningful and that it will thus require more subjects to demonstrate the statistical significance of this mean difference than it would if the mean difference were large.

There is a chance, of course, that when cost is the determining factor, it may prove more economical to use sophisticated multivariate statistical techniques to establish statistical significance than to enroll more patients or to conduct additional trials.

One problem arises when fewer subjects are studied, however, that has not often been discussed but deserves consideration and attention.

It is far simpler to demonstrate that a drug is active and efficacious than it is to describe, in detail and with precision, for whom it should be used and under what specific conditions. You may all recall that our regulations require that a prescription drug's labeling (professional package insert) provide the practitioner with adequate directions to use the drug in the population for whom it is intended.

The fewer patients studied in the premarketing phase of drug development, the more difficult it becomes to provide detailed and precise directions for the use of the drug.

Several of you were present at the recent Psychopharmacologic Drugs Advisory Committee meeting on December 3-4. You saw the advisory committee struggle with this very issue. Although convinced that two new antidepressant drug products were efficacious, it was difficult to describe, in detail, precisely for whom and under what conditions each drug should be used. It is obvious that current diagnostic categorizations (which have become possible with advances in the understanding of depressive disease) make it even more difficult to describe drug use with small numbers of subjects and limited number of trials.

In an idealized world, with an infinite amount of time, and where money was no object, we could block subjects on every diagnostic feature of potential interest and, conducting extensive trials of complicated design, determine precisely what portion of the potential patient population should take a new drug, and what would happen to them. Then we could write very complete and accurate drug labeling. But, as the English novelist Butler suggested approximately 100 years ago, *life is the task of drawing satisfactory inferences from inadequate premises.* If we are to follow the public mandate for less costly and speedier drug approval, we may have to accept broader labeling inferences from smaller and perhaps narrower data bases. Just how much smaller and how much narrower is an issue many of you in the audience will help decide while serving in your roles as our official advisors and outside experts. The issues involved are broad and beyond those covered by law. It is clearly a matter of informed judgment how much must be known about an active and efficacious drug before it is introduced into the market place. These are the questions we will all have to answer.

It is useful to remember, too, that there "is no free lunch." If we extensively modify the new drug development process as is now being actively considered in order to expedite the development and approval process of new drugs, a complete understanding of a new drug's best use may have to come from postmarketing experience and reassessment of the drug's benefit/risk ratio. Remember, there are no absolutes in this process. Words and phrases like "well controlled" and "substantial" and "adequate direction for use" are determined by the opinion of experts as much as by law. The FDA looks forward to your careful consideration and counsel on these important issues.

New Biological Approaches to Schizophrenia

Co-Chair: Philip A. Berger, M.D.
Department of Psychiatry and Behavioral Sciences
Stanford University School of Medicine
Stanford, California

and

Jack D. Barchas, M.D.
Department of Psychiatry and Behavioral Sciences
Stanford University School of Medicine
Stanford, California

Dopamine Neuronal Instability: A Model for the Schizophreniform Psychoses[1]

Roy J. King, M.D., Ph.D.;[2] Joachim D. Raese, M.D.,[2] Bernard A. Huberman, Ph.D.,[3] and Jack D. Barchas, M.D.[2]

The dopamine model of schizophrenia predicts that an excess in dopamine (DA) causes psychotic symptoms. Such a simple excess is not confirmed by the observed behavior of schizophrenics. Bleuler (1950) noted that schizophrenic individuals often manifest rapidly alternating and mutually contradictory affect, thought, and activity. Ellinwood et al. (1974), after injecting amphetamine chronically to cats, found a desynchronization and a fragmentation of their stereotypic behavior. Moreover, experimental evidence has not revealed an increase of dopamine function in schizophrenics. The authors propose here that, rather than an excess of DA, psychotic individuals exhibit an instability in dopaminergic function. This instability would be caused by an excessive dopaminergic feedback. Since the dopaminergic system appears to be well modulated with a variety of feedback mechanisms, including long-loop neuronal feedback, short-loop local inhibitory feedback, and regulation of dopamine synthesis through the activation of tyrosine hydroxylase, these mechanisms may be more crucial in determining psychotic symptoms. It is well know that systems with a high degree of negative feedback are relatively insensitive to slow changes in internal parameters or external input. However, they may become unstable with increasing feedback. These instabilities fall into three major classes:

1. the appearance of multiple equilibrium states;
2. the creation of autonomous oscillations; and
3. a chaotic behavior with a sensitive dependence on initial conditions and unpredictable variations in state.

It has been mathematically demonstrated that modeling the currently known feedback mechanisms of the dopaminergic system will lead

---

[1] This study was supported by USPHS Grant MH-23861 from the National Institute of Mental Health and by the Scottish Rite.

[2] Nancy Pritzker Laboratory of Behavioral Neurochemistry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305.

[3] Xerox Palo Alto Research Center, Palo Alto, CA 94304.

to the appearance of these instabilities (King et al. 1981). Herein the authors summarize the relationship between these instabilities and offer predictions about schizophrenic behavior. DA feedback mechanisms involve several time constants: neuronal feedback, occurring rapidly over a period of 1/3 to 2 seconds, activation and deactivation of dopamine synthesis proceeding over periods of 10 to 20 minutes, and long-term up-and-down regulation of dopaminergic receptors occurring over periods of days to weeks. The proposed increased feedback in psychotic individuals will lead to instabilities of behavior on all three time scales. This increased feedback can occur through a variety of mechanisms. For example, an increased release, decreased reuptake, increased synthesis, or increased postsynaptic DA receptor activity will all lead to an increased feedback gain. Likewise, an increased autoreceptor activity, a decreased DA synthesis, or a postsynaptic blockade of dopamine receptors will result in a net decreased feedback. Thus, the former procedures will lead to instability, whereas the latter modifications will rectify that instability. The authors now describe the effect of changing these parameters on the dynamical behavior.

One-third to Two Seconds. Because of the delays in activating and deactivating postsynaptic DA and GABA receptors, a simple stable equilibrium of dopaminergic activity can, by increasing feedback gain, bifurcate into periodic oscillations in dopaminergic firing. These oscillations will have a frequency of the order of the time constant for the delay, that is, 3 Hz to 1/2 Hz. Because the dopaminergic system projects directly to various regions of the limbic system and the striatum, and indirectly projects through the pars reticulata of the substantia nigra to the brainstem, one might expect that psychotic individuals would exhibit this periodic disturbance in activity. Such fluctuating activity has been reported by Ellinwood et al. (1974) in cats treated chronically with amphetamine and by Heath (1954) in subcortical recordings of electrical activity in schizophrenics. Behaviorally this autonomous slow-wave activity might manifest inself, for instance, in the thought disorder, perceptual changes, and eye-tracking disturbances observed in some schizophrenic patients.

Ten to Twenty Minutes. The dopaminergic system is unique among the monoamines in that with both an increase and a decrease in firing, there is an increased activation of dopamine synthesis (Nowycky & Roth 1978). It can be shown that for greater than a fourfold increase in dopamine synthesis at low firing rates, the single homeostatic equilibrium of the dopaminergic system will bifurcate into two stable equilibria. One of these equilibria has a relatively high mean DA output while the other has a lower DA activity. The low dopaminergic state will progressively, with increasing long-loop feedback gain, bifurcate further into oscillations and chaotic activity. This periodic or erratic activity will have a time constant of around 10-20 minutes. In addition, since the dopamine nuclei appear to be loosely coupled, that is, an activation of the one substantia nigra results in a deactivation of the contralateral substantia nigra (Nieoullon et al. 1977), this chaotic activity may decouple the left substantia nigra from the right substantia nigra or a substantia nigra nucleus from a ventral tegmental dopaminergic nucleus. One might, therefore, observe rapid transitions between high and low dopaminergic states as well as spatially decoupled simultaneously activated and deactivated dopaminergic states. This prediction may agree phenomenologically with Bleuler's reports on schizophrenic ambivalence of affect, will, and thought.

Furthermore, the addition of amphetamine, although initially causing a transition from a normal to a chaotic state, could remove a DA nucleus from a chaotic state and place it in a relatively stable high DA activity state. This might explain some of the results reported by van Kammen et al. (1980) on the stabilizing effect of amphetamine given to acutely psychotic individuals.

Days to Weeks. With the bifurcation of DA activity into a low and high DA state, long-term, up-and-down regulation of DA receptor activity could result in oscillations of dopamine function over a period of days to weeks. This behavior can take the form of either bistable oscillations or pulses with rapid transitions from a low to a high DA state. This would be followed by a plateau in DA activity, leading ultimately to a sudden post-plateau drop in DA activity at levels lower than those of the initial DA state. Antleman and Chiodo (1981) have shown that chronic amphetamine, tricyclic antidepressants, and rapid-eye-movement (REM) sleep deprivation may all lead to a subsensitivity of the dopaminergic nigral autoreceptors. Since a decrease in the sensitivity of the autoreceptors causes a net increase in feedback gain, these procedures could lead to a rapidly cycling transition between low to high DA states. Furthermore, if the feedback gain is initially large, the transitions between the low and high dopaminergic states will be chaotic and weakly correlated with transitions from low to high dopaminergic states in other dopaminergic nuclei. Such behavior might be similar to that of an acute schizophreniform psychosis. The schizoaffective psychoses additionally could manifest themselves in oscillations between high and low dopaminergic states that are relatively unsynchronized between neighboring nuclei.

In summary, it is proposed that psychosis results from an excessive DA long-loop feedback. The gain of this feedback circuit can be modified through a variety of mechanisms. Because of the large feedback, a schizophrenic and a nonschizophrenic individual may not differ in the mean values of any parameter monitoring DA activity. However, as a result of the increased instability in DA function, the psychotic individual will show greater spatio-temporal variability in DA activity. On a time scale of seconds, this instability will result in oscillations of neuronal activity that can spread to various subcortical and cortical regions. Over a period of minutes, DA activity will bifurcate into multiple stable states, periodic oscillations, and chaotic activity. On a time course of days to weeks, long-term regulation of DA receptor density can lead to the precipitation of that chaotic or oscillatory behavior. This model is consistent with a variety of genetic and environmental factors leading to a common instability in dopaminergic function.

References

Antelman, S., and Chioda, L. Dopamine autoreceptor subsensitivity: A mechanism common to the treatment of depression and the induction of amphetamine psychosis? *Biol. Psychiatry,* 16(8):717-727, 1981.

Bleuler, E. *Dementia Praecox; or, The Group of Schizophrenias.* New York: International Universities Press, 1950.

Ellinwood, E., Sudilovsky, A., and Nelson, L. Behavior and EEG analysis of chronic amphetamine effect. *Biol. Psychiatry,* 8(2):169-176, 1974.

Heath, R. *Studies in Schizophrenia.* Cambridge: Harvard University Press, 1954, pp. 157-194.

King, R., Raese, J.D., and Barchas, J.D. Catastrophe theory of dopaminergic transmission: A revised dopamine hypothesis of schizophrenia. *J. Theoret. Biol.,* 92:373-400, 1981.

Nieoullon, A., Cheramy, A., and Glowinski, J. Interdependence of the nigrostriatal dopaminergic systems on the two sides of the brain in the cat. *Science,* 198:416-418, 1977.

Nowycky, M., and Roth, R. Dopaminergic neurons: Role of the presynaptic receptor in the regulation of transmitter biosynthesis. *Prog. Neuropsychopharmacol.,* 2:139-158, 1978.

van Kammen, D.P., Docherty, J.P., Marder, S.R., Schulz, C., and Bunney, W.E., Jr. Lack of behavioral supersensitivity to *d*-amphetamine after pimozide withdrawal. *Arch. Gen. Psychiatry,* 37:287-290, 1980.

Retinal Oscillatory Potentials in Schizophrenia: Implications for the Assessment of Dopamine Transmission in Man[1]

Joachim D. Raese, M.D.,[2] Roy J. King, M.D., Ph.D.,[2] Debbie Barnes,[3] Philip A. Berger, M.D.,[2] Jack D. Barchas, M.D.,[2] Michael Marmor, M.D.,[3] and Peggy Hock, Ph.D.[3]

Recently, a new formulation of the dopamine (DA)-hypothesis of schizophrenia has been presented which shows that for certain unstable properties of dopaminergic feedback loops a spatial and/or temporal desynchronization will occur resulting in fragmentation of a dopaminergic nucleus into clusters of cells locked into high and low firing states (King et al. 1981, in press). This restatement of the DA-hypothesis does not predict net changes in DA or its metabolite concentrations.

This hypothesis was tested by examining the properties of the light-evoked oscillations in the retina which can be recorded from the anesthetized cornea. The rationale for this approach is based on several observations: 1) The mammalian contains a substantial concentration of DA (Haggendal & Malmfors 1963) as well as tyrosine hydroxylase (Juvone et al. 1978a, 1978b; Juvone & Neff 1981) in the amacrine cell layer. Retinal tyrosine hydroxylase is rapidly activated by exposure of the eye to light (Juvone et al. 1978a, 1978b). The activation is associated with kinetic changes of the enzyme identical to those occurring in nigrostriatal neurons (Nowycky & Roth 1978). 2) The activation of tyrosine hydroxylase is inhibited by gamma-aminobutyric acid (GABA) (Morgan & Kamp 1980) located together with DA-containing neurons in the amacrine cell layer, suggesting a DA-GABA feedback loop similar to central DA-GABA synaptic connections (Nowycky & Roth 1978). 3) DA-receptors modulate DA-turnover in the retina in a way which is analogous to the brain, i.e., dopamine-blocking drugs such as neuroleptics will increase, and activation of presynaptic receptors by apomorphine will decrease DA-turnover (Wassenaar & Korf 1976). 4) DA-depletion of the retina by reserpine will abolish the oscillatory potentials (OPs) in the rabbit (Hempel 1972-1973) which can be restored by intravitriol injection of the DA-precursor l-DOPA (Gutierrez & Spiguel 1973). The GABA antagonists bicuculline and picrotoxin also abolish the OPs (Wachtmeister 1980), indicating that both intact DA and GABA transmission are necessary for the OPs to be elicited.

---

[1] This study was supported by USPHS Grants MH-23861 and MH-30854 from the National Institute of Mental Health and by the Scottish Rite.

[2] Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305.

[3] Department of Ophthalmology, Stanford University School of Medicine, Stanford, CA 94305.

Address correspondence to Dr. Raese.

In this paper, data are presented which suggest that the OPs are modulated by dopaminergic activity in man. The investigators' approach consisted of: 1) a detailed statistical comparison of waveforms obtained from normal volunteers and drug-free schizophrenic subjects; and 2) stimulation of DA-transmission by amphetamine.

Methods

All patients participating in the study were men (ages 28-58) hospitalized at the Clinical Research Center at the Veterans Administration Medical Center in Palo Alto, California. The patients were managed without use of psychotropic medication for 2 weeks prior to the study. They were given diagnoses of schizophrenia or schizoaffective psychosis using Research Diagnostic Criteria (Spitzer et al. 1978) by three clinicians independently. Patients gave informed consent to the study, which was approved by the Committee on Research on Human Subjects at Stanford University. Patients were rated weekly by two clinicians using the Brief Psychiatric Rating Scale.

Subjects received intraocular drops into the right eye of mydriacyl and neosynephrine to maximally dilate the pupil. After dark adaptation of the eyes for 20 minutes, surface anesthesia was induced by applying novesine drops to the eye, and a contact lens (Burien-Allan) fitted with electrodes was placed on the cornea. A light source (Grass) was placed 25 cm from the eye, its power supply set to maximal intensity (W16), and light stimulation was carried out in 10-second intervals by triggering the lamp and simultaneously a sweep of 100 msec duration on a storage oscilloscope (Tektronix). Oscillatory potentials were recorded using a frequency filter attenuating frequencies below 100 Hz. Traces stored on the oscilloscope screen were photographed using a Polaroid camera.

The negative and positive deflections constituting the retinal light-evoked response were measured as shown in Fig 1-A and will be referred to as Relative Amplitudes (RA). Positive RA were assigned the labels 0[1], 0[2], and 0[3] in order of their latencies from the stimulus. Similarly, negative RA were termed N[1], N[2], and N[3] such that the alternating positive and negative RA of the waveform are described by the sequence 0[1] − N[1] − 0[2] − N[2] − 0[3] − N[4] (Figure 1-A). Latencies were measured as shown in Fig 1-B by determining the distance from the first negativity to the first peak 0[1] and assigned the label Δ0[1]. The distance representing the time elapsed from 0[1] to the trough N[1] was termed ΔN[1], etc. ΔO[1] through ΔN[3] will be referred to as Relative Latencies (RL).

All values of Relative Amplitudes were scaled by calculating their natural log. These natural logs were used to calculate the means, standard deviations, and variance of 5 to 11 measurements of each RA in each subject. The grand pooled variance for the RAs 0[1] through N[3] was determined for eight normal subjects and nine schizophrenic patients utilizing between 55 and 70 measurements for each RA for each of the two groups

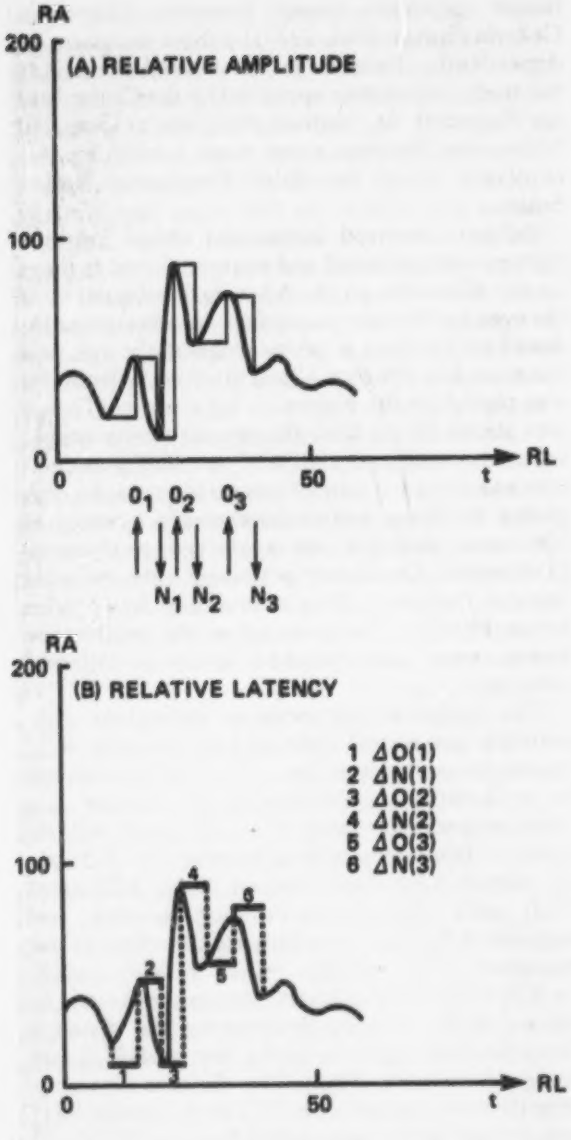


FIGURE 1. Determination of Values for the Major OP-Waveforms. We define the sequence 0[1], N[1], 0[2], . . . and A) determine the length RA = Relative Amplitude = $PA_i - PA_{i-1}$. B) Time (t) elapsed from stimulus (t = 0) is measured and the sequential periods labeled 1, 2, . . . 6 are assigned the labels Δ0[1], ΔN[1], . . .ΔN[3] = Relative Latencies.

Relative latencies were evaluated similarly except that unscaled values were used. Variances were compared by *F*-statistics, means by two-tailed *t*-test.

Results

Increased Variability of OPs in Schizophrenic Subject

Light stimulation of the dark adapted retina produces oscillatory waveforms characterized by increasing amplitude and stabilization of the oscillations in response to consecutive light flashes. Fig 2, A-C, illustrates that the OPs in three normal volunteers have stabilized after three light flashes.

Oscillatory potentials recorded from three schizophrenic patients are shown in Fig 2, D-F. Visual inspection reveals a lack of synchronization of the waveform.

In order to quantify this observation, the Relative Amplitudes and Latencies were determined as described in the Methods section. The Table shows the variances of RA and RL, respectively, of 11 normal and 11 schizophrenic subjects. Compared to normal subjects, schizophrenics had significantly greater variance of RA N[1] and N[3] while N[2] approached significance. The positive deflections 0[3] had similar variance in both groups. 0[1] and 0[2] had significantly higher variance in the control group. It should be noted that a major portion of this variance was contributed by one control subject who had extrememly high variance in this parameter. Interestingly, the subject has carried the diagnosis of dyslexia since childhood. This observation deserves further investigation.

The Table shows significantly higher variance in schizophrenia of RL ΔN[1] through Δ0[3], which corresponds to the time span encompassing the major OPs (*see* Figure 1, A and B), indicating that the time evolution of the central part of the evoked waveform is quite variable in schizophrenic subjects.

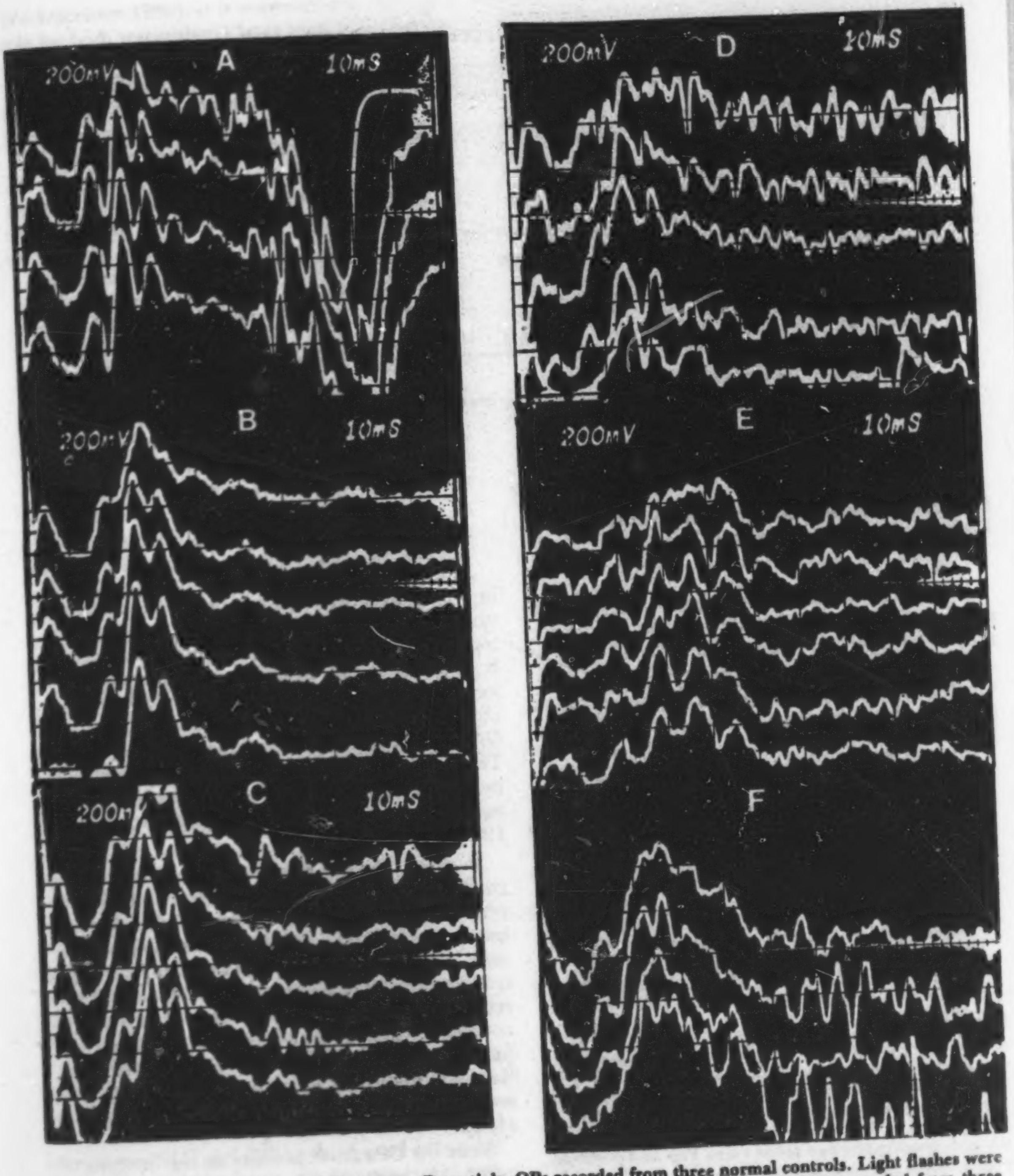


FIGURE 2. Oscilloscope Traces of Oscillatory Potentials. OPs recorded from three normal controls. Light flashes were given at a rate of 1 per 10 seconds. Sequence is from top to bottom of each panel (A - C). OPs recorded from three schizophrenic patients (D - F).

Table

Variance of Relative Amplitudes and Latencies of OPs

			Relative Amplitudes			
RA	0[1]	N[1]	0[2]	N[2]	0[3]	N[3]
Schizophrenia σ_p^2	.050	.150	.030	.190	.116	.073
Controls σ_p^2	.076	.106	.071	.142	.129	.043
p<	.026	.005*	.001	.08*	N.S.	.006*
			Relative Latencies			
RL	Δ0[1]	ΔN[1]	ΔN[2]	ΔN[2]	Δ0[3]	ΔN[3]
Schizophrenia σ_p^2	.012	.003	.008	.012	.003	.011
Controls σ_p^2	.012	.002	.003	.003	.002	.019
p<	N.S.	.05*	.001*	.001*	.05*	.005

*Schizophrenia > Controls
All others, Controls > Schizophrenia
Eleven controls and eleven schizophrenic subjects were studied and their OPs analyzed as described in the text. The variances (σ_p^2) of RA and RL values are shown. Significance was calculatec using the *F*-distribution.

Effect of Acute *D*-Amphetamine on the Relative Amplitude of the OPs

Baseline recordings were obtained from five subjects. One hour before their second recording they were given a single oral dose of 15 mg *d*-amphetamine. Amphetamine increased the mean relative amplitude (RA) of the oscillations (Fig 3) with the largest effects on 0[1], N[1], and N[2].

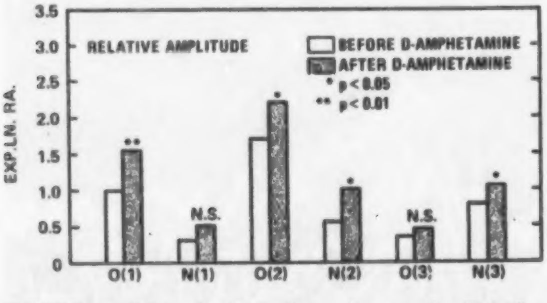


FIGURE 3. Effect of *d*-Amphetamine on the Relative Amplitude of Oscillatory Potentials. Two recordings were obtained from each subject. Subjects were given 15 mg of *d*-amphetamine orally 1 hour prior to their second recording session. The means of the natural log transforms of the RA obtained in the two sessions were calculated for each RA and compared by two-tailed *t*-test. Pre- and postdrug values of RA are plotted after exponentiation (exp. LN .RA).

Discussion

Animal studies suggest that the OPs originate in deeper layers of the retina, the earlier potentials originating in different layers than the later ones, indicating a radial flow of current (Wachtmeister & Dowling 1978). In addition to this particular anatomical organization, the individual OPs are characterized by differential sensitivity to the GABA antagonists bicuculline and picrotoxin. The latter observation is consistent with the hypothesis that different transmitters may be modulating earlier and later OPs (Wachtmeister 1980).

In this study, the OPs were recorded from the cornea, i.e., at a great distance from where they originate. The recording represents, therefore, an integration of the activity of entire cell populations which must be firing synchronously in sequence in order to generate the oscillatory evoked response. This behavior is consistent with that of coupled oscillators time-locked to a stimulus. It has been suggested that the OPs reflect the radial flow of current through feedback loops connecting retinal layers of different depths (Wachtmeister 1980).

Since the OPs are dependent on the integrity of both DA and GABA transmission (Hempel 1972-1973; Gutierrez & Spiguel 1973;

Wachtmeister 1980), it is reasonable to assume a role for both transmitters in at least some aspects of their regulation.

Several findings are presented suggesting a modulatory role for dopamine in the generation of OPs in man:

1) *d-amphetamine, a compound known to enhance DA-transmission, significantly increased the amplitude of the OPs.* To the best of our knowledge, this is the first report of a direct effect of DA-transmission on the OPs of man.

There are only two brief reports on pharmacological manipulation of DA on the raw electroretinogram (ERG). A single oral dose of thioridazine (50 mg) caused a prolongation of the a-wave latency and b-wave evolution time, as well as a diminution of b-wave amplitude in normal volunteers (Filip & Balik 1978). The same group reported the lack of an effect of 500 mg L-DOPA on the same ERG parameters (Balik & Filip 1978). In neither study, however, were the OPs recorded.

Since the OPs ride on the ascending slope of the b-wave, it is conceivable that amphetamine could influence the OPs through b-wave changes. Examination of b-waves obtained pre- and postdrug treatment, revealed no significant increase or decrease of the b-wave (data not shown). This finding is in keeping with the observations that b-wave and OPs originate in different layers of the retina and that compounds such as GABA and glutamate, which profoundly affect the OPs, have no effect on the b-wave (Wachtmeister 1980).

2) *Schizophrenic patients have higher variance of OPs than controls.* The variance of the RAs of the first six negative and positive deflections of the OPs and the Relative Latencies in 11 control and 11 schizophrenic subjects were analyzed (Table). The negative RAs N[1], N[2], and N[3] had greater variance in the schizophrenic group. This "selectivity" militates against the argument that a "nonspecific" increase in noise could account for the desynchronized appearance of the OPs (Figure 2). The variance of the RL in the schizophrenic group is significantly increased in $\Delta 0[2]$ through $\Delta 0[3]$ which together constitute the major part of the entire waveform.

It should be pointed out that the increased variances of 0[1] and 0[2] in the control group are due to one control subject who had extremely high variances in these parameters. The subject had no psychiatric history but suffered from developmental dyslexia. Further studies will be necessary to decide whether there is a causal relationship of ERG parameters and that diagnosis.

Ranking the 11 patients according to their OP variance revealed that the major contribution of the pooled group variance was contributed by five patients, all of whom suffered from auditory hallucinations.

Although our total group size is small, this finding suggests the existence of subgroups of schizophrenic patients who may be differentiated by using the OPs record as criterion. This preliminary finding would suggest that desynchronized OPs may be associated with productive symptoms such as auditory hallucinations.

References

Balik, J., and Filip, V. L-DOPA does not affect the electroretinogram in man. *Act. Nerv. Super. (Praha),* 20:259-260, 1978.

Filip, V., and Balik, J. Possible indication of dopaminergic blockade in man by electroretinograph. *Int. Pharmacol. Psychiatry,* 13:151-156, 1978.

Gutierrez, C., and Spiguel, R.D. Oscillatory potentials of the cat retina. *Life Sci.,* 13:991, 1973.

Haggendal, J., and Malmfors, T. Evidence for DA as retinal transmitter: Evidence of DA-containing neurons in the retina of rabbits. *Acta Physiol. Scand.,* 64:58-66, 1963.

Hempel, F.G. Modification of the rabbit electroretinogram by reserpine. *Ophthalmol. Res.,* 4:65, 1972-1973.

Juvone, P.M., Gall, C.L., and Neff, N.H. Retinal tyrosine hydroxylase: Comparison of short-term and long-term stimulation by light. *Mol. Pharmacol.,* 14:1212-1219, 1978a.

Juvone, P.M., Gall, C.L., Garrison-Gunt, C.K., and Neff, N.H. Light stimulates tyrosine hydroxylase activity and dopamine synthesis in retinal amacrine neurons. *Science,* 202:901-902, 1978b.

Juvone, P.M., and Neff, N.H. Dopamine neurons of the retina: A simple model system for studying synaptic regulatory mechanisms. *Essays Neurochem. Neuropharmacol.,* 5:75-94, 1981.

King, R., Raese, J.D., and Barchas, J.D. A mathematical model of central dopaminergic transmission and the dopamine hypothesis of schizophenia. In: Proceedings of the Second Conference on Monoamine Enzymes, Airlie House, Warrenton, Virginia, March 6-8, 1981. (In press)

King, R., Raese, J.D., and Barchas, J.D. Catastrophe theory of dopaminergic transmission: A revised dopamine hypothesis of schizophrenia. *J. Theoret. Biol.,* 92:373-400, 1981.

Morgan, W.W., and Kamp, C.W. A GABAergic influence on the light-induced increase in dopamine turnover in the dark adapted rat retina in vivo. *J. Neurochem.*, 34:1082-1086, 1980.

Nowycky, M.C., and Roth, R.H. Dopaminergic neurons: Role of the presynaptic receptor in the regulation of transmitter biosynthesis. *Prog. Neuropsychopharmacol.*, 2:139-158, 1978.

Spitzer, R.L., Endicott, J., and Robins, E. *Research Diagnostic Criteria (RDC) For A Selected Group of Functional Disorders*, 3d ed. New York:Biometrics Research, New York State Psychiatric Institute, 1978, pp. 9-13.

Wachtmeister, L. Further studies of the chemical sensitivity of the oscillatory potentials of the electroretinogram (ERG). *Acta Ophthalmol.*, 58:712-725, 1980.

Wachtmeister, L., and Dowling, J.E. The oscillatory potentials of the mud-puppy retina. *Invest. Ophthalmol. Visual Sci.*, 17:1176-1188, 1978.

Wassenaar, J.S., and Korf, J. Characterization of catecholamine receptors in rat retine. In: Bonting, S.L. (ed.), *Transmitters in the Visual Process*. Oxford:Pergamon Press, 1976, pp. 199-218.

A Convergence of Findings in the Psychophysiology of Schizophrenia[1]

Walton T. Roth, M.D.,[2] and Jared R. Tinklenberg, M.D.[2]

The history of the psychophysiology of schizophrenia has been similar to the history of other research approaches to this disease. Instead of steady progress over time, there have been sporadic reports of cardiovascular, electrodermal, EEG spectral, and, most recently, event-related potential (ERP) abnormalities that have proved minor, secondary, or unreplicable. Furthermore, there has been no theory to coordinate the diverse physiological measurements and give direction to experimental programs, except for the very general concept of activation or arousal, which is often applied in a post hoc fashion to explain whatever physiological differences are observed. Activation is probably more relevant to the understanding of anxiety states than to psychosis, though it would not be surprising to find high tonic levels of activation in patients whose psychosis has made them fearful.

Recently, a possible convergence of findings has become apparent that is consistent and unexpected. Skin conductance response (SCR) nonresponding and ERP P300 reduction have been observed in schizophrenic patients repeatedly in the last 10 years by groups of researchers who were quite unaware of each other's techniques, literature, and theories. That unawareness, though unfortunate in many ways, lends an element of independent verification to these findings, if a theoretical and empirical bridge can be built to show that the two phenomena have the same psychobiological basis.

---

[1] Preparation was supported by the Medical Research Service of the Veterans Administration, NIMH Special Research Center Grant MH-30854, and NIMH Grant MH-35330.

[2] Laboratory of Clinical Psychopharmacology and Psychophysiology, Veterans Administration Medical Center, Palo Alto, CA 94304 and Department of Psychiatry and Behavioral Science, Stanford University School of Medicine, Stanford, CA 94305.

Send reprint requests to Walton T. Roth, M.D., Psychiatry (116A3), VA Medical Center, 3801 Miranda Ave., Palo Alto, CA 94304, USA.

SCR is a transient decrease of skin resistance to novel or otherwise salient stimuli, usually measured on the palm where it has a latency of 2 or 3 seconds. The essential facts about SCR and psychosis are these:

1. SCR nonresponding is defined as responding once or not at all in a standard habituation paradigm with 75 dB sound pressure level, 1-second tones, and inter-stimulus interval (ISIs) from 25 to 45 seconds. According to this definition, 50 percent of schizophrenics are nonresponders, while only 15 percent of controls are nonresponders. Retarded depressives also have higher incidence of nonresponding than controls.
2. The ratio of evoked SCR/spontaneous SCR is much less for schizophrenics than for controls. This excludes simple arousal explanations.
3. Nonresponding schizophrenics become responders if the tone intensity in the habituation paradigm is increased or if a response is required.
4. Nonresponding schizophrenics are characterized clinically by emotional withdrawal, conceptual disorganization, and depressed mood.
5. There is some evidence that nonresponding is a trait: it has a higher incidence in preschizophrenics, and nonresponding schizophrenics continue to be nonresponders after clinical remission.

These assertions are based on investigations reviewed by Venables (1977) and Öhman (1981), who provide exhaustive lists of relevant references.

The phenomenon of nonresponding is extremely well-documented: at least five independent research groups in England, the USA, the Federal Republic of Germany,and Norway have observed it. Nonresponding is seen in both acute and chronic, medicated, and unmedicated patients, though not many first-episode, unmedicated schizophrenics have been tested. Although 15 percent of controls are nonresponders by standard criteria, these subjects may be nonresponders of a different kind than the majority of schizophrenics. Certain subjects fail to show SCRs to any stimuli, presumably because of innate differences that have no psychological meaning. More stringent criteria—for example, only considering subjects to be nonresponders if they evince "spontaneous" SCRs or SCRs to intense stimuli but fail to give SCRs in the standard habituation paradigm—may result in fewer false positives, i.e., nonresponding controls.

P300 by its designation is a positive ERP with a latency of about 300 msec. It has an amplitude on the order of 10 μV at a parietal midline location referenced to the ears or mastoids. Its latency and amplitude are not fixed, but vary widely according to the nature of the stimuli and the way the subject processes them. Table 1 lists 15 investigations of P300 in clinical groups. The investigations were carried out in eight independent laboratories in the USA, Canada, and the Federal Republic of Germany. P300 reduction is present in both unmedicated and medicated schizophrenics; however, as for SCR, few first-episode, unmedicated schizophrenics have been tested in P300 paradigms.

The most common paradigm for eliciting P300 has been designated the "oddball" paradigm in Table 1, following a usage in the ERP literature. The paradigm has the following properties: Two or more easily discriminable types of stimuli, often tones of two pitches, are presented repeatedly at a fixed ISI, usually between 1 and 3 seconds. One type of stimulus is less frequent than the other(s), and is usually made a target for a counting or reaction time (RT) task. These conditions are conducive to the generation of P300s to the infrequent stimuli, at least in normal subjects. Schizophrenics were found to have reduced P300s compared to controls in all paradigms except the two listed as 7C and 15, both of which deviated significantly from the oddball paradigm.

P300 reduction does not appear to be simply a reflection of poorer task performance on the part of schizophrenics. In Studies 6A, 10, and 13, differences remained even when performances were matched between groups. In Study 1, in which subjects were told to *ignore* the stimuli, the schizophrenic P300 reduction could be regarded as better performance since smaller P300s indicate that less attention was paid to the stimuli. However, the relation between ERPs and performance is a complex one, and the consequences of the reduced task involvement often found in psychotic experimental subjects are often subtle (for a review, see Roth, in press-a).

Are SCR nonresponding and P300 reduction in schizophrenics due to the same psychological or biological process? In the past 10 years a great deal has been learned about experimental

Table 1

P300 and Psychosis

Authors	Paradigm	Stimuli	Intensity	Probability	ISI (sec)	Results
1. Roth and Cannon (1972)	oddball, passive	noise, tone	70 dB SPL	.94/.06	1	P230: (S)chizophrenics <(C)ontrols for first 20 infrequents.
2. Levit et al. (1973)	guessing	noise, flash	30 dB HL	.50/.50	4-5	N1-P330:S<(D)depressed<C.
3. Verleger and Cohen (1978)	guessing (modeled after 2)	tone, flash	?	.50/.50	5-15	N1-P340:S<C.
4. Shagass et al. (1977; 1978)	stimulus differences, passive	checkerboard, 2 shocks to digits, click	see ref.	.25/.25/.25/.25	1.5-2	Visual P300:S<C, D<C. Auditory P360:S<C. P300 normal in non-psychotic patients.
5. Roth et al. (1979)	oddball with/without warning, passive	2 tones, chord	65/80 dB SPL	.70/.20/.10	1	P300:S<C but not significant due to large SDs in S and C.
6. Roth et al. (1980a; 1980b)	A. oddball, RT	2 tones; one is target	85 dB SPL	.85/.15	1	P330:S<C; RT: S>C; Hits: S<C; RTSD S>C, but P330:S<C even when RTs matched.
	B. stimulus differences, passive	tone, noise	70/100 dB SPL	.25/.25/.25/.25	4	P300 to 100 dB noise:S<C.
7. Roth et al. (1981)	A. oddball, RT	2 tones; one is target	85 dB SPL	.85/.15	1	P350:S<D<C; RT:S>D=C Hits: S<D=C; RTSD: S>D>C
	B. oddball, RT	3 tones; one is target	85 dB SPL	.80/.10/.10	1	P350 for target or non-target infrequent:S<D<C. RT:S=C=D. Hits: S<D=C; RTSD: S>D=C.
	C. intensity differences, passive	noise	85/100/115 dB SPL	.33/.33/.33	4	P320 for 115 dB:S=D=C.
8. Pass et al. (1980)	oddball, RT; "Continuous Performance"	6 visual letters; one is target	?	.17 for each	1	P300:S<C; RT:S>C. Errors of commission and omission: S>C.

Table 1 - (continued)

9. Josiassen et al. (1981)	oddball, count	4 shocks to digits; one is target	2 mA> threshold	.25 for each	2.3-3.3	P400: Patients <C. (Most patients were schizophrenics)
10. Steinhauer and Zubin (in press)	oddball, count	2 tones; one is target	65 dB SL	.75/.25 (see ref.)	3	P300:S< D< C. S< C even when only accurately counted blocks are considered. Pupillary dilation: S< C.
11. Friedman et al. (in press)	oddball, RT	2 tones, omitted tone; one is target	64 dB SPL	.66/.17/.17	0.8	P350 to target tone and P400 to missing tone: high risk children (10-18 yrs) < Control children.
12. Cohen et al. (1981)	oddball, count	2 clicks, click + light: one is target	70/50 dB SL	.80/.10/.10	1.65	P340: S< C = Alcoholics. P340 correlates with accuracy. No relation between SCR responsivity and P340.
13. Baribeau-Braun et al. (in preparation)	dichotic listening, RT	3 tones in two ears; one is target	65 dB SPL	.45/.05	.25-.75/ .50-1.50	P300: S< C even for trials with RT accurate and <500 msec.
14. Duncan-Johnson et al. (in preparation, a)	choice RT, sequential effects	2 tones; both are targets	85 dB SPL	.50/.50	1.5	P300:S< C though for P300 sequential effect: S = C. RT: S> C.
15. Duncan-Johnson et al. (in preparation, b)	simple RT, modality shift effects	tone, light; both are targets	40 dB SL (tone and light)	.50/.50	1.5-3.5	P300: S = C whether modality shifts or not. RT:S = C.

variables that control P300 amplitude and latency (for reviews, *see* Pritchard 1981, and Donchin 1981). When the findings are put in perspective, astonishingly close empirical and theoretical parallels can be drawn between P300 and SCR. The categories under which these similarities can be enumerated are listed in Table 2. Both P300 and SCR can be elicited by stimuli of diverse types, both are enhanced by various kinds of stimulus surprise, task relevance, and salience, and both show habituation. Neuronal and probabilistic models developed by Sokolov and others apply equally well to both responses. Cognitive and computer models of stimulus evaluation and context updating developed for P300 by Donchin and his students are being applied to SCR. A detailed documentation of these parallels can be found by Roth (in press-b).

Table 2

Parallels Between P300 and SCR

- I. Empirical Parallels
  - A. Stimulus Nonspecificity
  - B. Stimulus Properties Controlling P300 and SCR Amplitude
    - 1. Surprise
      - a. Occurrence uncertainty
      - b. Stimulus quality deviation
      - c. Temporal uncertainty
      - d. Temporal deviation
    - 2. Task Relevance
      - a. Signal value
      - b. Allotment of attentional resources
    - 3. Salience
  - C. Habituation
- II. Theoretical Parallels: P300 and the OR
  - A. Neuronal Models
  - B. Probabilistic Models
  - C. Cognitive Models
  - D. Computer Models

In a psychological sense, both SCR nonresponding and P300 reduction imply an inability to mobilize extra stimulus processing resources when the novelty or other features of the stimuli warn that additional resources may be required momentarily. These extra resources may actually turn out to be unnecessary, in that RT or counting tasks of a simple nature can be performed adequately with the available resources even when the stimulus comes as a surprise. The differences between psychotics and controls in mobilizing these resources may be apparent only at intermediate levels of stimulus novelty or task demand. When stimuli are expected and uninteresting, neither group responds; when stimuli are very novel, task-relevant, or intense, both groups may respond equally.

In a biological sense, SCR nonresponsivity and P300 reduction imply a failure of components of the orienting reflex. This innate basic mechanism for reacting to potentially dangerous stimuli in the environment is found in both vertebrates and invertebrates (e.g., Kandel 1981).

Our unitary interpretation of SCR and P300 could be challenged on the basis of the results of Cohen et al. (1981). Their study is up to now the only one to report SCR and ERP measures in the same patients, although from different paradigms. As usual, about half of the schizophrenics were SCR nonresponders in a habituation paradigm, but both SCR responders and nonresponders had reduced P300s in an oddball paradigm. Either their P300 paradigm was more sensitive than their SCR paradigm to a general schizophrenic deficit that differs quantitatively among schizophrenics, or their SCR paradigm differentiated subgroups of schizophrenics that differ qualitatively from each other. Although SCR and P300 are generally under the control of the same independent variables, it is possible that they reflect distinct and dissociable information processing mechanisms (*see* Roth, in press–b).

Since it has been suggested that there are at least two biologically distinct types of schizophrenics, one suffering from dopaminergic hyperactivity and the other from enlarged cerebral ventricles (Crow 1982), it is tempting to try to assign SCR nonresponders to one of these types. However, definite assignment of SCR or P300 abnormalities to specific subtypes of mental disease must await systematic investigations in which patients are studied from multiple perspectives simultaneously. Nonresponsivity should be assessed in various physiological systems from the brain to the periphery, and these data should be compared with biochemical, radiological, psychological, linguistic, and clinical-historical data. Converging findings may help us discover groups of patients with diseases of distinct etiologies and prognoses.

References

Baribeau-Braun, J., Picton, T., Gosselin, J.-Y, and Quan, F.W. A neurophysiological evaluation of selective attention in schizophrenia. Preliminary data presented at annual meeting of Society for Psychophysiological Research, October 1979. *Psychophysiology*, 18:176 (Abstr.) 1980. [Final report in preparation]

Cohen, R., Sommer, W., and Hermanutz, M. Auditory event-related potentials in chronic schizophrenics: Effects of electrodermal response type and demands on selective attention. In: Perris, C., Kemali, D., and Vacca, L. (eds.), *Electroneurophysiology and Psychopathology* (Series: *Advances in Biological Psychiatry.)* Basel, Switzerland: S. Karger AG, Vol. 6, 1981, pp. 180-194.

Crow, T.J. Two dimensions of pathology in schizophrenia—Dopaminergic and non-dopaminergic. Psychopharmacol. Bull., 18(3):22-29, 1982.

Donchin, E. Surprise!....Surprise? *Psychophysiology*, 18:493-513, 1981.

Duncan-Johnson, C.C., Roth, W.T., and Kopell, B.S. Effects of stimulus sequence on P300 and reaction time in schizophrenics: A preliminary report. Presented at Sixth International Conference on Event-related Potentials of the Brain (EPIC VI), Lake Forest, Illinois, June 21-27, 1981. [Final report in preparation (a)]

Duncan-Johnson, C.C., Roth, W.T., Callaway, E., Fujii, J., and Kopell, B.S. Shift of sensory modality: Effects on P300 and RT. Preliminary data presented at Annual Conference of the Society for Psychophysiological Research, Washington, D.C., October 1981. [Final report in preparation (b)]

Friedman, D., Vaughan, H.G. Jr., and Erlenmeyer-Kimling, L. Cognitive brain potentials in children at risk for schizophrenia: Preliminary findings and methodological considerations. *Schizophr. Bull.* (In press)

Josiassen, R.S., Shagass, C., Roemer, R.A., and Straumanis, J.J. The attention-related somatosensory evoked potential late positive wave in psychiatric patients. *Psychiatry Res.*, 5:147-156, 1981.

Kandel, E. Towards a cellular biology of anticipatory and chronic anxiety in simple animal models. Paper presented at 20th Annual Meeting of the American College of Neuropsychopharmacology, San Diego, California, December 16-18, 1981.

Levit, R.A., Sutton, S., and Zubin, J. Evoked potential correlates of information processing in psychiatric patients. *Psychol. Med.*, 3:487-494, 1973.

Öhman, A. Electrodermal activity and vulnerbility to schizophrenia: A review. *Biol. Psychol.*, 12:87-145, 1981.

Pass, H.L., Klorman, R., Salzman, L.F., Klein, R.H., and Kaskey, G.B. The late positive component of the evoked response in acute schizophrenics during a test of sustained attention. *Biol. Psychiatry*, 15:9-20, 1980.

Pritchard, W.S. Psychophysiology of P300. *Psychol. Bull.*, 90:506-540, 1981.

Roth, W.T. Specific and non-specific ERP characteristics of clinical groups. In: Cohen, J., Karrer, R., and Tueting, P. (eds.), *Proceedings of the Sixth International Conference on Event Related Slow Potentials of the Brain*. New York: New York Academy of Sciences. (In press-a)

Roth, W.T. A comparison of P300 and the skin conductance response. In: Gaillard, A.W.K., and Ritter, W. (eds.), *Tutorials in ERP Research — Endogenous Components*. Amsterdam: North-Holland Publishing Co. (In press-b)

Roth, W.T., and Cannon, E.H. Some features of the auditory evoked response in schizophrenics. *Arch. Gen. Psychiatry*, 27:466-471, 1972.

Roth, W.T., Horvath, T.B., Pfefferbaum, A., Tinklenberg, J.R., Mezzich, J.E., and Kopell, B.S. Late event-related potentials and schizophrenia. In: Begleiter, H. (ed.), *Evoked Brain Potentials and Behavior*, Vol. 2, Downstate Series of Research in Psychiatry and Psychology. New York: Plenum Publishing, 1979, pp. 499-515.

Roth, W.T., Horvath, T.B., Pfefferbaum, A., and Kopell, B.S. Event-related potentials in schizophrenics. *Electroencephalogr. Clin. Neurophysiol.*, 48:127-139, 1980a.

Roth, W.T., Pfefferbaum, A., Horvath, T.B., Berger, P.A., and Kopell, B.S. P300 reduction in schizophrenics. *Electroencephalogr. Clin. Neurophysiol.*, 49:497-505, 1980b.

Roth, W.T., Pfefferbaum, A., Kelly, A.F., Berger, P.A., and Kopell, B.S. Auditory event-related potentials in schizophrenia and depression. *Psychiatry Res.*, 4:199-212, 1981.

Shagass, C., Straumanis, J.J., Roemer, R.A., and Amadeo, M. Evoked potentials of schizophrenics in several sensory modalities. *Biol. Psychiatry*, 12:221-235, 1977.

Shagass, C., Roemer, R.A., Straumanis, J.J., and Amadeo, M. Evoked potential correlates of psychosis. *Biol. Psychiatry*, 13:163-184, 1978.

Steinhauer, S., and Zubin, J. Vulnerability to schizophrenia: Information processing in the pupil and event-related potential. In: Hanin, I., and Usdin, E. (eds.), *Biological Markers in Psychiatry and Neurology*. Oxford: Pergamon Press. (In press)

Venables, P.H. The electrodermal psychophysiology of schizophrenics and children at risk for schizophrenia: Controversies and developments. *Schizophr. Bull.*, 3:28-48, 1977.

Verleger, R., and Cohen, R. Effects of certainty, modality shift, and guess outcome on evoked potentials and reaction times in chronic schizophrenics. *Psychol. Med.*, 8:81-93, 1978.

What Is Vital Depression (Endogenous Depression or Melacholia), and How Can It Be Reliably Assessed

Chair: **Robert M.A. Hirschfeld, M.D.**
Clinical Research Branch
National Institute of Mental Health
Rockville, Maryland

Pituitary-Adrenal Assessment in Identifying Subtypes of Depression

Walter Armin Brown, M.D.,[1] and C. Brandon Qualls, M.D.[2]

About 50 percent of patients with primary major depressive disorder show pituitary-adrenal disinhibition while they are depressed but not after recovery. This endocrine phenomenon provides a model for examining the value of a biological marker in subtyping depressive illness.

The dexamethasone suppression test (DST), because of its procedural simplicity, lack of risk, minimal discomfort to the patient, relative ease with which normal and abnormal responses are differentiated, and demonstrated clinical correlates has been the method most widely applied for assessing pituitary-adrenal activity in studies of psychiatric patients. Recent studies using the DST in depressed patients have examined the clinical correlates of normal and disinhibited pituitary-adrenal activity. With respect to existing diagnostic categories, Brown and Shuey (1980) and others (Schlesser et al. 1980) have found that nonsuppression after dexamethasone occurs almost exclusively in patients with primary major depressive disorder; very few patients with secondary depression (those with a preceding psychiatric diagnosis other than affective) show nonsuppression. Carroll and his associates (Carroll et al. 1981) have reported that nonsuppression occurs exclusively in patients with endogenous depression or melancholia; patients with nonendogenous depression showing normal suppression. Yet whether one examines patients who meet criteria for melancholia, primary depression, or endogenous depression, one finding has been consistent from study to study: Patients in each of these diagnostic categories are heterogenous in their pituitary-adrenal activity. Depending on the DST protocol, 30 to 65 percent are nonsuppressors and the remainder suppressors. This heterogeneity has focused the authors' attention on dimensions of depressive illness other than diagnosis that might correlate with pituitary-adrenal activity.

Although in a few studies (Davis et al. 1981) nonsuppressors have been observed, on the basis of rating scale scores, to have a more severe depression than suppressors, this is not a consistent finding (Brown & Qualls 1981). A few patients who have been nonsuppressors during one major depressive episode have been studied during subsequent periods of depression. Nonsuppression has occurred in these patients only in the context of severe depressive symptomatology, not with minor or transient depression (Brown & Qualls, unpublished observations). Thus there may be a severity threshold for nonsuppression.

---

[1] Department of Psychiatry, Providence Veterans Administration Medical Center and Brown University, Providence, RI 02908.

[2] Department of Psychiatry, Brown University and Butler Hospital, Providence, RI 02908.

However, since many suppressors have, by any criteria, a severe illness, the differences in pituitary-adrenal activity among depressed patients are not likely to be accounted for by differences in severity of illness.

Nor do suppressors and nonsuppressors differ consistently in the occurrence or intensity of suicidal ideation, agitation, anorexia, sleep disturbance, or other specific depressive symptoms. Yet one symptom dimension in depressed patients—cognitive impairment—does appear to consistently correlate with pituitary-adrenal activity. Nonsuppressors have more difficulty than suppressors in completing self-rating scales (Brown & Shuey 1980), have longer reaction times (Brown & Qualls 1981), are rated as having greater thinking disturbance (Reus 1982), and make more errors of commission on a recognition task (Reus, unpublished observations). Further, a significant positive correlation has been observed between urinary cortisol and number of errors on the Halstead Categories Test (Rubinow, unpublished observations). In summary, the studies to date have consistently shown that depressed patients with pituitary-adrenal disinhibition have a greater degree of cognitive impairment than those with normal pituitary-adrenal regulation.

Nonsuppressors have been found to differ from suppressors on three dimensions of illness course: they are older at both the index episode and their first depressive episode (this age difference appears to be sex related; it occurs most clearly in depressed women); irrespective of treatment, nonsuppressors seem to undergo greater improvement during hospitalization (Brown & Qualls 1981; Greden et al. 1980); and, retrospective studies show that nonsuppressors have more episodes of depression (Brown & Qualls 1981; Schlesser et al. 1980).

A few studies, all of which must be considered preliminary, suggest that nonsuppressors and suppressors differ in their response to specific treatment. Whereas nonsuppressors appear to respond well to desipramine and imipramine (Brown & Qualls 1981; Greden et al. 1981), they show a poor response to clomipramine (Brown et al. 1980) and mianserin (Cobbin et al. 1981). Suppressors, on the other hand, seem to respond equally well to these antidepressants. Clearly, more data are needed to definitively answer the question of whether suppressors and nonsuppressors respond preferentially to different antidepressants. The little data available so far lend themselves to the interpretation that nonsuppressors respond better to drugs having their predominant effects on noradrenergic rather than serotonergic systems. This preferential drug response would be consistent with the known serotonergic excitatory and noradrenergic inhibitory input to pituitary-adrenal regulation.

Suppressors and nonsuppressors appear to differ in their response to electroconvulsive therapy (ECT). The authors have found that of 13 suppressors and 12 nonsuppressors treated with ECT clinical improvement occurred in all of the suppressors but in only six (50%) of the nonsuppressors. Six nonsuppressors did not respond to ECT according to both rating scale criteria and their clinician's impressions. These observations are consistent with those of Papakostas et al. (1981) who, although not directly addressing the predictability of the DST for ECT response, reported that 5 of 14 nonsuppressors treated with ECT did not improve, a higher than usual rate of nonresponse.

Suppressors and nonsuppressors differ in their responses to methylphenidate and sleep deprivation, treatments which induce in some patients a transient relief of depressive symptoms. Significantly more suppressors than nonsuppressors show an antidepressant response to methylphenidate (Sternbach et al. 1981), but more nonsuppressors than suppressors respond to sleep deprivation (Nasrallah & Coryell 1982).

The apparent differences between suppressors and nonsuppressors in course of illness and response to specific treatments suggest that the depressive illnesses associated with normal and abnormal pituitary-adrenal regulation differ in their pathophysiology. Two other bits of data support this concept. Schlesser and his associates (1980) reported that nonsuppressors are more likely to have a family history of depression than suppressors; and, the authors have found (1982) that people are consistently suppressors or nonsuppressors over multiple depressive episodes. These observations suggest that the depression associated with pituitary-adrenal disinhibition may, more so than other depressive illnesses, have a genetic component and, consistent with this, there may be stable individual differences in the propensity to develop pituitary-adrenal disinhibition with depression. Thus pituitary-adrenal assessment may identify a subtype of depression having a distinct pathophysiology with characteristic clinical and treatment response features.

Diagnostic categories based on symptomatic phenomenologic criteria rarely identify illnesses which are homogeneous with respect to etiology, pathophysiology, or treatment requirements. Many illnesses that differ little if at all symptomatically have differing underlying pathophysiologies that are critical in determining effective treatment and prognosis. Pneumonia, hypertension, and probably depression as well, are among them. On the other hand, as with vitamin deficiencies, porphyria, and syphilis, a single pathophysiologic process which must be identified for effective treatment, can have differing symptomatic presentations. Pituitary-adrenal disinhibition may be associated with a psychiatric illness having a number of symptomatic presentations, depression perhaps the most common. Such an illness might respond, however, to one or more specific treatments. One study has shown that among patients with mixed psychiatric diagnoses including catatonia, schizoaffective disorder depressed, and paranoid schizophrenia, nonsuppressors regardless of "diagnosis" but not suppressors, respond to thymoleptic treatments—lithium, ECT, and secondary amine tricyclics (Carman et al. 1980).

Among depressed patients pituitary-adrenal disinhibition is associated with cognitive impairment, a tendency to recurrence, and an emerging profile of response to specific treatments. This neuroendocrine dysfunction and other neuroendocrine and neurochemical markers may help reorient our thinking about the dimensions of psychiatric illness relevant to "diagnosis" and provide a stepping stone to a classification of depression more closely tied to pathophysiology and treatment than current phenomenologic approaches.

References

Brown, W.A., Haier, R.J., and Qualls, C.B. Dexamethasone suppression test identifies subtypes of depression which respond to different antidepressants. *Lancet*, I:928-929, 1980.

Brown, W.A., and Shuey, I. Response to dexamethasone and subtype of depression. *Arch. Gen. Psychiatry*, 37:747-751, 1980.

Brown, W.A., and Qualls, C.B. Pituitary-adrenal disinhibition in depression: Marker of a subtype with characteristic clinical features and response to treatment? *Psychiatry Res.*, 4:115-128, 1981.

Carman, J.S., Crews, E.L., Wyatt, E.S., Dohn, H.H., and Hall, K.R. Prediction of response to psychotropic medications. *Ala. J. Med. Sci.*, 17(2):161-165, 1980.

Carroll, B.J., Feinberg, M., Greden, J.F., Tarika, J., Albala, A. Haskett, R., James, N., Kronfol, Z., Lohr, N., Steiner, M., de Vigne, J.P., and Young, E. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry*, 38:15-22, 1981.

Cobbin, D.M., Cairncross, K.D., Jurd, S., Veltman, and Pohlen. Urinary and MHPG levels and the dexamethasone test predict clinical response to the antidepressant drug mianserin. *Neuroendocrinol. Lett.*, 3(3):133-138, 1981.

Davis, K.L., Hollister, L.E., Mathe, A.A., Davis, B.M., Rothpearl, A.B., Faull, K.F., Hsieh J.Y.K.,, Barchas, J., and Berger, P. Neuroendocrine and neurochemical measurements in depression. *Am. J. Psychiatry*, 138(12):1555-1562, 1981.

Greden, J.F., Takika, J.S., de Vigne, J., Kronfol, Z., and Carroll, B.J. Dexamethasone test predicts treatment response. Proceedings of the American Psychiatric Association, New Research Abstracts, NR 36, 1980.

Greden, J.F., Kronfol, Z., Gardner, R., Feinberg, M., Mukhopadhyay, S., Albala, A.A., and Carroll, B.J. Dexamethasone Suppression Test and selection of antidepressant medications. *J. Affect. Disord.*, 3:389-396, 1981.

Nasrallah, H.A., and Coryell, W.H. Dexamethasone nonsuppression predicts the antidepressant effects of sleep deprivation. *Psychiatry Res.*, 6:61-64, 1982.

Papakostas, Y., Fink, M., Lee, J., Irwin, P., and Johnson, L. Neuroendocrine measures in psychiatric patients: Course and outcome with ECT. *Psychiatry Res.*, 4:55-64, 1981.

Reus, V.I. Pituitary-adrenal disinhibition as the independent variable in the assessment of behavior symptoms. *Biol. Psychiatry*, 17(3):317-326, 1982.

Schlesser, M.A., Winokur, G., and Sherman, B.M. Hypothalamic-pituitary-adrenal axis activity in depressive illness. *Arch. Gen. Psychiatry*, 37:737-743, 1980.

Sternbach, H., Gwirtsman, H., and Gerner, R.H. The Dexamethasone Suppression Test and response to methylphenidate in depression. *Am. J. Psychiatry*, 138(12):1629-1632, 1981.

Benzodiazepine Abuse: What Are the Data?

Chair: Charles P. O'Brien, M.D., Ph.D.
University of Pennsylvania
VA Medical Center
Philadelphia, Pennsylvania

Subjective Effects of Benzodiazepines and Methaqualone in Recreational Sedative Users

Jonathan O. Cole, M.D.,[1] Maressa Hecht Orzack, Ph.D.,[1] Francine M. Benes, M.D., Ph.D.,[1] Barbara J. Beake, A.B.,[1] Michael P. Bird, A.B.,[1] Yoram Bar Tel, M.A.,[1] and Martin Ionescu-Pioggia, A.B.[1]

Sedative drugs, including methaqualone and various barbiturates, are generally agreed to have abuse potential and are used recreationally as "street" drugs. Some individuals become physically and psychologically dependent on these agents. Recreational use of benzodiazepines is less well documented, though some reports exist, and physical dependence is believed to be relatively uncommon. Nevertheless, a number of cases of physical dependence have been documented in the world literature.

If one assumes that the relative abuse liabilities of various benzodiazepines are unclear, one feasible approach to documenting their abuse liabilities would be to compare them, first, to each other and, second, to a sedative drug of known abuse potential such as methaqualone. Our group is currently engaged in a program of studies which is working toward this objective. The present paper should be viewed as a progress report on work completed to date. Two studies, one comparing methaqualone in single doses of 200 mg and 400 mg with placebo and a second comparing 20 mg of prazepam with 10 mg of diazepam and placebo, have been completed. Studies directly comparing a higher dose of diazepam (20 mg) with higher doses of prazepam (40 mg) and with methaqualone are now in progress.

Methaqualone had been selected as a "standard" abuse-liable sedative because of its popularity with recreational sedative users in the Boston area. It is a chemically synthesized molecule which belongs to a group of compounds called the oxoquinazolines. As such, it is structurally similar to piperidone and barbiturate hypnotic drugs (Brown & Goenechea 1974). Methaqualone is absorbed rapidly after oral administration (Meyer & Boggan 1977) and, in man, average peak plasma levels occur at 2 hours after administration (Morris et al. 1972). Unbound plasma methaqualone is free to diffuse passively into the cerebrospinal fluid compartment in proportion to its concentration (Christensen & Holfort 1975). The primary route of metabolism of the drug is through the hepatic microsomal mixed oxidase enzymes (Prabhu et al. 1964). SKF 525-A, a compound which inhibits the liver metabolism of methaqualone, enhances its distribution into various subcellular compartments within the brain, including cytoplasm, myelin, and, to a much lesser degree, synaptosomes, mitochondria, and microsomes (Kuhn & Shah 1978). Within 8 hours of oral administration, 80-90 percent of the drug present in plasma has been cleared (Morris et al. 1972), the principal route or excretion for methaqualone and its metabolites being through the urine. In human subjects, its rate of elimination is quite variable, and the estimated half-life of methaqualone in urine can be as long as 74 hours (Heck et al. 1978).

---

[1] Psychopharmacology Program, McLean Hospital-Harvard Medical School, Belmont, MA 02178.

Methaqualone is a short-acting anesthetic and muscle relaxant which in man produces slow wave changes in the electroencephalogram (EEG) similar to those observed with barbiturates (Saxena et al. 1977). The ability of methaqualone to reduce seizure susceptibility in mice (Boggan et al. 1977) appears to be associated with enhancement of transmission at GABA-nergic synapses in the central nervous system (Naik et al. 1978). Although methaqualone is a potent inhibitor of specific ^{3}H-diazepam binding to rat brain synaptosomal membranes (Muller et al. 1978), its central depressant effects do not appear to be mediated through a direct action of GABA receptors (Naik et al. 1978). As a lipophilic substance which has been demonstrated in various brain compartments, the range of possibilities to account for its various actions is very broad and its interaction with GABA-nergic neurons may be only one of many possible mechanisms of action in the central nervous system.

In addition to its clinically useful physiological effects, methaqualone has euphoriant, relaxant, and anxiolytic properties which have been associated with its recent widespread nonmedical use (Gerald & Schwirian 1973). Individuals who take methaqualone consistently report its preferred use in social settings (Gerald & Schwirian 1973; Kochansky et al. 1975), and its apparent aphrodisiac properties appear to be among its most desirable effects (Gerald & Schwirian 1973). Studies of methaqualone effects in monkeys have demonstrated an increase of "affiliative activities" including grooming, huddling, and sitting together, although curiously, sexual functions while under the influence of the drugs were primarily autoerotic (Claus et al. 1980).

The accumulated experience with nonmedical use of methaqualone has revealed that a variety of complications can arise. Interference with memory recall and stimulus discriminability (Rundell et al. 1975), tolerance (Faulkner et al. 1979), physical dependence (Singh et al. 1980), abstinence syndromes with potentially life-threatening seizures (Swartzburg et al. 1973), and peripheral neuropathy (Mark & Sloggem 1976) are among the more serious complications of long-term methaqualone abuse. In addition, methaqualone-diphenhydramine (Mandrax®), a commercially produced combination drug, has also been associated with dose-related psychotic reactions, intoxication-related suicide attempts, and violent episodes (Tennant 1973).

Despite its potential complications, methaqualone is a sedative hypnotic with considerable abuse potential which appears to derive from its recreationally desirable effects. As such, it represents a useful investigative tool to explore the effects of such agents on individuals and their social interactions under controlled laboratory conditions. Such a controlled laboratory setting employing standardized assessment batteries, once established, could later be applied to the study of other sedative hypnotic drugs to determine their respective abuse liability relative to methaqualone as a reference standard. Methaqualone has been evaluated for subjective and physiological effects by Jasinski et al. (1977) and found generally comparable to pentobarbital in its subjective effects.

The prazepam-diazepam comparison was undertaken on the presumption that diazepam's relatively rapid absorption, which gives peak blood levels 30-90 minutes after oral ingestion (Bliding 1974), might make it more subjectively reinforcing than prazepam which is converted into desmethyldiazepam in the body and gives peak plasma levels of this compound only at about 6 hours (Chang et al. 1978). In our clinical experience patients often feel more rapid relief from anxiety on diazepam than on other benzodiazepines. The doses were selected as representing high standard clinical dosage units (Woody et al. 1975). Higher dosages are often selected for recreational purposes, but lower dosages were chosen to work out a useful methodology before higher levels were studied.

The designs for both studies were essentially identical. Subjects were recruited by notices posted in various local colleges. Most were students from socio-economically upper middle or upper class families who were college educated. All participants were casual users of sedative-hypnotics, such as barbiturates, methaqualone, and benzodiazepines, and had used one or more of these drugs at least six times in doses above the usual prescribed levels. Subjects were required to complete the Minnesota Multiphasic Personality Inventory (MMPI) (Dahlstrom et al. 1972) and undergo a clinical interview. The latter was conducted by a clinical psychologist who determined previous drug usage, probed for areas of personality dysfunction and adverse reactions to stress, and reviewed the psychiatric history of the subject and his family of origin. Results from both the MMPI and the clinical interview were used as criteria on which to judge the subjects' suitability for participation. The mean MMPI profile of male and female subjects showed elevations of scales 4 (Pd — psychopathic deviate) and 9 (Ma — mania), but these were below a T-score of 70. This pattern is characteristic of a hypomanic and sociopathic personality style that is generally within the range of normal behavior (Dahlstrom et al. 1972). In addition, subjects had a normal physical examination, no history of drug dependence including alcohol, and had no unusual side effects during their previous drug experiences.

Separate groups of 24 subjects, 12 male and 12 female, were recruited for the methaqualone and the diazepam-prazepam studies. Four subgroups of six subjects each, two male subgroups and two female subgroups, were created.

Measures

The major dependent measure for the present report was List 116 of the Addiction Research Center Inventory (ARCI), a 102-item inventory which characterizes the subjective effects of a drug compared with those of other well-known drugs of abuse (Haertzen 1974). This version contains seven standard scales in addition to an 11-item Amphetamine scale developed by Martin et al. (1971) plus Euphoria and Sedation scales established by Jasinski et al. (1977). The utility of these scales in investigating the subjective effects of various substances is well documented (Martin et al. 1971; Jasinski 1977; Jasinski et al. 1977).

Although the ARCI was originally a true/false questionnaire, we devised two variants for use in these studies. For the methaqualone study, a 7-point version was used; subjects were asked to rate themselves on intensity from 0 to 6. For the prazepam study, a 10-point version was used; subjects were asked to rate themselves on each item from −5 to +5. The same scales were used in both studies, but the actual numerical scores obtained on the scales are not strictly comparable across studies. Different versions of the Profile of Mood States (POMS) (McNair et al. 1971) were used in the two studies; neither version seemed as sensitive to drug-placebo differences as the ARCI. The POMS results will not be presented at this time.

Testing Procedures

Subjects were run in groups of six, with each group coming in for three 5-hour sessions, 1 week apart. Each subject in fact received all three treatments (20 mg of prazepam, 10 mg of diazepam and placebo, or 400 mg and 200 mg of methaqualone and placebo) in random order and double-blind. Thus, each subject served as his or her own control for the experiment. Randomization of treatments ensured that only two subjects in each group were receiving the same drug during each session. Subjects themselves were not aware that they would receive a different treatment at each session, and only knew the possible treatments they *could* receive.

Subjects were instructed to abstain from drug usage for 72 hours and alcohol for 12 hours prior to each session; they were asked to give a urine sample at the beginning of the session to be screened for illicit drug usage that might interfere with the validity of their ratings. No illicit use was detected. Initial physiological measures including pulse, temperature, and blood pressure were obtained. Pulse determinations were repeated hourly, while blood pressures were obtained only at the beginning and the end of each session.

The POMS and ARCI self-rating questionnaires were administered at the outset (predrug) and then hourly for 4 (methaqualone) or 5 (prazepam) hours following drug ingestion. Subjects were also asked to guess which drug they thought they and the other subjects received, what rate they would pay for what they had received, and how high they felt during the session.

Groups were run in a living-room-like atmosphere in which subjects were free to play games, talk, read, listen to music, and eat, starting 1 hour after drug ingestion during the times when they were not filling out ratings. Each rating took about 25 minutes, leaving the subjects a substantial amount of free time.

Table 1

Covariance F-Ratios of ARCI Scores: Methaqualone Study

Scale	Drug	Time	Sex	Drug-Time	Time-Sex	Drug-Sex
Amphetamine	16.90**	37.25**	4.72*	7.27**	1.98	0.34
Drunkenness	31.66**	26.42**	5.83*	12.83**	1.85	1.35
Excitement	5.32**	35.45**	7.67**	7.37**	0.34	0.02
LSD	13.64**	27.68**	1.12	4.81**	2.77*	1.01
MG	4.77**	14.34**	1.39	3.00**	0.07	0.06
MPG	12.35**	54.31**	5.93**	8.66**	1.05	0.01
PCAG	11.03**	2.96*	0.19	3.06**	2.04	1.78
Sedation	15.47**	0.86	1.09	3.61**	2.33	1.17
Euphoria	9.56**	41.41**	2.40	7.42**	1.12	1.26

* Significant at .05 level (two-tailed)

** Significant at .01 level (two-tailed)

Table 2

Covariance F-Ratios of ARCI Scores: Prazepam Study

Scale	Drug	Time	Sex	Drug-Time	Time-Sex	Drug-Sex
Amphetamine	1.36	30.27**	0.79	1.67	0.56	2.37
Drunkenness	4.00*	21.78**	1.88	4.22**	0.14	0.68
Euphoria	1.24	31.97**	0.15	2.88**	4.55**	0.41
Excitement	2.53	2.78*	2.37	1.57	0.58	1.09
LSD	4.12*	7.30**	0.73	0.79	0.43	0.58
MG	0.01	2.49*	4.71*	2.06*	1.31	1.04
MBG	1.32	19.50**	0.35	2.29*	1.80	1.46
PCAG	1.63	3.12*	7.37**	2.61**	0.13	0.26
Sedation	2.88	4.00**	6.50*	2.93**	0.26	0.27

* Significant at .05 level (two-tailed)

** Significant at .01 level (two-tailed)

Data Analysis

The F values and corresponding probabilities for main drug effects, time effects, sex effects, and interaction among these variables were obtained by an analysis of covariance (grouped by sex) which adjusted for variations in the subjects' predrug ratings. The baseline scores (predrug) depicted in the figures represent raw means for each scale, while postdrug scale scores have been covaried. No significant differences between the three treatment groups were observed on baseline ratings in either study. Results of this analysis for the ARCI are presented in Table 1 for the methaqualone study and in Table 2 for the prazepam study. Where main drug effects, drug-by-time interactions, or trends were observed, an analysis of variance of adjusted mean scores was performed for each separate time point on that measure. Differences between drug conditions at these time points were analyzed using a Neuman-Keuls multiple comparison statistic.

Results

Within both studies in the major analysis of covariance, main drug effects and drug-by-time interactions significant at the $p < .05$ level were taken as clear evidence of drug treatment differences. Significant main drug effects occurred when, by inspection, level differences between treatments, usually drug and placebo, were evident throughout the entire study period, while drug-by-time interactions were statistically significant when drug-placebo differences were marked at one or two time periods, usually 1 and/or 2 hours after drug ingestion and then dwindled as the study period continued.

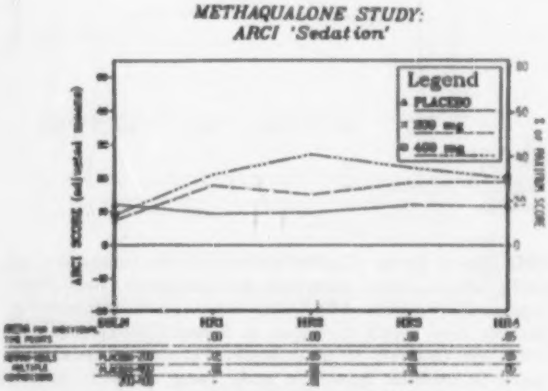


FIGURE 1. Drug vs. time curves for the comparison of orally administered methaqualone. Each point represents the mean ARCI scale score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-66): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

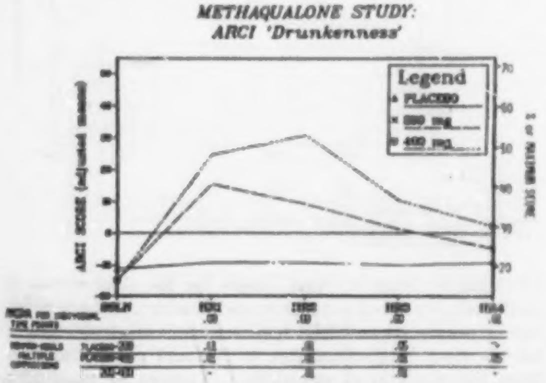


FIGURE 2. Drug vs. time curves for the comparison of orally administered methaqualone. Each point represents the mean ARCI scale score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (-30-96): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

Treatment differences in the methaqualone study were highly significant by analysis of covariance (Table 1) at the $p < .001$ level for drug or drug-by-time or both on seven of the eight ARCI scales presented. The morphine group (MG) scale, designed to pick up characteristic effects of opiates, reached significance at the $p < .01$ level. Several of the measures, Sedation (Figure 1), Drunkenness (Figure 2) and PCAG (a scale to detect effects of pentobarbital, chlorpromazine, and alcohol group drugs) are measures of sedation or sedative-type intoxication. These scales did discriminate between 200 mg and 400 mg of methaqualone at the second and sometimes the third hour, showing the higher dose to be more sedative than the lower dose of methaqualone. On the Euphoria (Figure 3), Excitement, Amphetamine (Figure 4), and morphine-benzedrine group (MBG) scales, the two dosages of methaqualone were almost identical in the course and degree of drug effect with maximum effect occurring at 1 hour after drug ingestion.

In the prazepam-diazepam-placebo study (Table 2), main drug effects were less striking and drug-by-time interactions were more common, while significance levels were more modest than those seen in the methaqualone study. Sedative effects as measured by the Sedation (Figure 5),

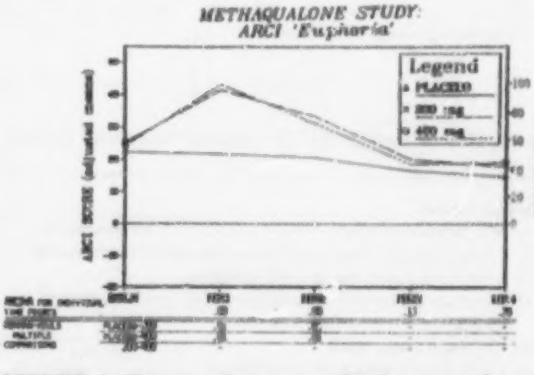


FIGURE 3. Drug vs. time curves for the comparison of orally administered methaqualone. Each point represents the mean ARCI scale score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-42): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

Drunkenness (Figure 6), and PCAG scales were clearly significant. The sedation produced by both prazepam and diazepam in fact appeared equivalent to the 400 mg dose of methaqualone, while the degree of drunkenness produced by these agents was only comparable to the 200 mg dose range. Euphoriant effects were seen only on the Euphoria (Figure 7) and MBG scales, while a dysphoric effect was detected by the LSD scale.

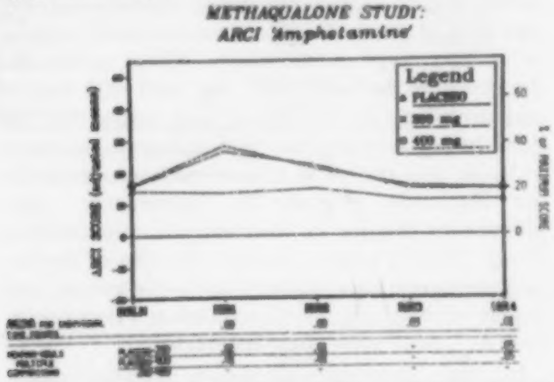


FIGURE 4. Drug vs. time curves for the comparison of orally administered methaqualone. Each point represents the mean ARCI scale score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-72): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

Table 3

Items Contained in ARCI 'Abuse Potential' Scale

Positive Items:

1) My movements are free, relaxed, and pleasurable.
2) Things around me seem more pleasing than usual.
3) I am sure I will sleep well tonight.
4) I feel as if something pleasant had just happened to me.
5) My head feels light.
6) I feel a very pleasant emptiness.

Negative Items:

1) My face feels hot.
2) I feel as if I have the flu.
3) I feel like avoiding people, although I usually do not feel this way.
4) I have been getting cramps.
5) I have a feeling of just dragging along rather than coasting.
6) My head feels as it does during a hangover.

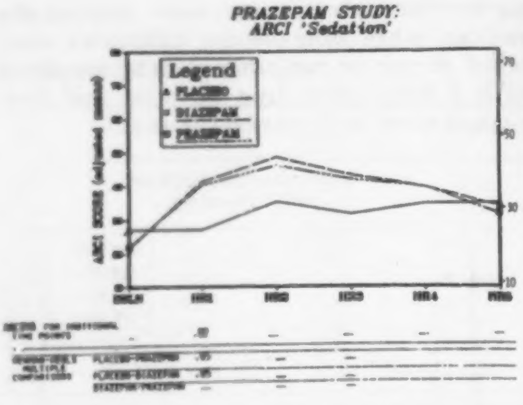


FIGURE 5. Drug vs. time curves for the comparison of orally administered prazepam and diazepam. Each point represents the mean ARCI scale score of each treatment at the six time levels (baseline to 5 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-110): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

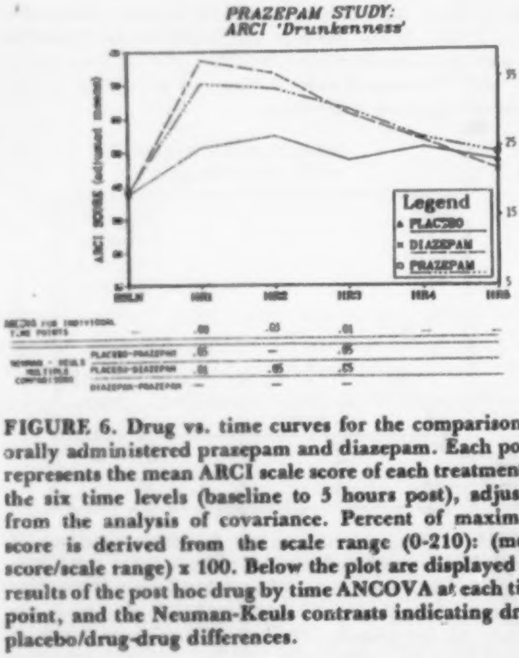


FIGURE 6. Drug vs. time curves for the comparison of orally administered prazepam and diazepam. Each point represents the mean ARCI scale score of each treatment at the six time levels (baseline to 5 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-210): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

By Neuman-Keuls analysis, diazepam-placebo differences were seen at more time points on the sedative scales than were prazepam-placebo differences, suggesting a tendency toward a more sedative effect for 10 mg of diazepam than for 20 mg of prazepam. No Neuman-Keuls contrasts were significant on the Euphoria scale for either drug though diazepam, by inspection, appears to be a bit more euphoriant. On the Excitation scale (Figure 8), an unexpected significance level of $p = .05$ showing diazepam to be more "exciting" than prazepam at 1 hour was uncovered, but its statistical meaningfulness is reduced by the main analysis of covariance significance level (a $p = .09$ main drug effect).

We have created an artificial "Abuse Potential" scale from the ARCI based on items correlating with the price the subject would have paid for the drug dose he received at any given study session. These items are listed in Table 3. The correlations

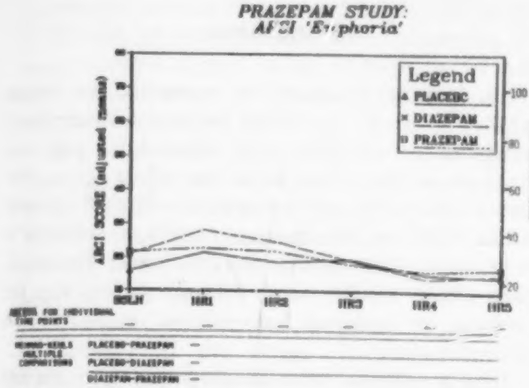

PRAZEPAM STUDY:
ARCI 'Euphoria'

FIGURE 7. Drug vs. time curves for the comparison of orally administered prazepam and diazepam. Each point represents the mean ARCI scale score of each treatment at the six time levels (baseline to 5 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-70): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

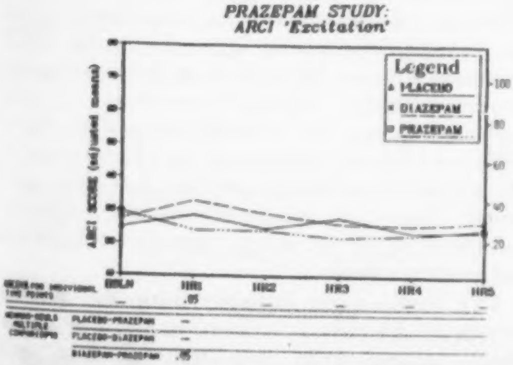

PRAZEPAM STUDY:
ARCI 'Excitation'

FIGURE 8. Drug vs. time curves for the comparison of orally administered prazepam and diazepam. Each point represents the mean ARCI scale score of each treatment at the six time levels (baseline to 5 hours post), adjusted from the analysis of covariance. Percent of maximum score is derived from the scale range (0-70): (mean score/scale range) x 100. Below the plot are displayed the results of the post hoc drug by time ANCOVA at each time point, and the Neuman-Keuls contrasts indicating drug-placebo/drug-drug differences.

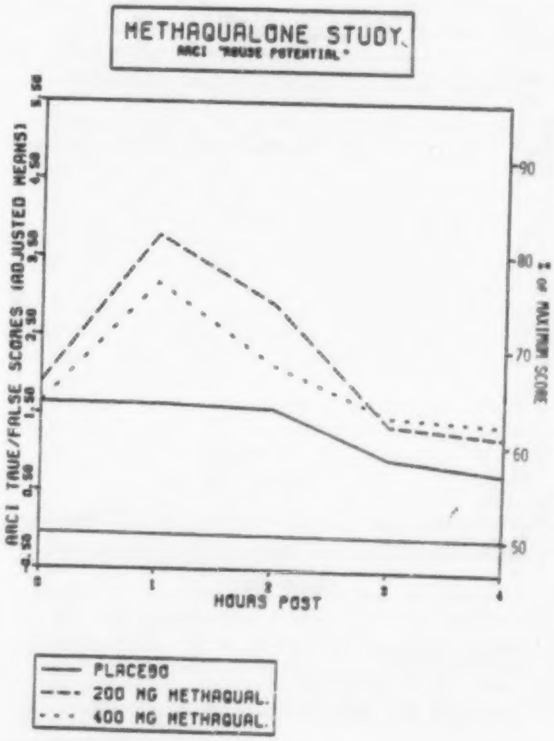

METHAQUALONE STUDY
ARCI "ABUSE POTENTIAL"

FIGURE 9. Drug vs. time curves for the comparison of orally administered methaqualone. Each point represents the mean ARCI "Abuse Potential" score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Items were scored true/false to standardize values. Percent of maximum score is derived from the scale range (-6-6): (mean score/scale range) x 100.

(which had to reach ± .32 for statistical significance) were obtained from combining data from the methaqualone study described above and from a similar 24-subject study comparing 15 mg and 30 mg of dextro-amphetamine with placebo. By scoring the "Abuse Potential" items in the ARCI used in both the methaqualone and prazepam-diazepam studies true-false, we have been able to create comparable graphs for the two studies showing adjusted means on this measure (Figures 9 and 10). This measure showed highly significant drug-placebo differences for methaqualone ($p = .004$) and also showed the lower 200 mg methaqualone dose to be "preferred" to the 400 mg dose. This phenomenon is probably a function of the higher euphoria to sedation ratio in the 200 mg dose. Drug-placebo differences in the prazepam-diazepam study, however, were not statistically significant. Despite this, a visible tendency for diazepam to look more "abuse liable" than prazepam at the dosages studied is apparent.

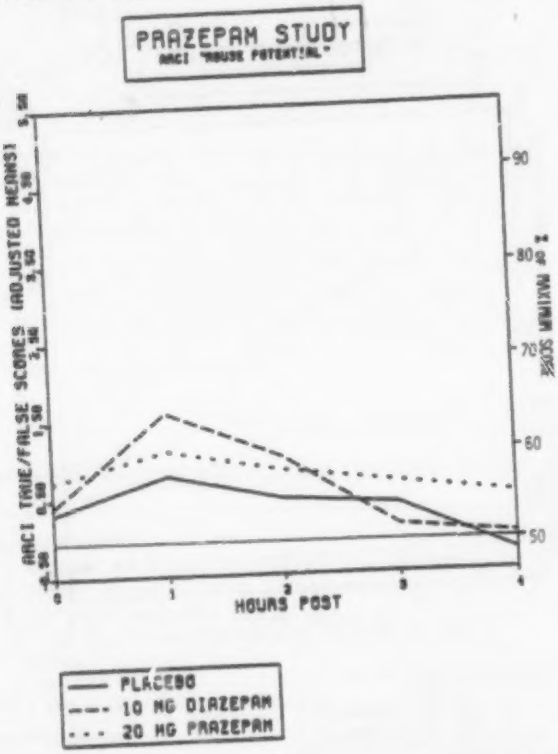


FIGURE 10. Drug vs. time curves for the comparison of orally administered prazepam and diazepam. Each point represents the mean ARCI "Abuse Potential" score of each treatment at the five time levels (baseline to 4 hours post), adjusted from the analysis of covariance. Items were scored true/false to standardize values. Percent of maximum score is derived from the scale range (-6-6): (mean score/scale range) x 100.

Discussion

The general approach to assessing the abuse liability of drugs described here, involving four groups of six subjects each selected for past experience in the recreational use of drugs in the class under study and the use of a reduced version of the ARCI as the main measure of subjective drug effects, is supported by the results obtained. Dose-effect results were obtained for methaqualone on sedative but not on euphoria-like measures.

Effects of the two benzodiazepines appear similar in direction but less in degree. Since only moderate clinical dosages were studied, the major questions about the abuse potential of benzodiazepines, as potentially measurable by our methodology, are not answerable. Very weak trends in the prazepam-diazepam data suggest that at higher doses of both drugs diazepam *might* be clearly more euphoriant. This possibility was strengthened by data presented by Jasinski (1981) in which a dose-response effect of both diazepam and chlordiazepoxide was obtained on the ARCI Sedation scale. Diazepam, but not chlordiazepoxide, showed dose-related increases on the ARCI Euphoria scale, suggesting that benzodiazepines may well differ among themselves in their euphoriant properties. A comparison of the effects of 20 mg of diazepam and 40 mg of prazepam in 12 recreational sedative users has just been completed. These data will be examined for differential effects of the two drug regimens on Euphoria and related scales.

The authors are also revising the scoring system for the ARCI. A factor analysis of 2-hour ARCI scores from our methaqualone and *d*-amphetamine studies has yielded three factors which measure euphoria, sedation, and dysphoria. These factors should provide clearer and, hopefully, more sensitive scales than the empirical ARCI scales we have been using. Jasinski et al. (1977) have used only the Sedation and Euphoria scales. Since PCAG and its subscale Sedation, and Drunkenness correlate between 0.76 and 0.96, while MBG and its subscale

Euphoria, Excitement, and Amphetamine correlate between 0.83 and 0.95, this limited assessment may be justified. The LSD scale, by contrast, seems to measure somatic and psychic dysphoria and correlates moderately well (0.46 to 0.70) with all other ARCI scales. It remains to be seen whether a new, factor analytic set of ARCI scales will be more sensitive or sensible than other approaches used to date.

The next difficult question is whether the system being used is a valid way of assessing the abuse liability of sedative drugs. It is unclear to what extent the benzodiazepines are actually abused, and the newer agents, such as prazepam, may not be abused at all. Illicit use probably reflects past and present popularity, as well as availability of the drugs. Methaqualone and diazepam are both known to illicit users, but prazepam may not be. After consideration of higher dose studies, the authors will be better able to assess the relative euphoriant and sedative qualities of benzodiazepines. If their methods do ultimately show methaqualone to have a higher euphoria/sedation ratio than diazepam, they will have more tangible data with which to characterize the abuse liability of the latter. Prazepam appears to be even less euphoriant than diazepam, and thus may be less liable to be abused. Illicit drug abuse as measured by epidemiologic surveys or law enforcement data may show a pattern of abuse popularity and/or frequency which reflects the trends observed in these studies. Unfortunately, good quality data on frequency of illicit use is lacking. At present, methods such as theirs are the most feasible approach to assessing the abuse potential of sedative drugs.

References

Bliding, A. Effects of different rates of absorption of two benzodiazepines on subjective and objective parameters. *Eur. J. Clin. Pharmacol.*, 7:201-207, 1974.

Boggan, W.O., Meyer, H.S., Steinberg, R.M., and Worthington, C. Effects of methaqualone on the seizure susceptibility of mice. *Psychopharmacology (Berlin)*, 54:45-49, 1977.

Brown, S.S., and Goenechea, S. Methaqualone: Metabolic, kinetic, and clinical pharmacologic observations. *Clin. Pharmacol. Ther.*, 14:314-319, 1974.

Chang, T., Johnson, E., Peterson, F., and Glazko, A.J. Research Report #740-0012, May 12, 1978, Department of Pharmacology Project #3.11.848A, Warner-Lambert-Parke-Davis Pharmaceutical Research Division, Ann Arbor, Michigan.

Christensen, J.M., and Holfort, S. Methaqualone in human serum and cerebrospinal fluid after oral intake. *J. Pharm. Pharmacol.*, 27:538-539, 1975.

Claus, G., Kling, A., and Bolander, K. Effects of methaqualone on social behavior in monkeys *(Macaca mulatta)*. *Brain Behav. Evol.*, 17:391-410, 1980.

Dahlstrom, W.G., Welsh, G.S., and Dahlstrom, L.E. *An MMPI Handbook*, Vols. 1 and 2, Minneapolis, University of Minnesota Press, 1972.

Faulkner, T.P., Hayden, J.H., Mehta, C.M., Olson, D.A., and Comstock, E.G. Dose-response studies on tolerance to multiple doses of secobarbital and methaqualone in a polydrug abuse population. *Clin. Toxicol.*, 15:23-37, 1979.

Gerald, M.C., and Schwirian, P.M. Nonmedical use of methaqualone. *Arch. Gen. Psychiatry*, 28:627-631, 1973.

Haertzen, C.A. An Overview of the Addiction Research Center Inventory (ARCI): An Appendix and Manual of Scales, National Institute of Drug Abuse, Rockville, MD, 1974.

Heck, H.d'A., Maloney, K., and Anbar, M. Long-term urinary excretion of methaqualone in a human subject. *J. Pharmacokinet. Biopharm.*, 6:111-122, 1978.

Jasinski, D.R. Clinical evaluation of sedative-hypnotics for abuse potential, 285. In: Thompson, T., and Unna, K. (eds.), *Predicting Dependence Liability of Stimulant and Sedative Drugs*. Baltimore: University Park Press, 1977.

Jasinski, D.R. Clinical evaluation of benzodiazepines for abuse potential. Abstracts presented at the annual meeting of the American College of Neuropsychopharmacology, Coronado, California, December 16-18, 1981.

Jasinski, D.R., Griffith, J.D., Pevnick, J., Gorodetzky, C., Cone, E., and Kay, D. Progress Report from the Clinical Pharmacology Section of the NIDA Addiction Research Center. Presented to the Committee on Problems of Drug Dependence, National Research Council, Cambridge, MA, 1977.

Kochansky, G.E., Hemenway, T.S., III, Salzman, C., and Shader, R.I. Methaqualone Abusers: A preliminary survey of college students. *Dis. Nerv. Syst.*, 36:348-351, 1975.

Kuhn, D.M., and Shah, N.S. Subcellular localization of (^{14}C) methaqualone in mouse brain: Effects of hepatic microsomal enzyme inhibition. *Toxicol. Appl. Pharmacol.*, 46:109-116, 1978.

Marks, P., and Sloggem, J. Peripheral neuropathy caused by methaqualone. *Am. J. Med. Sci.*, 272:323-326, 1976.

Martin, W.R., Sloan, J.W., Sapira, J.D., and Jasinski, D.R. Physiologic, subjective and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetramine, and methylphenidate in man. *Clin. Pharmacol. Ther.*, 12:245-258, 1971.

McNair, D., Lorr, M., and Droppleman, L. Profile of Mood States Manual, San Diego, Educational and Industrial Testing Service, 1971.

Meyer, J.S., and Boggan, W.O. The effects of methaqualone on pituitary-adrenocortical activity in mice. *Psychopharmacology (Berlin)*, 54:51-55, 1977.

Morris, R.N., Gunderson, G.A., Babcock, S.W., and Zaroslinski, J.F. Plasma levels and absorption of metha-

qualone after oral administration to man. *Clin. Pharmacol. Ther.*, 13:719-723, 1972.
Muller, W.E., Schlafer, U., and Wollert, U. Benzodiazepine receptor binding: The interactions of some nonbenzodiazepine drugs with specific (^{3}H) diazepam binding to rat brain synaptosomal membranes. *Arch. Pharmacol.*, 305:23-26, 1978.
Naik, S.R., Naik, P.R., and Sheth, U.K. Involvement of gamma-amino butyric acid (GABA) in the anticonvulsant action of methaqualone. *Psychopharmacology (Berlin)*, 57:103-107, 1978.
Prabhu, C.G., Browne, R.K., and Zarosinski, J.F. Studies on the metabolism in rat and mouse of a new hypnotic – methaqualone. *Arch. Int. Pharmacodyn Ther.*, 148:228-236, 1964.
Rundell, O.H., Williams, H.L., and Lester, B.K. Comparative effects of alcohol, secobarbital, methaqualone, and meprobamate on information processing and memory. *Adv. Exp. Med. Biol.*, 85A:617-628, 1977.
Saxena, R.C., Thacore, V.R., Suri, T.N., Agarwal, T.N., and Bhargava, K.P. Electroencephalographic studies with I.V. methaqualone in man. *Electroencephalogr. Clin. Neurophysiol.*, 43:876-879, 1977.
Singh, N., Nath, R., Kulshreatha, V.K., and Kohli, R.P. An experimental evaluation of dependence liability of methaqualone diphenhydramine (combination) and methaqualone in rats. *Psychopharmacology (Berlin)*, 67:203-207, 1980.
Swartzburg, M., Lieb, J., and Schwartz, A.H. Methaqualone withdrawal. *Arch. Gen. Psychiatry*, 29:46-47, 1973.
Tennant, F.J., Jr. Complications of methaqualone-diphenhydramine (Mandrax®) abuse. *Br. J. Addict.*, 68:327-330, 1973.
Woody, G.E., O'Brien, C.P., and Greenstein, R. Misuse and abuse of diazepam: An increasingly common medical problem. *Int. J. Addict.*, 10:843-849, 1975.

What Is the Effect of "Stress" on Neuroendocrine Function? In-Depth Consideration of Recent Theorizing

Chair: **Redford B. Williams, Jr., M.D.**
Duke University Medical Center
Durham, North Carolina

Heterogeneity in the Response Pattern of Organ Systems to Stress: Mediators and Mechanisms

Cynthia M. Kuhn, Ph.D.,[1] Alberto Grignolo, Ph.D.[1] Mark Johnson,[1] and Saul M. Schanberg, M.D., Ph.D.[1]

Ornithine decarboxylase (ODC, E.C.4.1.1.17) catalyzes the first step in the synthesis of the polyamines putrescine, spermidine, and spermine. This enzyme is an extremely useful index of cellular response to stimulation because its activity changes rapidly in response to numerous physiological events that affect the metabolic activity of the cell. In this laboratory, ODC has been used as a tool to characterize the effects of a number of hormones and neuroeffectors on tissue function, and to identify mediators of stress effects in developing and adult rats. Previous studies have shown that pharmacologic or physiologic stimulation of the sympathetic nervous system (SNS) by alpha or beta adrenergic agonists, insulin-induced hypoglycemia, or other simuli increases ODC activity in several organs including heart, kidney, liver, and aorta (Thadani & Schanberg 1979; Slotkin 1979; Grignolo et al. 1982). In the present study, the pattern of tissue ODC response to stress and neural and nonneural mediators of stress effects have been investigated. These studies show that ODC responses to stress are determined by the organ, age of the animal, and the type of stress.

Two hours of continuous immobilization (IMM) increase ODC activity in liver, heart, kidney, and aorta. However, with longer periods of IMM, a more complex pattern is observed. ODC activity continues to increase in kidney and liver, while heart ODC decreases. In contrast,

---

[1] Department of Pharmacology, Duke University Medical Center, Durham, NC 27710.

shaker stress, which has been reported to cause sympathoadrenal activation and hypertension in experimental animals (Bunag et al. 1980), causes a marked decrease in heart ODC activity but no change in kidney or liver ODC activity (Table 1). Interestingly, these stresses evoke different patterns of ODC response despite the fact that both cause a marked increase in serum levels of corticosterone (Table 2). Corticosterone is a potent inducer of liver and kidney ODC activity (Panko & Kenny 1971; Nicholson et al. 1976), yet ODC activity increased during IMM but not shaker stress, despite significant elevations in serum corticosterone during both stress paradigms. These findings suggest that some other physiologic response associated with these stress paradigms contributes to the regulation of ODC activity.

Table 1

Effects of Shaker Stress on Tissue ODC Activity

Organ	Control		ODC Activity (percent control)			
			2 hours		6 hours	
Kidney	100 ± 19	(47)	113 ± 20	(11)	111 ± 19	(18)
Heart	100 ± 35	(48)	95 ± 15	(10)	32 ± 5*	(18)
Liver	100 ± 18	(40)	107 ± 16	(9)	71 ± 5	(19)

Animals were shaken in a group at 175 oscillations/minute for 2 or 6 hours or left undisturbed in the home cage, then killed and tissue ODC activity determined. Results are expressed as percent control ± SEM. N is indicated in parentheses.

* Indicates statistically different from control activity, $p < .05$ or better. Control ODC activity = 0.68 nmole/g/hr for heart, 4.99 nmole/g/hr for kidney, and 0.185 nmole/g/hr for liver.

Table 2

Effect of Shaker Stress and Immobilization on Serum Corticosterone Concentration

	Corticosterone (ng/ml)	
Control	45 ± 11	(13)
IMM	338 ± 74*	(15)
Shaker	267 ± 34*	(15)

Animals were left undisturbed (control), immobilized in wire mesh cages or shaken in a group (175 oscillations/minute) for 4 hours, then killed and serum corticosterone determined by radioimmunoassay. Results are expressed as ng/ml ± SEM.

*Indicates statistically different from control, $p < .001$. N is indicated in parentheses.

The fact that stimulation of the sympathetic innervation elevates ODC activity in several peripheral tissues (Thadani & Schanberg 1979; Slotkin 1979) suggested that stress effects might be mediated neurally. This possibility was investigated by determining the effect of the ganglionic blocker chlorisondamine on the ODC elevation associated with IMM. Chlorisondamine markedly inhibited the increase in heart ODC associated with IMM in 26-day-old rats (Table 4). These results suggest that the ODC increase after IMM is mediated primarily by neural mechanisms and helps explain the discrepancy between serum corticosterone levels and ODC activity that is observed during IMM and shaker. The finding that the ODC increase associated with IMM could be almost completely blocked by chlorisondamine indicates that the marked corticosterone elevation which occurs during IMM does not significantly stimulate ODC activity. This finding further suggests that tissue ODC sensitivity to glucocorticoid hormones is altered during stress. Suppression of GH sensitivity during stress has already been reported (Kuhn et al. 1979).

An effect of stress that cannot be explained by SNS activation is the decrease in heart ODC which is observed during shaker stress and after long periods of IMM. Findings from other laboratories suggest that certain stresses including prolonged IMM can increase *vagal* activity (Fitzgerald 1975). To investigate this possibility, animals were pretreated with atropine, and then exposed to shaker stress. Atropine did not affect basal ODC activity, but almost completely prevented the decline associated with shaker stress (heart ODC values in shaker animals = 30 ± 7% of control, while values in atropine-treated animals = 84 ± 12% of control). These results indicate that vagal activity contributes to the decline in ODC associated with shaker stress, and suggest that the decrease in heart ODC activity that occurs after 6 hours of IMM might also reflect increased vagal tone to the heart.

The ODC responses to stress described above are not constant throughout an animal's lifetime, but change as the animal develops. ODC responsivity to stress in immature animals differs from that observed in adults in two ways. First, certain environmental stimuli change ODC activity in neonates, but not in adults. Second, the changes

Table 3

Effect on Stress on Tissue ODC Activity in Neonatal Rats

	Tissue ODC Activity (percent control)					
	Heart		Liver		Brain	
Control	100 ± 13	(35)	100 ± 24	(49)	100 ± 13	(14)
Maternal Deprivation	40 ± 9*	(57)	14 ± 4*	(48)	39 ± 3*	(15)
Deprived + Immobilized	101 ± 14**	(35)	98 ± 49**	(20)		
Deprived + Cold	151 ± 32**	(35)	140 ± 31**	(17)	70 ± 9**	(15)

Eight-day-old rat pups were deprived in an incubator, placed in an incubator in wire restraining cages, or placed in a 4° cold room for 2 hours. Controls were left with the mother for this time period. At the end of 2 hours, all animals were killed and tissue ODC activity was determined. Results are expressed as percent control ± SEM. *N* is indicated in parentheses.

*Indicates statistically different from control, $p < .05$ or better.

**Indicates statistically different from deprived animals, $p < .05$ or better.

Table 4

Effect of Chlorisondamine on ODC Activity During Immobilization

	ODC Activity (percent control)					
	Heart		Liver		Kidney	
Day 26						
Control	100 ± 13	(20)	100 ± 16	(18)	100 ± 17	(16)
Immobilized	297 ± 23*	(10)	277 ± 83*	(10)	1010 ± 300*	(9)
Chlorisondamine	85 ± 14	(20)	78 ± 16	(18)	162 ± 39*	(19)
Chlor + IMM	144 ± 21**	(10)	117 ± 11**	(10)	79 ± 20**	(10)
Day 10						
Control	100 ± 14	(8)				
Immobilized	171 ± 27*	(8)				
Chlorisondamine	106 ± 18*	(9)				
Chlor + IMM	200 ± 27*	(10)				

Animals were injected with saline or chlorisondamine, then immobilized for 2 hours in wire mesh cages and tissue ODC activity determined. Results are expressed as percent control ± SEM. *N* is indicated in parentheses.

*Indicates $p < .05$ or better relative to control.

**$p < .05$ or better relative to immobilized.

Control ODC activity = .295 nmole/g/hr for hearts on Day 26, 0.735 for Day 10. .238 nmole/g/hr for kidney and .399 nmole/g/hr for liver.

induced by classical stress paradigms are mediated by different physiological mechanisms in adults and neonates. Maternal deprivation (MD) of neonatal rats causes an immediate and long-lasting decline in ODC activity in most organs (Butler & Schanberg 1977). This decline is observed only in preweanling rats, and is initiated by the loss of a specific form of tactile stimulation of the pups by the mother (Butler & Schanberg 1977; Evoniuk et al. 1979). On the other hand, IMM or cold stress elevates ODC activity significantly in preweanling rat pups (Table 3). This finding suggests that maternal deprivation and the "classical" stress paradigms IMM and cold evoke distinct biochemical responses in developing rats. Furthermore, the heart ODC increase following IMM is not mediated neurally in pups, as chlorisondamine did not block stress effects in 10-day-old pups (Table 4). This finding is consistent with reports that functional sympathetic innervation of most peripheral organs is established between Days 12 and 16 postnatally (Slotkin 1979) and suggests that SNS activation is not the sole mediator of stress effects in developing animals.

These studies show that ODC responses to stress are a function of the type of stress, the organ, and the age of the animal. First, IMM and shaker evoke very different patterns of ODC response in adult rats, indicating that stress is not "nonspecific." Second, the sensitivity of a given organ to a hormone during stress appears to be modulated by concomitant changes in the activity of the autonomic nervous system and other endocrine systems. Furthermore, stress-induced secretion of certain hormones (e.g., corticosterone) does not necessarily lead to predictable biochemical responses in individual organs; that is, different tissue responses can be obtained in the presence of hormonal responses that are qualitatively and quantitatively identical. Third, certain stresses are effective only at certain maturational stages (e.g., maternal deprivation); others are effective at all ages but activate different effector pathways (e.g., neural vs. nonneural) depending upon the age of the animal and the maturity of those pathways.

Our studies of stress-induced changes in ODC activity suggest that this enzyme is an extremely useful tool for investigating hormonal and neural mediators of stress. By correlating ODC activity with endocrine and neural response patterns, we can obtain valuable information about the physiological responses of adult and immature animals to environmental challenges.

References

Bunag, R.D., Takeda, K., and Riley, E. Spontaneous remission of hypertension in awake rats chronically exposed to shaker stress. *Hypertension,* 2:311-318, 1980.

Butler, S.R., and Schanberg, S.M. Effect of maternal deprivation on polyamine metabolism in preweanling rat brain and heart. *Life Sci.*, 21:877-884, 1977.

Evoniuk, G.E., Kuhn, C.M., and Schanberg, S.M. The effect of tactile stimulation on serum growth hormone and tissue ornithine decarboxylase activity during maternal deprivation in rat pups. *Commun. Psychopharmacol.*, 3:363-370, 1979.

Fitzgerald, R. Involvement of vagal activity in the unconditioned heart rate responses of restrained rats. *Physiol. Behav.*, 17:785-788, 1975.

Grignolo, A., Kuhn, C.M., and Schanberg, S.M. Maturation of growth hormone stimulation of kidney ornithine decarboxylase in the rat. *Life Sci.*, 30:383-390, 1982.

Kuhn, C.M., Evoniuk, G., and Schanberg, S.M. Loss of tissue responsivity to growth hormone during maternal deprivation in rats. *Life Sci.*, 25:2089-2097,1979.

Nicholson, W.E., Levine, J.H., and Orth, D.N. Hormonal regulation of renal ornithine decarboxylase activity in the rat. *Endocrinology,* 98:123-128, 1976.

Panko, W.B., and Kenney, F.T. Hormonal stimulation of hepatic ornithine decarboxylase. *Biochim. Biophys. Acta.* 43:346-350, 1971.

Slotkin, T.A. Ornithine decarboxylase as a tool in developmental neurobiology. *Life Sci.*, 24:1623-1630, 1979.

Thadani, P.V., and Schanberg, S.M. Effect of stress and sympathetic activity on rat cardiac and aortic ornithine decarboxylase activity. *Life Sci.*, 25:1009-1016, 1979.

Neurotransmitter Receptors: Heterogeneity, Regulation, and Function

Chair: **Henry I. Yamamura, Ph.D.**
Department of Pharmacology
University of Arizona Health Sciences Center
Tucson, Arizona

Correlation Between Pharmacological Activity and the Influence of GABA on the Binding of Flunitrazepam and the Specific Benzodiazepine Antagonist, Ro 15-1788[1]

Frederick J. Ehlert, Ph.D.,[2] William R. Roeske, M.D.,[2] Andrew Chen, B.S.,[2] and Henry I. Yamamura, Ph.D.[2]

Several lines of evidence indicate that gamma-aminobutyric acid (GABA) mechanisms are involved in the mediation of the pharmacological effects of benzodiazepines. The results of electrophysiological studies, for example, have shown that benzodiazepines potentiate the effects of GABA in a variety of neuronal systems (Tallman et al. 1980). Insight into the nature of the link between the pharmacological actions of benzodiazepines and GABA has come from biochemical experiments in which co-purification of GABA receptors and benzodiazepine receptors was demonstrated, and also from binding experiments in which GABA has been shown to enhance the binding of benzodiazepines (Olsen 1981). Results such as those described above have led to the suggestion that at least some benzodiazepine receptors are coupled to GABA receptor-chloride ionophore complexes. If the effects of GABA on the benzodiazepine receptor are related to the mechanism of action of benzodiazepines, then a correlation between the GABA modulation of binding and the pharmacological efficacy of a series of drugs which interact with the benzodiazepine receptor might be anticipated. Accordingly, we have found recently that GABA enhances the binding of the novel anxiolytic, CL218,872 (3-methyl-6-[3-trifluoromethylphenyl]-1,2,-4-triazolo[4,3-b]pyridazine) (Regan et al. 1981) but has little or no effect on the binding of presumptive pharmacological antagonist of benzodiazepines, propyl-carboline-3-carboxylate (Ehlert et al. 1981). Since a new class of compounds, the imidazodiazepines, have been reported to bind with high affinity to the benzodiazepine receptor and to antagonize selectively the pharmacological effects of tranquilizing benzodiazepines (Hunkeler et al. 1981), a quantitative study of the influence of GABA on the binding of the representative antagonist imidazodiazepine, Ro15-1788 (ethyl-8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxylate), might provide additional evidence for a correlation between GABA modulation of binding and pharmacological activity. In the present report, the results of such a study are presented and are shown to be consistent with the postulate that GABA enhances the benzodiazepine receptor binding activity of anxiolytics, like flunitrazepam (FLU), whereas the binding of benzodiazepine antagonists, like Ro15-1788, is largely insensitive to the influence of GABA.

---

[1] The authors thank Dr. William Haefely of Hoffman-La Roche, Basel, Switzerland, for providing the Ro 15-1788. Part of this work was supported by USPHS Grants MH-27257, MH-30626, HL-21486 and Program Project Grant HL-20984. H.I.Y. is a recipient of a USPHS Research Scientist Development Award, Type II (MH-00095), from the National Institute of Mental Health, and W.R.R. is a recipient of a USPHS Research Scientist Development Award (HL-00776) from the National Heart, Lung, and Blood Institute.

[2] Departments of Pharmacology, Psychiatry, Biochemistry, and Internal Medicine and the Arizona Research Laboratories, University of Arizona Health Sciences Center, Tucson, AZ 85724.

Benzodiazepine receptor binding assays were carried out on the rat cerebral cortex using [^{3}H]FLU (83.6 Ci/mmole); the details of the assay have been given in a previous report (Ehlert et al. 1981). Briefly, cortical homogenates (20 mg original wet tissue weight/ml buffer) were washed five times by centrifugation and resuspension in fresh phosphate buffer (pH 7.4, 9.5 mM K$^+$, 81 mM Na$^+$, 50 mM PO$_4$). Binding was measured by the filtration method, and incubation lasted 30 min at 37°C.

Table

Effect of GABA on the Competitive Inhibition of [^{3}H]FLU Binding by FLU and Ro 15-1788

	IC_{50}[1]		IC_{50}control
	Control (nM)	10μM GABA (nM)	IC_{50} GABA
FLU (100 mM NaCl)	17.8	5.6[2]	3.2 (2.1 - 4.7)[3]
Ro15-1788	5.6	6.3	0.89 (0.64 - 1.2)
Ro15-1788 (100 mM NaCl)	7.1	6.3	1.1 (0.89 - 1.3)

[1] The IC_{50} represents the concentration of non-labeled drug that caused 50% inhibition of specific [^{3}H]FLU binding. Each IC_{50} value represents the geometric mean of values from four experiments.
[2] Significantly different from control, $p < 0.005$.
[3] 95% confidence limits.

The results of FLU/[^{3}H]FLU and Ro15-1788/[^{3}H]FLU competition experiments carried out in the presence or absence of GABA (10^{-5} M) are shown in the Table. In the presence of 100 mM NaCl, GABA caused a 3.2-fold reduction in the IC_{50} of FLU from 17.8 nM in controls to 5.6 nM in the presence of GABA. Since the concentration of [^{3}H]FLU (0.5 nM) used in the competition experiment was much less than the IC_{50} values, correction from IC_{50} to K_i led to negligible changes in the results. We have shown previously that in the absence of 100 mM NaCl GABA (10^{-5} M) only causes a 1.9-fold reduction in the IC_{50} of FLU at 37°C (Ehlert et al. 1981). In contrast, no significant effects of GABA (10^{-5} M) on the binding of Ro15-1788 were detected in the presence or absence of 100 mM NaCl (*see* Table). Identical results were obtained in the presence of 10^{-4} M GABA (data not shown).

The present results illustrate that under conditions in which GABA causes a moderate increase in the potency of FLU, no significant effects of GABA on the binding of the imidazodiazepine analogue Ro15-1788 are demonstrable. Since the results of pharmacological studies indicate that Ro15-1788 is a specific antagonist of tranquilizing benzodiazepines (Hunkeler et al. 1981), the present data are consistent with our previous suggestion that measurement of the influence of GABA on the binding of ligands to the benzodiazepine receptor may be a useful technique for determining if a drug has pharmacological properties agonistic or antagonistic to benzodiazepines (Ehlert et al. 1981).

References

Ehlert, F.J., Roeske, W.R., and Yamamura, H.I. Multiple benzodiazepine receptors and their regulations by γ-aminobutyric acid. *Life Sci.*, 29:235, 1981.

Hunkeler, W., Möhler, H., Pieri, L., Polc, P., Bonetti, E.-P., Cumin, R., Schaffner, R., and Haefely, W. Selective antagonists of benzodiazepines. *Nature*, 290:514-516, 1981.

Olsen, R.W. GABA-benzodiazepine-barbiturate receptor interactions. *J. Neurochem.*, 37:1, 1981.

Regan, J.W., Roeske, W.R., Malick, J.B., Yamamura, S.H., and Yamamura, H.I. GABA enhancement of CL-218,872 affinity and evidence of benzodiazepine receptor heterogeneity. *Mol. Pharmacol.*, 20:477, 1981.

Tallman, J.F., Paul, S.M., Skolnick, P., and Gallager, D.W. Receptors for the age of anxiety: Pharmacology of the benzodiazepines. *Science*, 207:274, 1980.

Down Regulation and Heterogeneity of Opiate Receptors

Kwen-Jen Chang, Ph.D.,[1] and Steven G. Blanchard, Ph.D.[1]

One of the adaptative responses of cells or neurons to chronic exposure to ligands is regulation of receptor number. While for most polypeptide hormones and some neurotransmitters the receptor number is decreased after chronic ligand treatment, for the opiate receptor no alteration of receptor numbers after chronic opiate treatment in animals has been observed despite the development of opiate tolerance and dependence. The investigators reexamined this phenomenon in a simple system, the cultured neuroblastoma cell.

Cultured mouse neuroblastoma cells (N4TG1) serve as a useful model for studies on the molecular and cellular action of opiates and opioid peptides (Chang et al. 1978; Chang & Cuatrecasas 1979). Direct receptor binding studies with a labeled enkephalin analog on neuroblastoma cells did not indicate internalization of opiate receptors since nearly all cell associated label was dissociated as intact molecules (Chang et al. 1978). Using the fluorescent enkephalin analog, rhodamine-conjugated [D-Ala^2,Lys^6] leu-enkephalin and image-intensified fluorescence microscopy, enkephalin (δ) receptors in neuroblastoma cells were found to slowly form clusters which do not appear to be internalized (Hazum et al. 1979a,b, 1980). This result differs from many polypeptide (hormones) receptors (*see* review by Hazum et al. 1981) such as for insulin, epidermal growth factor, nerve growth factor, α_2-macroglobulin, chemotactic peptide, and gonadotropin releasing hormone, in which the receptors are internalized following the initial receptor-ligand interactions. This internalization is believed to be related to the so-called down regulation or desensitization.

Chang et al. (1982b) reported that after one to several hours' exposure of neuroblastoma cells in monolayer culture to enkephalin, the number of enkephalin receptors measured subsequently in the extensively washed membrane preparations is greatly reduced. This action is referred to as down regulation. This reduction in receptor number seems selective for opioid peptides and is antagonized by a variety of opiate agonists and antagonists.

Confluent monolayers of cultured mouse neuroblastoma cells (N4TG1) were pretreated with ligand, the cells were then washed extensively with phosphate buffered saline (PBS) to remove ligand remaining bound, and membrane particulate fractions were prepared and washed again with Na+-containing buffer to dissociate any remaining ligand. The enkephalin receptor binding was then measured with ^{125}I-labeled [D-Ala^2, D-leu^5] enkephalin (DADLE) on those cell membrane particulate preparations. Similar results were also obtained when [^{3}H]DADLE or [^{3}H]diprenorphine was used as labeled ligand. Pretreatment of the cell monolayer for 4 hours with 0.1 μM DADLE led to a large reduction of the binding activity of labeled ligands. This reduction induced by the DADLE pretreatment is time, temperature, and dose dependent (Chang et al. 1982b). At 37°C, significant reduction was observed after half-hour pretreatment, and had nearly reached maximum (about 80% reduction) after 1 hour. At 24°C, this reduction in binding is greatly decreased with respect to both the rate and the extent of reduction. The DADLE-induced down regulation is dose dependent with an EC_{50} value of about 2 nM. This value is in reasonable agreement with the previously determined dissociation constant (K_d) of DADLE for enkephalin receptor of this cell line (Chang et al. 1978; Chang & Cuatrecasas 1979).

Down regulation induced by DADLE is specific for opiate receptors, since this effect can be antagonized by the presence of an excess of opiate antagonists such as naloxone, nalorphine, and diprenorphine (Figure 1A). These antagonists do not induce down regulation when they are present alone (Figure 1A). The natural endogenous peptides, met- and leu-enkephalin as well as β-endorphin, and their metabolically stable analogs [D-Ala^2,NMePhe^4,Met(O)ol^5] enkephalin (FK 33824) and [D-Ala^2,Met^5] enkephalinamide can also induce similar down regulation at concentrations of less than μM.

Morphine and benzomorphan drugs such as ketocyclazocine, a κ-agonist, and N-allylnormetazocine, a σ-agonist, at high concentrations induce only a slight and nonsignifi-

---

[1] Molecular Biology Department, Wellcome Research Laboratories, Research Triangle Park, NC 27709.

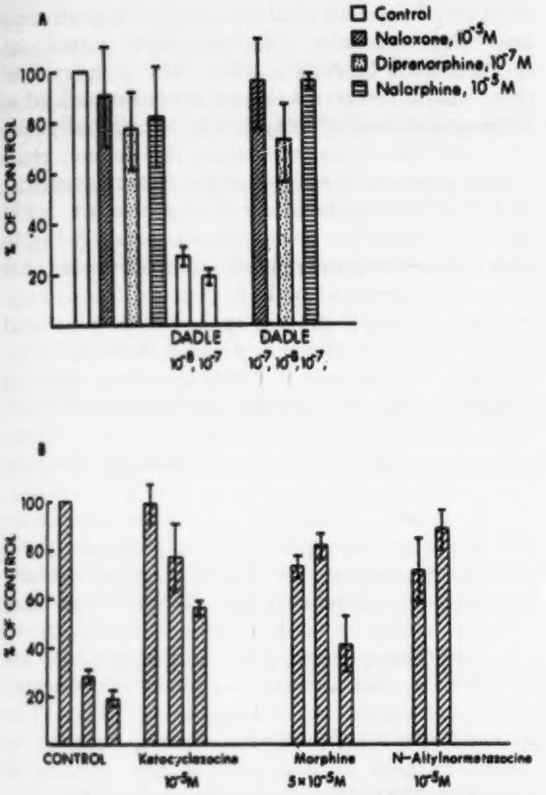


FIGURE 1: Specificity of the ligand-induced opiate receptor down regulation.

N4TG1 cells were grown to confluence in DMEM supplemented with 75 units/ml penicillin, 75 μg/ml streptomycin sulfate and either 7 or 5% newborn calf serum (GIBCO) in a 95% air/5% CO_2 humidified atmosphere at 37°. Cells were incubated with or without various opiate agonists (B) and antagonists (A) in the absence and presence of DADLE as indicated in the figure for 4 hours at 37°C. After completion of the incubation the medium was withdrawn, the monolayers rinsed with PBS and the cells were detached using 0.05% EDTA in PBS. The cells were pelleted by centrifugation, resuspended in PBS and incubated for 30 minutes at 37° to remove bound ligand. This incubation was repeated once and then the cell pellet was resuspended in ice cold 50 mM Tris, pH 7.7, and the cells were homogenized using a Model PT-20 Polytron (setting 3.5, 20 sec). The homogenates were centrifuged at 40,000 xg for 30 minutes and the resulting pellets were resuspended in 50 mM Tris, pH 7.7, containing 100 mM NaCl and the suspensions were incubated at room temperature for 1 hour. The membranes were again pelleted, resuspended, and pelleted once in Tris buffer lacking sodium, and assayed for ^{125}I-DADLE binding.

cant receptor reduction (usually about 20%). They can also antagonize the effect of opioid peptides (Figure 1B). This antagonistic effect of opiates against peptides is also dose dependent. Opiates are more effective against a dose of 10^{-8} M than of 10^{-7} M DADLE, as would be expected for competitive inhibition (Figure 1B).

Incubation of cell monolayers with 10^{-8}M [^{3}H]DADLE at 37° for 4 hours followed by washing and preparation of membrane particulates in manner identical to that used for the nonradioactive ligand showed that only 10 percent of the ligand initially associated with the cells remained bound. This corresponds to a concentration of DADLE of less than 10^{-10}M in the final assay. Because incubation of cells with the 10^{-8}M DADLE caused about 70 percent down regulation, the loss of binding activity could not simply be attributed to the competition of ^{125}I-DADLE with ligand that remained after preparation of the membrane fragments. Furthermore, diprenorphine, a ligand known to have an affinity greater than DADLE (Chang et al. 1980), does not cause significant receptor reduction after similar pretreatment, suggesting that peptide-induced receptor loss could not be simply explained by the high affinity of the ligand that may not be washed away.

The enkephalin-induced binding reduction is manifested by a decrease in the number of high affinity binding sites, presumably enkephalin (δ) receptors. The Scatchard plots of the saturation binding curves of ^{125}I-DADLE for control and DADLE (0.1 μM) pretreated cell membranes revealed the loss of total high affinity binding sites without changing the slope (Figure 2). Thus, binding sites remaining after DADLE pretreatment have an affinity similar to that of the control membranes. This is further confirmed by the competition binding studies of DADLE and morphine against ^{125}I-DADLE binding. No significant difference in IC_{50} values (the concentrations which cause 50 percent inhibition of labeled binding) between control and pretreated membranes was observed (Chang et al. 1982a). IC_{50} values of about 50 nM for morphine and 1 nM for DADLE were observed for both control and pretreated membranes in agreement with previously reported values (Chang & Cuatrecasas 1979; Chang et al. 1978, 1979).

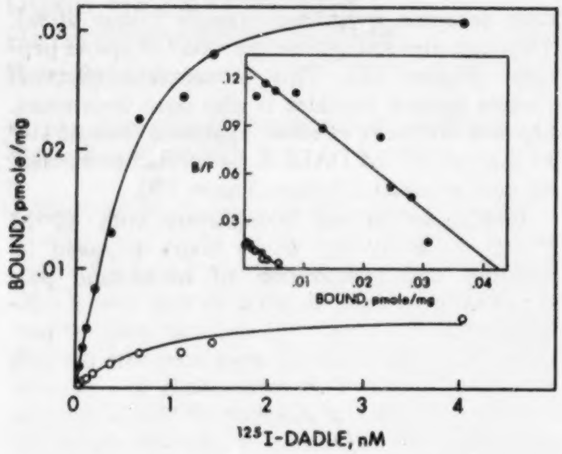


FIGURE 2: Binding of ^{125}I-DADLE to N4TGl membranes before and after preincubation of cells with unlabeled DADLE.

Confluent cultures of N4TGl cells were incubated with or without 10^{-8}M unlabeled DADLE and membranes were prepared as described in the legend to Figure 1. Aliquots of the membranes were incubated for 1 hour with various concentrations of ^{125}I-DADLE after which time bound ligand was determined by rapid filtration through glass fiber filters. Nonspecific binding was determined in the presence of 10^{-5}M unlabeled DADLE. Plots of control (●) and treated (O) membranes are shown. *Inset:* Scatchard plots of the data are shown. The control membranes had a Kd of 0.76 nM and B_{max} of 42.8 fmol/mg while the values for the treated membranes were 0.83 nM and 6.4 fmol/mg, respectively.

The decrease in receptors specifically induced by opioid peptides is intriguing. Numerous *in vivo* and *in vitro* experiments have indicated that enkephalin can mimic the biological effects of morphine, including the development of tolerance and physical dependence (Wei & Loh 1976). To our knowledge, the present results are the first demonstration of opiate receptor down regulation and appear to contradict the conventional concept. Opioid peptides, but not opiate alkaloids, induce down regulation. It will be interesting to know whether this selective effect for opioid peptides is due to the particular opiate receptor subtype in neuroblastoma cells or to neoplastic properties of this cell line. It also will be interesting to know whether the same effect can be observed in the other subtypes of opiate receptors.

Currently it is believed that there are at least five opiate receptor subtypes (Chang & Cuatrecasas 1981). There are $\mu,\varkappa,\sigma,\delta$, and ϵ receptors based on pharmacological experiments and four receptor binding sites based on radioreceptor binding studies. The properties of these opiate receptor subtypes are summarized as follows: $\mu,\varkappa$, and σ receptors were originally proposed by Martin to account for the distinct pharmacological actions of morphine, ketocyclazocine, and N-allylnormetazocine. For μ-receptor, morphine is a selective prototype μ-agonist. A highly selective μ-receptor peptide, morphiceptin, has also been identified to be a peptide fragment of β-casein, a major protein in cow milk (Chang et al. 1981a). Kosterlitz, Paterson, & Robson (1981) and others (Handa et al. 1981) have also obtained a highly selective peptide ([D-Ala^2,NMePhe^4, Gly^{5}ol]enkephalin) for μ-receptor. Either μ-Receptors predominate in guinea pig ileum or the intrinsic activity of μ-receptor in guinea pig ileum is greater. Naloxone is a potent antagonist. Mu-receptors are predominately localized in brain areas associated with analgesia and sensory functions (Goodman et al. 1980). They may mediate analgesic and cataleptic activities in animals (Chang et al. 1982a). The possible existence of μ_1 and μ_2-receptors has also been suggested recently by Pasternak (1981). The μ_1-receptor is inhibited irreversibly by naloxazone treatment both *in vivo* and *in vitro* (Zhang & Pasternak 1981; Wolozin & Pasternak 1981).

For $\varkappa$-receptors, ethylketocyclazocine (EKC) is the typical $\varkappa$-agonist. Recent data from Wüster et al. (1980) and Chavkin and Goldstein (1981) have suggested that dynorphin may serve as a natural ligand for $\varkappa$-receptors. Mouse vas deferens and guinea pig ileum tolerant to μ- and δ-agonists do not show tolerance to dynorphin. High cross tolerance occurs between the typical $\varkappa$-agonists and dynorphin. These receptors show less antagonistic sensitivity to naloxone. They may mediate sedation in animals and hallucinatory and dysphoric effects in man.

Although it was originally postulated that σ-receptor is a subtype of opiate receptor (Gilbert & Martin 1976), the data currently available suggest that it may be a non-opiate type receptor. The typical hyperactivity caused by σ-agonists, is not antagonized by naloxone, only the (+) stereoisomer is active and the effects resemble those of phencyclidine. In studies on stimulus-discriminative procedure, Herling and Wood (1981) showed that rats trained to discriminate phencyclidine generalize to σ-agonists such as

N-allylnormetazocine and cyclazocine. Furthermore, using binding studies, several laboratories (McLowhon et al. 1981; Zukin & Zukin 1981) have also provided evidence that perhaps the σ-agonists bind to the phencyclidine binding sites in addition to their opiate receptor activities.

Delta-receptors were proposed by Lord et al. (1977) to account for the high potency of enkephalin in mouse vas deferens. Many available cultured neuroblastoma cells also contain homogenous δ-receptors (Chang & Cuatresasas 1979). Naloxone is known to be less active in this system than in the μ-receptor system. Delta-receptors are predominately located in the limbic system, as shown by Goodman et al. (1980), and may mediate the action of epileptic seizures (Frenk et al. 1978a, 1978b; Liebeskind 1978) and possibly the reward behavior described by Stein and Belluzzi (1978) and other affective actions of opiates.

Schulz et al. (1979) proposed ϵ-receptors to account for the unusual selective potency of β-endorphin in rat vas deferens. In this system, both enkephalin and morphine are poor ligands. Interestingly, κ-agonists such as ethylketocyclazocine, bremazocine, and MR2034 behave as rather potent competitive antagonists (Huidoboro et al. 1980; Gillan et al. 1981).

Biochemical receptor binding studies utilizing highly specific radioisotope labeled ligands have confirmed at least three topographically distinct opiate receptor binding sites in brain (Chang et al. 1981b). They are opiate alkaloid morphine preferring binding sites, peptide enkephalin preferring binding sites, and binding sites selective for benzomorphan drugs. Morphine binding sites represent μ-receptors which can be studied with low concentrations of [^{3}H]-labeled dihydromorphine, naloxone, naltrexone or ^{125}I-labeled FK 33-824. Enkephalin binding sites labeled by low concentrations of labeled enkephalins and DADLE are δ-receptors. After quenching μ and δ-receptors with a μ-agonist, morphiceptin and a δ-agonist, DADLE, [^{3}H]diprenorphine binds to a third opiate receptor which we call benzomorphan binding site (Chang 1981). Excluding σ-receptor as an opiate receptor, at present, it is still not clear whether the benzomorphan binding site corresponds to κ or ϵ receptors, since both have similar high affinity for benzomorphan drugs and low affinity for enkephalin and morphine. Kosterlitz et al. (1981) and Pfeiffer and Herz (1981) have claimed that a similar κ-binding site is identified by using [^{3}H]EKC. However, etorphine which is believed to have no κ-agonist activity has high affinity for this [^{3}H)EKC binding site. Beta-endorphin also shows high affinity compared to enkephalin. It remains to be established whether benzomorphan binding sites are identical to the κ-binding sites.

Using ^{125}I-labeled [D-Ala^2]β_h-endorphin, Hazum et al. (1979c) have reported the existence of a non-opiate but β-endorphin specific binding site. A similar non-opiate β-endorphin specific binding has also been observed in a neuroblastoma cell line N18TG2 by Hammonds and Li (1981) who use [^{3}H]labeled β-endorphin.

Previous *in vivo* morphine chronic experiments have led to the conclusion that neither the number nor the affinity of receptors are altered after chronic treatment with morphine (Pert et al. 1973; Klee & Streaty 1974; Hölt et al. 1975; Simon & Hiller 1978). Similar experiments to measure the binding activities of three subtypes of opiate receptors including morphine (μ), enkephalin (δ), and benzomorphan binding sites after chronic morphine treatment *in vivo* have been carried out in this investigator's laboratory. The results confirmed the previous conclusion that neither the number nor the affinity of any opiate receptor subtype are altered after chronic morphine treatment. Thus, the effect of reducing receptor numbers may be selective for opioid peptides and differ from the phenomena of *in vivo* morphine tolerance and dependence.

However, the recent demonstration of the lack of cross-tolerance between a δ-agonist (DADLE) and a μ-agonist (sulfentanyl) in mouse vas deferens after chronic *in vivo* treatment with either ligand (Schulz et al. 1980) suggests that tolerance selective for a receptor subtype may occur in certain systems. N4TG1 cells contain δ-receptors only. The present studies demonstrate that only opioid peptides induce the down regulation of enkephalin receptors. Morphine (a μ-agonist), ketocyclazocine (a κ-agonist), and N-allylnormetazocine (a σ-agonist) are ineffective in inducing this effect. In fact, they antagonize the effects of opioid peptides. These observations resemble the studies on mouse vas deferens (Schulz et al. 1980). Selective desensitization due to the loss of opiate receptors may develop for δ-receptors after chronic opioid peptide treatment for certain systems. The previous failure to detect the change of opiate receptors after chronic treatment may be because peptides have not been used.

There are many possible mechanisms for the ligand-induced loss of receptors reported here. For instance, desensitized low affinity receptors may be induced by peptides which can no longer be detected by the present binding method. Our preliminary experiments suggest that this is not the case. It may also be possible that the receptors are cryptic after treatment with opioid peptides. The formation of (essentially) irreversible receptor-ligand complexes may also occur during the pretreatment. Understanding of the mechanism of receptor reduction may have important implications for understanding the physiological, pharmacological, and pathological actions of opioids.

References

Chang, K.-J., Miller, R.J., and Cuatrecasas, P. Interaction of enkephalin with opiate receptors in intact cultured cells. *Mol. Pharmacol.*, 14:961-970, 1978.

Chang, K.-J., and Cuatrecasas, P. Multiple opiate receptors: Enkephalins and morphine bind to receptors of different specificity. *J. Biol. Chem.*, 254: 2610-2618, 1979.

Chang, K.-J., Cooper, B.R., Hazum, E., and Cuatrecasas, P. Multiple opiate receptors; different regional distribution in the brain and differential binding of opiates and opioid peptides. *Mol. Pharmacol.*, 16:91-104, 1979.

Chang, K.-J., Hazum, E., and Cuatrecasas, P. The possible role of distinct morphine and enkephalin receptors in mediating the actions of benzomorphan drugs (putative κ and σ agonists). *Proc. Natl. Acad. Sci. USA*, 77:4469-4473, 1980.

Chang, K.-J. Multiple opiate receptors and *in vitro* methodology for opioid peptides. *Psychopharmacol. Bull.*, 17:108-111, 1981.

Chang, K.-J., and Cuatrecasas, P. Heterogeneity and properties of opiate receptors. *Fed. Proc.*, 40:2729-2734, 1981.

Chang, K.-J., Killian, A., Hazum, E., Cuatrecasas, P., and Chang, J.-K. Morphiceptin (Tyr-Pro-Phe-Pro-HN$_2$): A potent and specific agonist for morphine (μ) receptors. *Science*, 212:75-77, 1981a.

Chang, K.-J., Hazum, E., and Cuatrecasas, P. Novel opiate binding sites selective for benzomorphan drugs. *Proc. Natl. Acad. Sci. USA*, 78:4141-4145, 1981b.

Chang, K.-J., Cuatrecasas, P., Wei, E.T., and Chang, J.-K. Analgesic activity of intracerebroventricular administration of morphiceptin and β-casomorphins. "Correlation with the morphine (μ) receptor binding affinity." *Life Sci.*, 30:1547-1551, 1982a.

Chang, K.-J., Eckel, R.W, and Blanchard, S.G. Opioid peptides induce reduction of enkephalin receptors in cultured neuroblastoma cells. *Nature* (London), 296:446-448, 1982b.

Chavkin, C., and Goldstein, A. Demonstration of a specific dynorphin receptor in guinea pig ileum myenteric plexus. *Nature* (London), 291:591-593, 1981.

Frenk, H., Urca, G., and Liebeskind, J.C. Epileptic properties of leucine and methionine-enkephalin: Comparison with morphine and reversibility by naloxone. *Brain Res.*, 147: 327-337, 1978a.

Frenk, H., McCarty, B.G., and Liebeskind, J.C. Morphine and enkephalin: Analgesic and epileptic properties. *Science*, 200:335-337, 1978b.

Gilbert, P.E., and Martin, W.R. The effects of morphine- and nalorphine-like drugs in the nondependent morphine-dependent, and cyclazocine-dependent chronic spinal dog. *J. Pharmacol. Exp. Ther.*, 198: 66-82, 1976.

Gillan, M.G.C., Kosterlitz, H.W., and Morgnan, J. Unexpected antagonism in the rat vas deferens by benzomorphans which are agonists in other pharmacological tests. *Br. J. Pharmacol.*, 72:13-15, 1981.

Goodman, R.R., Snyder, S.H., Kuhar, M.J., and Young, W.S. Differentiation of δ and μ opiate receptor localizations by light microscopic autoradiography. *Proc. Natl. Acad. Sci. USA*, 77:6239-6243, 1980.

Hammonds, R.G., and Li, C.H. Human β-endorphin-specific binding in neuroblastoma N18TG2 cells. *Proc. Natl. Acad. Sci. USA*, 78:6764-6765, 1981.

Handa, B.K., Lane, A.C., Lord, J.A.H., Morgan, B.A., Rance, M.J., and Smith, C.F.C. Analogues of β-LPH$_{61-64}$ possessing selective agonist activity at μ-opiate receptors. *Eur. J. Pharmacol.*, 70:531-540, 1981

Hazum, E., Chang, K.-J., and Cuatrecasas, P. Opiate (enkephalin) receptors of neuroblastoma cells: Occurrence in clusters on the cell surface. *Science*, 206: 1007-1079, 1979a.

Hazum, E., Chang, K.-J., and Cuatrecasas, P. Role of disulphide and sulphydryl groups in the clustering of enkephalin receptors in neuroblastoma cells. *Nature*, 282: 626-628, 1979b.

Hazum, E., Chang, K.-J., and Cuatrecasas, P. Specific nonopiate receptors for β-endorphin. *Science*, 205:1033-1035, 1979c.

Hazum, E., Chang, K.-J., and Cuatrecasas, P. Cluster formation of opiate (enkephalin) receptors in neuroblastoma cells: Difference between agonist and antagonists and possible relationships to biological functions. *Proc. Natl. Acad. Sci. USA*, 77: 3038-3041, 1980.

Hazum, E., Chang, K.-J., and Cuatrecasas, P. Receptor redistribution induced by hormones and neurotransmitters: Possible relationship to biological functions. *Neuropeptides*, 1:217-230, 1981.

Herling, S. and Woods, J.H. Discriminative stimulus effects of narcotics: Evidence for multiple receptor-mediated actions. *Life Sci.*, 28:1571-1584, 1981.

Höllt, V., Dum, J., Bläsrg, J., Schubert, P., and Herz, A. Comparison of *in vivo* and *in vitro* parameters of opiate receptor binding in naive and tolerance/dependent rodents. *Life Sci.*, 16:1823-1828, 1975.

Huidoboro, F., Huidoboro-Toro, J.P., and Miranda, H. Interactions between morphine and the opioid-like peptides in the rat vas deferens. *Br. J. Pharmacol.*, 70:519-525, 1980.

Klee, W.A., and Streaty, R.A. Narcotic receptor sites in morphine-dependent rats. *Nature*, 248:61-63, 1974.

Kosterlitz, H.W., Paterson, S.J., and Robson, L.E. Characterization of the κ-subtype of the opiate receptor in the guinea pig brain. *Br. J. Pharmacol.*, 73:939-949, 1981
Lord, J.A.H., Waterfield, A.A., Hughes, J., and Kosterlitz, H.W. Endogeneous opioid peptides: Multiple agonists and receptors. *Nature* (London), 267:495-500, 1977.
McLawhon, R.W., West, R.E., Jr., Miller, R.J., and Dawson, G. Distinct high-affinity binding sites for benzomorphan drugs and enkephalin in a neuroblastoma-brain hybrid cell line. *Proc. Natl. Acad. Sci. USA*, 78:4309-4313, 1981.
Pasternak, G.W. Opiate, enkephalin, and endorphin analgesia: Relation to a single subpopulation of opiate receptors. *Neurology*, 31:1311-1315, 1981.
Pert, C.B., Pasternak, G.W., and Snyder, S.H. Opiate agonists and antagonists discriminated by receptor binding in brain. *Science*, 182:1359-1361, 1973.
Pfeiffer, A., and Herz, A. Demonstration and distribution of an opiate binding site in rat brain with high affinity for ethylketo cyclazocine and SKF 10047. *Biochem. Biophys. Res. Comm.*, 101:38-44, 1981.
Schulz, R., Wüster, M., Krenss, H., and Herz, A. Selective development of tolerance without dependence in multiple opiate receptors of mouse vas deferens. *Nature* (London), 285:242-243, 1980.
Schulz, R., Faase, E., Wüster, M., and Herz, A. Selective receptors for β-endorphin on the rat vas deferens. *Life Sci.*, 24:843-849, 1979.
Simon, E.J., and Hiller, J.M. *In vitro* studies on opiate receptors and their ligands. *Fed. Proc.*, 37:141-146, 1978.
Stein, C., and Belluzzi, J.D. Brain endorphins and the sense of well-being: A psychobiological hypothesis. *Adv. Biochem. Psychopharmacol.*, 18:299-311, 1978.
Wei, E., and Loh, H. Physical dependence on opiate-like peptides. *Science*, 193:1262-1263, 1976.
Wolozin, B.L., and Pasternak, G.W. Classification of multiple morphine and enkephalin binding sites in the central nervous system. *Proc. Natl. Acad. Sci. USA*, 78:6181-6185, 1981.
Wüster, M., Schulz, R., and Herz, A. Highly specific opiate receptors for dynorphin (1-13) in the mouse vas deferens. *Eur. J. Pharmacol.*, 62:235-236, 1980.
Zukin, R.S., and Zukin, S.R. Demonstration of [^{3}H]cyclazocine binding to multiple opiate receptor sites. *Mol. Pharmacol.*, 20:246-254, 1981.

Alpha Adrenergic Receptor Subtypes: Physiological Relationships and Mechanisms

Brian B. Hoffman, M.D.[1]

Alpha adrenergic receptors have been grouped into two major subtypes, termed alpha$_1$ and alpha$_2$ receptors. Radioligand binding techniques have been utilized to measure the number of alpha$_1$ and alpha$_2$ receptors in a variety of tissues. [^{3}H]dihydroergocryptine labels the entire alpha receptor population; the alpha receptor subtypes may be delineated by constructing competition curves with unlabelled selective antagonists and analyzing the data with computer modeling techniques (Hoffman et al. 1979). Alternatively, alpha$_1$ and alpha$_2$ receptors may be directly identified with selective radioligands such as [^{3}H] prazosin and [^{3}H]yohimbine.

Using these methods, human platelets have been found to contain alpha$_2$ receptors (Hoffman et al. 1979). Rabbit uterus contains both alpha$_1$ and alpha$_2$ receptors. Studies in intact strips of rabbit uterus demonstrated that catecholamines induced smooth muscle contraction by activating alpha$_1$ receptors; alpha$_2$ receptors do not seem to play a direct role in this response (Hoffman et al. 1981). Estrogens increase the number of alpha receptors in the uterus; interestingly, this change occurs exclusively in the alpha$_2$ receptor population which is not involved in mediating contraction. Rat liver membranes contain both alpha$_1$ (80%) and alpha$_2$ (20%) receptors (Hoffman et al. 1980b). In isolated hepatocytes, the alpha$_1$ receptors mediate glycogen phosphorylase activation, whereas the physiological significance of the alpha$_2$ receptors in liver is unclear. In experiments designed to study the regulation of alpha receptors, it is important to delineate the subtypes rather than merely the total number of receptors since alpha$_1$ and alpha$_2$ receptors may mediate distinct physiological effects and be separately regulated.

Alpha$_1$ and alpha$_2$ receptors seem to have quite distinct mechanisms of action, although the molecular details for neither receptor are well understood. $Alpha_1$ receptors have been associated with changes in intracellular calcium metabolism in a variety of tissues; $alpha_1$ receptors have not been found to regulate intracellular cAMP concentration. $Alpha_2$ receptors have been found to inhibit adenylate cyclase activity in a host of cells. The inhibition of adenylate cyclase is dependent on the presence of GTP. Perhaps related to the different mechanisms of the two receptors is the observation that GTP regulates the affinity of agonists such as epinephrine at $alpha_2$ receptors but not at $alpha_1$ receptors. Indeed, radioligand binding studies have shed some light on the mechanism of $alpha_2$ receptor function. Agonist competition curves with [^{3}H]dihydroergocryptine at the human platelet's $alpha_2$ receptor may be resolved into two affinity components, interconvertable by guanine nucleotides (Hoffman et al. 1980a). These data suggest the possibility of an agonist-promoted association of the $alpha_2$ receptor with an additional membrane component. More direct evidence in favor of this possibility was demonstrated by the increase in sedimentation velocity of solubilized agonist labeled receptor on sucrose density gradients, compared to either unoccupied or antagonist labeled receptor (Michel et al. 1981). A future area of active investigation will involve efforts to further characterize this component which presumably leads to the inhibition of adenylate cyclase.

---

[1] Division of Clinical Pharmacology (S-155), Department of Medicine, Stanford University Medical Center, Stanford, CA 94305.

References

Hoffman, B. B., DeLean, A., Wood, C. L., Schocken, D.D., and Lefkowitz, R.J. Alpha adrenergic receptor subtypes: Quantitative assessment by ligand binding. *Life Sci.*, 24:1739-1749, 1979.

Hoffman, B. B., Mullikin-Kilpatrick, D., and Lefkowitz, R. J. Heterogeneity of radioligand binding to alpha adrenergic receptors: Analysis of guanine nucleotide regulation of agonist binding in relation to receptor subtypes. *J. Biol. Chem.*, 255:4645-4652, 1980a.

Hoffman, B. B., Michel, T., Mullikin-Kilpatrick, D., Lefkowitz, R.J.,, Tolbert, M.E.M., Gilman, T.H., and Fain, J.N. Agonist versus antagonist binding to alpha adrenergic receptors. *Proc. Natl. Acad. Sci. USA*, 77:4569-4573, 1980b.

Hoffman, B. B., Lavin, T. N., Lefkowitz, R.J., and Ruffolo, R. R. Alpha adrenergic receptor subtypes in rabbit uterus: Mediation of myometrial contraction and regulation by estrogens. *J. Pharmcol. Exp. Ther.*, 219:290-295, 1981.

Michel, T., Hoffman, B. B., Lefkowitz, R.J., and Caron, M.G. Different sedimentation properties of agonist- and antagonist-labelled platelet $alpha_2$ adrenergic receptors. *Biochem. Biophys. Res. Commun.*, 100:1131-1136, 1981.

Psychobiology of Premenstrual Change

Co-Chair: Jean Endicott, Ph.D.
New York State Psychiatric Institute
New York, N.Y.
and
Uriel Halbreich, M.D.
Department of Psychiatry
Albert Einstein College of Medicine
Bronx, N.Y.

Retrospective Report of Premenstrual Depressive Changes: Factors Affecting Confirmation by Daily Ratings[1]

Jean Endicott, Ph.D.,[2] and Uriel Halbreich, M.D.[3]

Daily ratings made across one or more menstrual cycles at times confirm, and at other times fail to confirm, premenstrual changes reported by women on retrospective questionnaires (Abplanalp et al. 1980; Dalton 1964; Golub 1974; May 1976; McCance et al. 1937; Sampson & Jenner 1977). The authors have begun a series of studies to help determine 1) which types and levels of severity of reported premenstrual changes are most likely to be confirmed by daily ratings; 2) the most efficient ways of obtaining such ratings; and 3) the possible consequences of a failure to confirm reported changes when selecting subjects for biological or treatment studies.

Retrospective Reports of Premenstrual Changes. All subjects described their usual premenstrual changes during the prior three cycles on the Premenstrual Assessment Form (PAF). The PAF, described in detail elsewhere (Halbreich et al. in press), is a 95-item questionnaire designed to describe premenstrual changes with a greater degree of specificity than that of other available procedures (Moos 1968; Steiner et al. 1980). The PAF items are scored to obtain summary measures of 7 Bipolar Continua, 18 Unipolar Dimensional Scales, and 18 Typological Categories. After completion of the PAF, the women made daily ratings for at least one menstrual cycle. A PAF was also completed at the end of the cycle over which daily ratings were made with the focus upon the premenstrual period just experienced.

This preliminary report focuses only upon the typological category of "Depressive Syndrome." The criteria, presented in abbreviated form, are: A. – Depressed or low mood (one of five items rated at least mild), or irritable mood (one of two items rated at least mild); and B. – If depressed mood, at least four of eight items, if irritable or loss of interest or pleasure only, at least five of the eight items. The eight items report change in appetite, sleep, psychomotor function, anergia, loss of interest, low level of social activity, self-deprecation, concentration difficulties, and suicidal ideation.

Daily Ratings. After completing the PAF, the women begin making daily ratings on 21 items of particular interest in ongoing studies by the authors. Each item is rated on a scale of 1 for "not present at all" to 6 for "extreme" manifestation of the mood or behavior in question.

Activity Monitors. Two types of premenstrual depressive syndrome are of particular interest to the authors, that with hypersomnia, lethargy, and decreased activity level, and that with anxiety and increased activity level. Large-scale integrated

---

[1] Supported in part by New York State Department of Mental Hygiene, Grant #30906-04 and Grant #36186-01 from the National Institute of Mental Health.

[2] Director, Research Assessment and Training Unit, New York State Psychiatric Institute, New York, NY 10032.

[3] Director, Division of Behavioral Endocrinology, Department of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461.

(LSI) activity monitors (McPartland et al. 1975) are worn by some subjects when they are making daily ratings in an attempt to obtain objective measures of activity level across the cycle.

Subjects. The subjects were participating in a number of different studies and were recruited in varying ways. Some were co-workers of the senior author, others responded to notices posted about the medical center seeking women for studies across the menstrual cycle, and others contacted the investigators as a result of a newspaper article and a television program reporting on the authors' interest in premenstrual changes. Many of the women in the latter groups were seeking treatment or referral for treatment. At the time of the ACNP meeting, 48 women had completed daily ratings across at least one menstrual cycle, in addition to the initial PAF.

Results

Range of Severity. Women responding to posted notices and co-workers of the senior author tended to report fewer changes and changes of much lower levels of severity than women seeking treatment.

Agreement Between Pre- and Post-PAF. Although the pattern of reported changes was similar for the two PAFs, the severity ratings completed after the cycle of daily ratings tended to be lower. For example, on the PAF Summary Scale for Depressed Mood and Ideation, the mean on the pre-PAF was 26 and that on the post-PAF was 23. The number of subjects whose PAF ratings met criteria for Major Depressive Syndrome pre was 41 and post was 27. The severity levels of the daily ratings also tend to be lower than those noted on the pre-PAF. Some women commented afterward that their premenstrual changes had not been as severe as expected. Both of these findings suggest that women may tend to describe their "worst case" when they report on premenstrual changes in the absence of special attention having been paid to them during the prior month or months.

Likelihood of Confirmation of Depressive Syndrome by Daily Ratings. Confirmation required that the average daily ratings on specified items be at least two points higher during the premenstrual than during the postmenstrual period. Furthermore, ratings during the nonpremenstrual days should not be indicative of a tendency to have frequent depressive changes throughout the cycle.

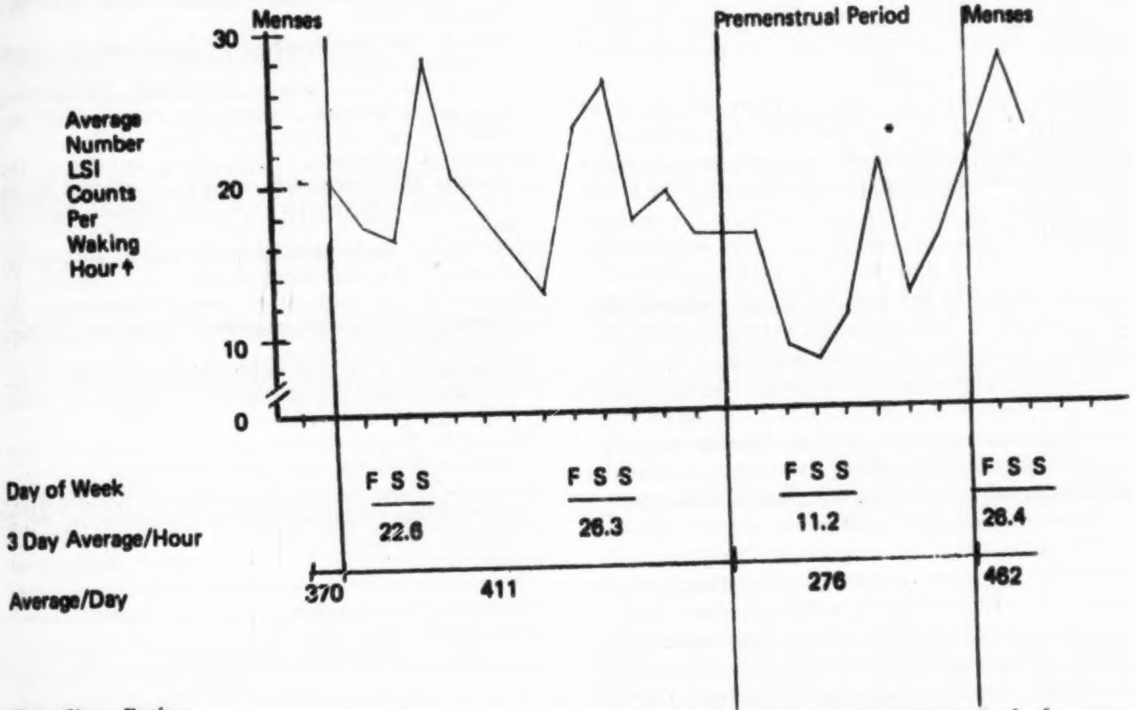
The overall rate of confirmation of the presence or absence of a premenstrual depressive syndrome was only 59 percent for the total sample of 48 women. Fifteen women reported severe depressive changes on the pre-PAF, 13 of these were confirmed, while only 6 of the 14 who reported moderate depressive changes and 5 of the 12 who reported depressive changes at the mild level were confirmed. The pre-PAF ratings for 7 women indicated that they did *not* meet the criteria for a premenstrual depressive syndrome. Their daily ratings confirmed such an absence in only 4, while 3 of the 7 were found to have depressive changes of a syndromal type at the mild level. Two of these women commented on this spontaneously, indicating that they had not noticed premenstrual depression previously. Thus, the likelihood of confirmation of either the presence or absence of a premenstrual depressive syndrome was clearly related to the severity of the reported change, with high levels of confirmation limited to those reporting a severe syndrome.

Although some of the women whose ratings failed to confirm reports of mild or moderate change had daily ratings indicating premenstrual depressive changes on some items, the number of items and level of severity of change were not sufficient to confirm a clear syndromal change of a depressive nature.

The major reason for a lack of confirmation for the women who described severe or extreme changes were ratings indicative of frequent or chronic depressive symptoms throughout the cycle. Although some of these women had premenstrual exacerbations on some items, there was not a clear difference in level of severity for the entire syndrome.

Confirmation of Changes in Activity. Although only a few subjects have worn the LSI, it is already apparent that reported changes of activity may or may not be confirmed. Some women report lethargy, but are actually more active premenstrually. Others report hypersomnia, but are not less active when they are awake. Daily ratings and LSI readings are given for one subject in which both measures confirmed the retrospective reports made on the PAF (*see* Figure).

Example of Confirmation of Reported Premenstrual Changes of Depression, Mood, and Reduced Activity Level



Time Chart Rating																									
Sleep more	1	1	1	1	1	1	1	1	2	1	1	1	1	1	2	3	3	4	4	4	5	4	1	1	1
Depressed	1	1	1	2	2	1	1	2	1	1	1	1	2	3	1	4	4	4	4	5	5	5	2	1	1
Malaise	1	1	1	1	1	1	1	1	2	1	1	1	1	1	3	3	3	3	3	5	6	6	3	1	1
Lower performance	1	1	1	1	1	1	1	1	1	1	1	3	1	1	1	3	3	4	3	3	5	5	2	1	1

*Day with outside demands for unusual levels of activity for a week day.

†Since the number of waking hours varied from 15 to 19.5 each day, the average waking hour was calculated.

FIGURE

Discussion

The preliminary findings have clear relevance for studies of premenstrual changes, particularly biological and/or treatment studies.

Subjects should not be selected on the basis of retrospective reports alone, whether they are chosen to have particular types of changes or to be free of them. Daily ratings made across one or more cycles are needed to confirm such reports. This is particularly true for changes of a syndromal nature. Reports of changes in activity levels should also be objectively confirmed through the use of activity monitors.

A possible explanation for the high rate of "placebo" response in treatment studies for premenstrual dysphoria is the rather consistent finding that women report less severe changes after at least one cycle of careful attention to their moods and behavior. Had the women involved in the current studies been on placebo, the scores on the second PAF would have "indicated" that they had a "placebo response." Thus it is not only advisable to use daily ratings to confirm reported changes, but also to establish a new baseline against which placebo or active treatment response may be judged.

Many studies of daily ratings which have reported a lack of confirmation of premenstrual changes have used college students or volunteers who have not been seeking treatment. The levels of severity reported by such women are usually minimal, mild, or moderate. The relationship between level of severity and likelihood of confirmation found in the current study suggests that this may have been a major reason for the low level of confirmation in such studies.

Another reason for lack of confirmation is that many women who reported premenstrual changes of a depressive nature also had depressive symptoms frequently throughout the month so that the premenstrual period was not clearly different.

Some investigators interview women at two points in their cycle to determine if they are clearly more depressed premenstrually than during midcycle. Unfortunately, in the absence of daily ratings, the conclusions drawn from contrasting the two interviews may be misleading if the aim is to select women who are relatively free of depressive symptoms during the nonpremenstrual days of the cycle. Some women appear to have a few days to a week during midcycle when they feel better and are depressed most of the remaining days, with some worsening premenstrually.

The degree to which other nondepressive changes are confirmed by daily ratings is also under study. The findings reported here, as well as those of prior investigators, strongly support the need for the use of daily ratings and other measures of premenstrual change if one is attempting to select homogeneous groups of subjects with contrasting types of changes and levels of severity. Questionnaires such as the PAF are best used for screening of subjects.

References

Abplanalp, J.M., Haskett, R.F., and Rose, R.M. The premenstrual syndrome. *Psychiatric Clin. No. Am.*, 3:327-347, 1980.

Dalton, K. *The Premenstrual Syndrome.* Springfield, Ill.: Charles C Thomas, 1964.

Golub, S. The effect of premenstrual anxiety and depression on cognitive function. *J. Person. Soc. Psychol.*, 34:99-104, 1976.

Halbreich, U., Endicott, J., Schacht, S., and Nee, J. The diversity of premenstrual changes as reflected in the Premenstrual Assessment Form. *Acta Psychiatr. Scand.* (In press)

May, R. R. Mood shifts and the menstrual cycle. *J. Psychosom., Res.*, 20:125-130, 1976.

McCance, R. A., Luff, M. C., and Widdowsom, E. E. Physical and emotional periodicity in women. *J. Hyg.*, 37:571-605, 1937.

McPartland, R.J., Kupfer, D.J., Foster, G., Reisler, K.L., and Matthews, G. Objective measurement of human motor activity. *Biotelemetry*, 2:317-323, 1975.

Moos, R.H. The development of a menstrual distress questionnaire. *Psychosom. Med.*, 30:853-867, 1968.

Sampson, G., and Jenner, F. A. Studies of daily recordings for the Moos Menstrual Distress Questionnaire. *Br. J. Psychiatry*, 130:265-271, 1977.

Steiner, M., Haskett, R. F., and Carroll, B. J. Premenstrual tension syndrome: The development of research diagnostic criteria and new rating scales. *Acta Psychiatr. Scand.*, 62:177-190, 1980.

Premenstrual Tension in Biochemical and Psychotropic Drug Assessment

Richard I. Shader, M.D.,[1] and
Jerold S. Harmatz

During its earliest years, this unit focused on identifying differential response tendencies among young men taking neuroleptics. Promising typologies were developed to predict, for example, contrasting responses in extroverted athletic men and rather more introspective aesthetes, and in men differing in anxiety traits. These differences seemed to arise from both constitutional and psychological predilections. We were intrigued by the possibility that some of our procedures might be applied to young women, perhaps differentiated in terms of their athletic background. Very soon, however, we were obliged to recognize that for many women, within-month variation in (especially affective) symptomatology was greater than any expectable neuroleptic effect in healthy volunteers. As part of our attempts to identify women with more pronounced tendencies to experience these exaggerated emotional shifts, we found ourselves embarked on a series of studies of the premenstrual tension syndrome.

A 55-symptom checklist was constructed following a review of the literature available at that time (1966). Together with three rating scales of impairment in physical, emotional, and task/social functioning, it was administered to 457 healthy, young women not currently using oral contraceptive medication (Table 1). Rating scale distributions were superimposed and cut-off criteria established for distinguishing between women who experienced minimal and maximal premenstrual tension symptoms across the domain of their somatic and affective lives. These groups are subsequently referred to as the minimal and maximal groups. A residual group was acknowledged as inconsistent with regard to this distress. Indeed, among the maximal group, five prevalent symptoms, viz. anxiety, irritability, depression, fatigue, and abdominal distension were determined regularly to co-occur (Table 2). Such co-occurrence suggested that these symptoms comprise the basis of a premenstrual syndrome (Table 3). A series of multivariate procedures, including obverse factor analysis and discriminant function analysis, were subsequently carried out to identify some five major patterns of premenstrual experience among our volunteers: Group 1 was characterized mostly by depression and irritability; Group 2 by depression and breast enlargement; Group 3 by abdominal pain and autonomic symptoms; and Group 4 by reduced energy, irritability, weight gain, and abdominal distension. Group 5 was nearly symptom-free.

The authors then undertook to relate selected biochemical and treatment parameters to their understanding of premenstrual tension as differently experienced by especially the minimal and maximal groups of women. Inspired by the early work of Loraine and Bell (1963), they examined urinary progesterone and estrogen in 18 healthy, normally ovulating women. Fractionated estrogens (estrone, estriol, estradiol) were determined by the method of Brown (1955) Pregnanetriol was assessed using the procedure of Fotherby and Love (1960). Klopper's Method (1955) was used for pregnanediol. Ten women had self-ratings that met the minimal premenstrual tension criteria and eight were maximal. For the analysis, complete data were available in 13 cases. Their cycles were divided into follicular and luteal phases by subtracting 15 days from the lengths of their cycles. Temperature records confirmed the occurrence of ovulation during the study month.

Table 4 shows lower luteal pregnanediol levels for the maximal cohort. Table 5 illustrates an essentially bimodal distribution of pre-ovulatory estrogen with significant differences between the two cohorts. In Table 6 luteal pregnanediol is shown to differ according to level of pre-ovulatory estrogen. This last observation is consistent with Dalton's demonstrations that natural progesterone is an effective treatment for premenstrual tension syndrome.

Although plasma MAO had earlier been studied for its relationship to premenstrual tension, the authors wanted to understand platelet MAO activity through the cycles of women contrasted for their characteristic premenstrual experience. For 1 month, on alternate days, blood was drawn from 11 high and 10 low premenstrual tension women. Belmaker (1974), who used similar biochemical procedures, collected the data shown in Figure 1. Figure 2, however, illustrates that when the data were separated according to premenstrual cohort, the authors found a follicular decrement for our low group and a luteal increment for the high group. On the average, on paper-and-pencil measures, the high premenstrual group evidenced greater dysphoric tendencies during both phases of their cycles.

---

[1] Psychopharmacology Research Unit, New England Medical Center Hospital, Boston, MA 02111.

Table 1

Premenstrual Symptoms
(% of 457 Healthy Women Reporting)

Symptom	Absent	Present	
		Slight	Marked
Anxiety	24.9	43.8	31.3
Lack of concentration	54.5	33.9	11.6
Decreased alertness	64.8	25.8	9.4
Confusion	75.7	15.8	8.5
Nervous	26.0	39.8	34.1
Wanting to cry	32.6	37.0	30.4
Irritability	12.5	39.6	47.9
Depression	17.7	40.5	41.8
Moody	22.5	39.4	38.1
Antagonistic	45.7	34.8	19.5
Easily upset	19.5	41.8	38.7
Fatigue	28.2	37.9	33.9
Listlessness	48.1	35.2	16.6
Lethargy	53.6	31.1	15.3
Malaise	56.7	31.3	12.0
Energetic	65.4	20.6	14.0
Insomnia	82.7	11.6	5.7
Drowsiness	52.5	33.9	13.6
Weakness	56.0	34.6	9.4
Increased libido	39.6	28.9	31.5
Decreased libido	79.6	15.5	4.8
Muscle tightness	52.3	30.0	17.7
Tightness of finger	81.8	13.1	5.0
Dizziness	85.3	12.0	2.6
Weight gain	34.1	45.7	20.1
Swelling feet	80.5	12.9	6.6
Perspiring hands	80.5	13.8	5.7
Leg ache	70.9	16.8	12.3
Pruritus	95.6	3.5	0.9
Headache	52.5	30.9	16.6
Blurred vision	94.1	5.0	0.9
Eyes sore	88.8	9.2	2.0
Breasts tender	31.3	41.8	26.9
Breasts sore	60.0	23.6	16.4
Breasts painful	79.0	13.6	7.4
Breasts enlarged	49.0	32.8	18.2
Nausea	84.9	12.0	3.1
Vomiting	96.9	2.4	0.7
Increased appetite	62.6	19.0	18.4
Decreased appetite	75.3	18.6	6.1
Craving sweets	67.4	23.0	9.6
Thirst	57.3	26.0	16.6
Constipation	71.3	18.2	10.5
Diarrhea	77.9	16.4	5.7
Abdominal distention	26.0	38.5	35.4
Increased urine premenstrually	59.3	26.5	14.2
Increased urine at menses	61.3	25.4	13.3
Decreased urine premenstrually	90.8	7.4	1.8
Lower abdominal pain	35.7	37.4	26.9
Lower-sided pain	82.7	8.8	8.5
Lower-left-sided pain	85.1	8.1	6.8
Vaginal discharge	42.2	39.2	18.6
Backache	42.2	37.4	20.4
Weakness of legs	73.3	17.9	8.8
Acne	32.6	50.3	17.1

Table 2

Coincidental Occurrence of Five Prevalent Symptoms (% of 457 Healthy Women Reporting)

Combination	Present
Anxiety + depression	0.2
Anxiety + depression + abdominal distension	0.2
Depression + abdominal distension	0.2
Depression + fatigue + abdominal distension	0.4
Anxiety + irritability	0.4
Anxiety	0.4
Fatigue + abdominal distension	0.4
Irritability	0.7
Depression + fatigue	0.7
Anxiety + depression + fatigue	0.7
Anxiety + irritability + fatigue	0.7
Depression	0.9
Anxiety + fatigue + abdominal distension	0.9
Abdominal distension	1.1
Fatigue	1.1
Irritability + fatigue	1.1
Irritability + depression + fatigue	1.3
Irritability + fatigue + abdominal distension	1.5
Anxiety + irritability + abdominal distension	1.8
Anxiety + depression + fatigue + abdominal distension	2.0
Irritability + abdominal distension	2.0
Anxiety + irritability + fatigue + abdominal distension	2.4
Irritability + depression	2.6
Irritability + depression + abdominal distension	3.3
Anxiety + irritability + depression	3.5
Irritability + depression + fatigue + abdominal distension	5.5
Anxiety + irritability + depression + fatigue	8.5
Anxiety + irritability + depression + abdominal distension	8.8
Anxiety + irritability + depression + fatigue + abdominal distension	43.5

Table 3

Occurrence of Five Prevalent Symptoms in Minimally and Maximally Impaired Women (% Reporting)

	Minimally impaired*			Maximally impaired*		
Symptom	Absent	Present Slight	Present Marked	Absent	Present Slight	Present Marked
Anxiety	44.2	40.0	15.8	11.8	43.1	45.1
Irritability	28.4	51.6	20.0	2.9	22.5	74.5
Depression	34.7	47.4	17.9	8.8	24.5	66.7
Fatigue	41.1	36.8	22.1	14.7	35.3	50.0
Abdominal distension	41.1	37.9	21.1	16.7	34.3	49.0

*The two groups differed significantly ($p < .001$) on each symptom

Table 4

Urinary Pregnanediol: Mean Values in μG/24 Hours

Days prior to flow	-10-9	-8-7	-6-5	-4-3	-2-1
Subjects without PMT	2.75 ($N = 2$)	2.02 ($N = 5$)	3.06 ($N = 7$)	3.33 ($N = 9$)	1.97 ($N = 7$)
Subjects with PMT	0.84 ($N = 5$)	1.16 ($N = 12$)	1.67 ($N = 13$)	1.39 ($N = 14$)	1.61 ($N = 8$)
p value*	.08	.17	.08	.0078	N.S.

**T*-test for independent samples (two-tailed).

Table 5

Preovulatory Urinary Estrogens: Mean Values in μG/24 Hours

Days after flow onset	+6+7	+8+9	+10+11	+12+13
Subjects without PMT	24.75 ($N = 8$)	31.50 ($N = 8$)	42.38 ($N = 8$)	55.25 ($N = 8$)
Subjects with PMT	21.50 ($N = 8$)	36.63 ($N = 8$)	32.77 ($N = 9$)	37.22 ($N = 9$)
p value*	N.S.	N.S.	N.S.	N.S.

**T*-test for independent samples (two-tailed).

Table 6

Urinary Pregnanediol: Mean Values in μG/24 Hours

Days prior to flow	-10-9	-8-7	-6-5	-4-3	-2-1
Subjects with PMT					
Hi-preov-estrogen	1.10 ($N = 1$)	2.17 ($N = 3$)	2.73 ($N = 4$)	1.50 ($N = 4$)	2.07 ($N = 3$)
Lo-preov-estrogen	0.85 ($N = 2$)	0.75 ($N = 4$)	0.65 ($N = 4$)	0.60 ($N = 4$)	0.70 ($N = 2$)
p value*	N.S.	.015	.033	.168	N.S.

**T*-test for independent samples (two-tailed).

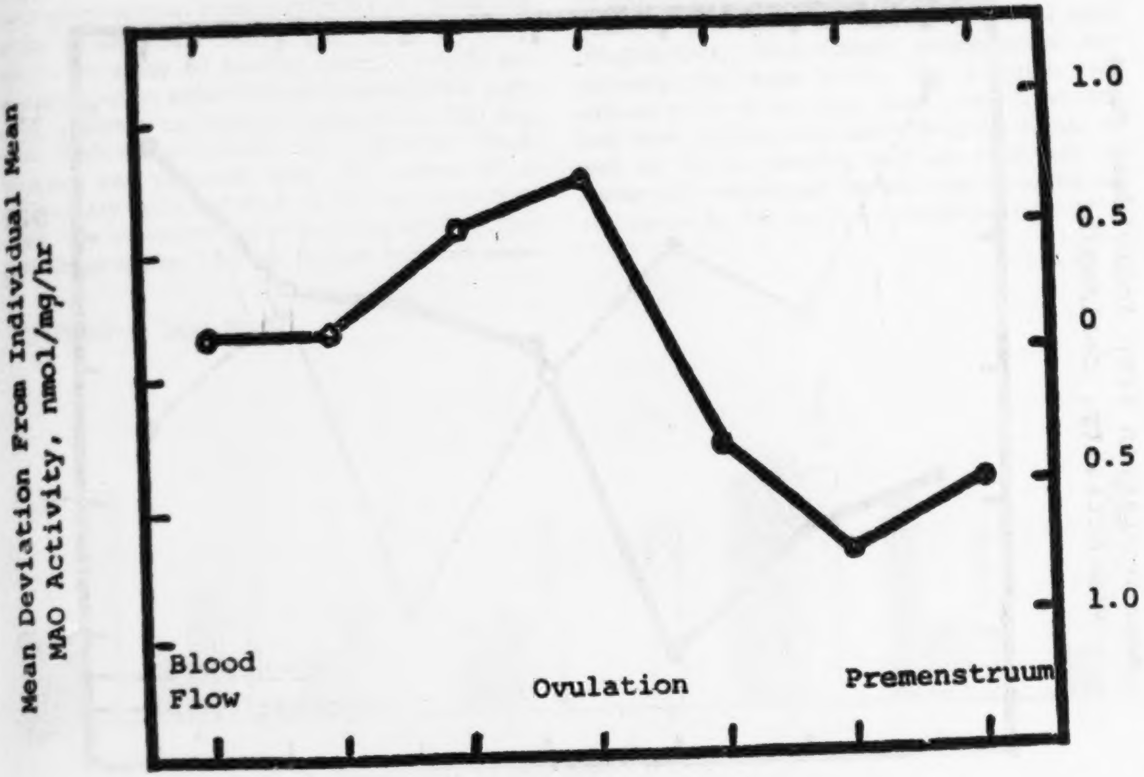

Mean Deviation From Individual Mean
MAO Activity, nmol/mg/hr
1.0
0.5
0
0.5
1.0
Blood
Flow
Ovulation
Premenstruum

FIGURE 1

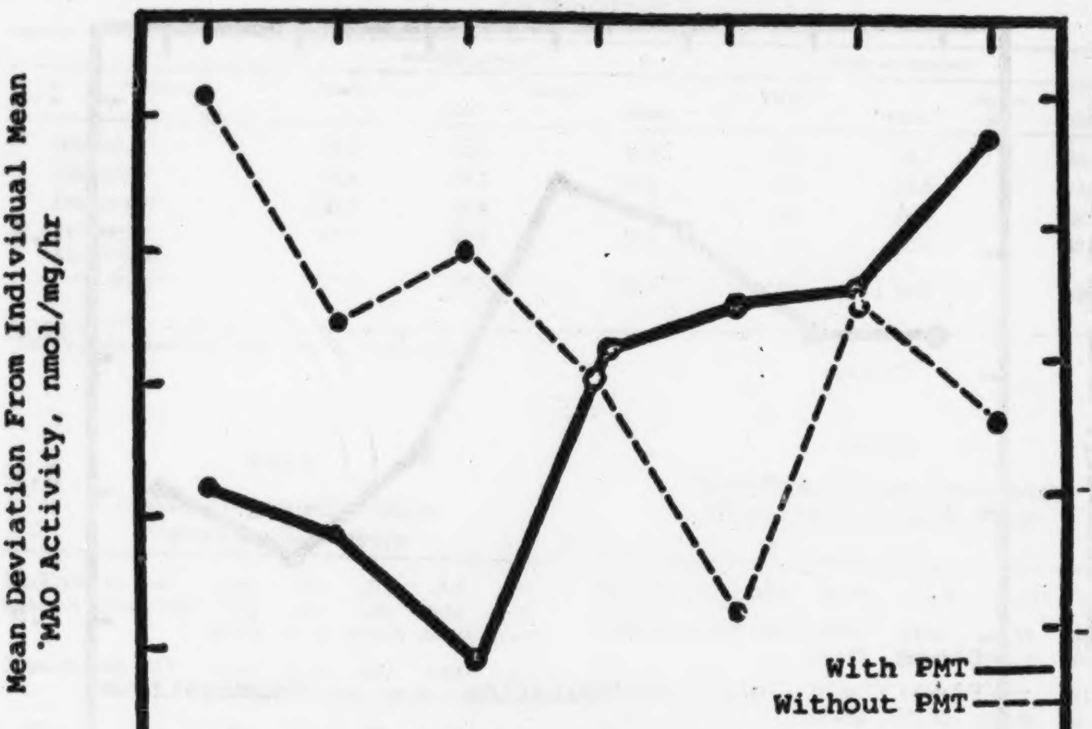

Mean Deviation From Individual Mean
MAO Activity, nmol/mg/hr
1.0
0.5
0
-0.5
-1.0
With PMT
Without PMT

FIGURE 2

With regard to treatment, staff was encouraged by open trials with lithium to undertake a controlled trial of lithium among women who met their premenstrual tension criteria (i.e., members of the MAXIMAL cohort). (*see* Figure 3.) They set out to study 60 healthy women, evenly assigned to receive either lithium carbonate (900 mg/day), placebo, or Dyazide (triamterene 100 mg and hydrochlorothiazide 50 mg/day). Each woman was screened over the course of a preliminary cycle and then, in the next or treated cycle, was evaluated before and after her follicular and luteal weeks. The test battery included standard measures of anxiety, depression, and hostility, as well as self-ratings of functional capacity. Over 60 percent of the screened applicants had to be dropped by the end of the first cycle because of health or procedural anomalies, menstrual cycle irregularities, inconsistent premenstrual experience. In other words, the program was tedious to carry out, and when after 13 women had been run on each active drug condition, as well as 10 on placebo, and no consistent or statistically significant benefit was observed on any measure, the study was terminated.

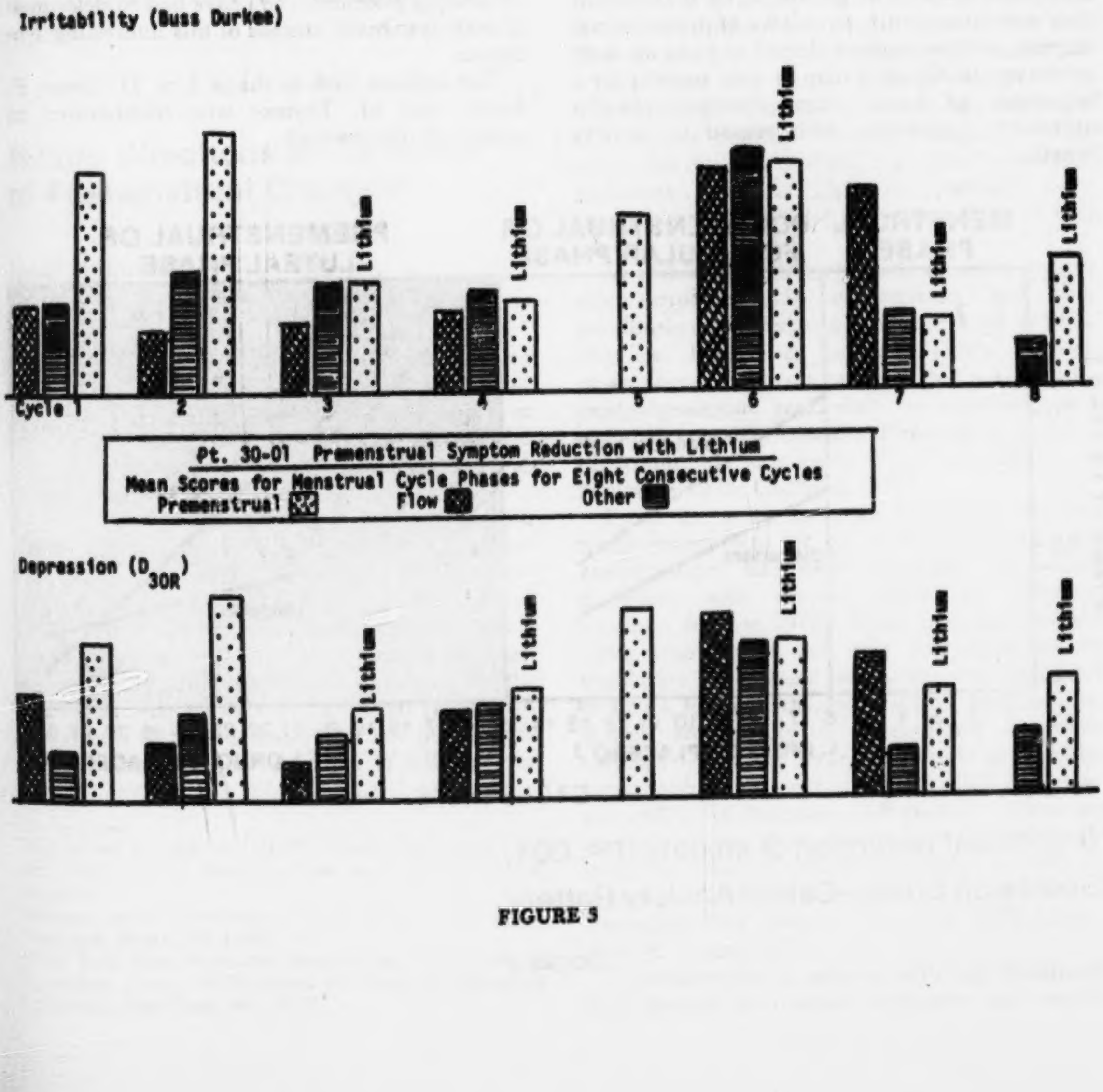
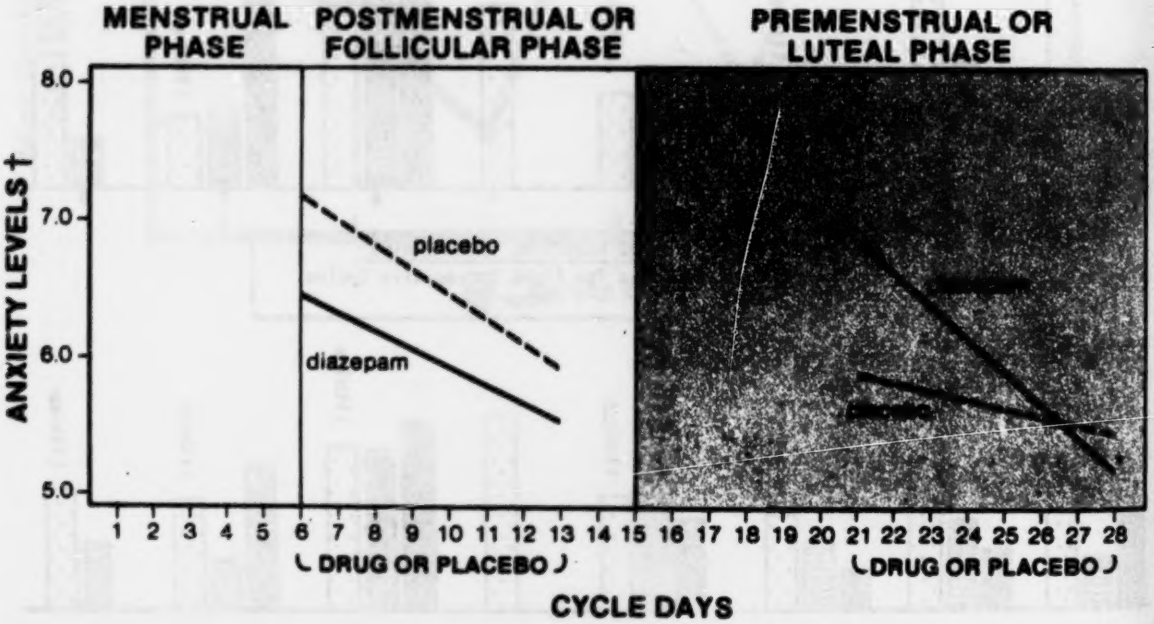


FIGURE 3

In a study of diazepam, 6 mg/day, the authors burdened themselves with an even more cumbersome selection strategy, but with more fortunate results. In this design, they tried to stratify by premenstrual criteria, and by level of anxiety trait to allow comparability with previous work with young men. Considerable overlap obtained between self-reports of premenstrual tension and indices of neuroticism like anxiety. They found it inordinately difficult to find subjects with low anxiety who consistently experienced high premenstrual tension. Forty-nine subjects were stratified by anxiety level and then evaluated on measures of anxiety, depression, and hostility. Only 13 of these cases proved to be invariant in their month-to-month experience of premenstrual distress, and the authors elected to focus on their responses. In Figure 4 may be seen support for a hypothesis of luteal phase diazepam/placebo superiority, especially with regard to anxiety benefit.

The investigations have generally confirmed that menstrual cycle effects might be an important source of variance in psychotropic drug and biochemical trials, especially when female subjects are predisposed to these molimina. It is also true, however, that we have found conventional factorial designs too impractical to fulfill. Their current preference is to include in a multivariate consideration, like a regression equation, a variable which can index a given proband's susceptibility, i.e. which is coded "yes" if the case characteristically suffers from premenstrual tension and whose experimental trial happens to involve her luteal phase. Otherwise, with changes in funding priorities, they have had to defer most of their systematic studies of this interesting syndrome.

The authors wish to thank Drs. D. Osser, P. Soloff, and M. Taymor who collaborated on aspects of this research.



*Significant reduction of anxiety (P<.001)

†Scores on Sheier-Cattell Anxiety Battery

FIGURE 4

References

Belmaker, R.H., Murphy, D.L., Wyatt, R.J., and Loriaux, D.L. Human platelet monoamine oxidase changes during the menstrual cycle. *Arch. Gen. Psychiatry,* 31:553-556, 1974.

Brown, J.B. A chemical method for the determination of oestriol, oestrone, and oestradiol in human urine. *Biochem. J.,* 60:185-193, 1955.

Fotherby, K., and Love, D.N. A modified method for the estimation of pregnanetriol in urine. *J. Endocrinol.,* 20:157-162, 1960.

Klopper, A., Michie, E.A., and Brown, J.B. A method for the determination of urinary pregnanediol. *J. Endocrinol.,* 12:209-219, 1955.

Loraine, J.A., and Bell, E.T. Hormone excretion during the normal menstrual cycle. *The Lancet,* 1340-1342, June 22, 1963.

Future Directions in the Study of Premenstrual Changes[1]

Uriel Halbreich, M.D.,[2] and
Jean Endicott, Ph.D.[3]

The physical, behavioral, and mood changes which may occur during the premenstrual period are very prevalent and sometimes may be severe enough to warrant treatment. However, the etiology and pathophysiology of premenstrual changes (PMC) are unclear.

A recent wave of interest in PMC has been manifested by an increase in the number of articles and symposia on the subject. Many of these share a widely held misconception in that the entire gamut of premenstrual changes is treated as a single syndrome. Studies by the authors (Halbreich & Endicott 1982; Halbreich et al., 1982b, 1982c) as well as others (Moos & Leiderman 1978) have indicated that PMC are better conceived as consisting of a number of different but partially overlapping subtypes and dimensions.

Subtypes of PMC are differentially related to affective disorder (Endicott et al. 1981), even among women who meet criteria for a premenstrual depressive syndrome. Three subtypes of premenstrual depressive changes have been shown to have different external correlates (Halbreich et al., in press). Furthermore, some of the major types of change are bipolar (e.g., decreased and increased activity or appetite, depression but also elevation of mood).

Once the concept of a single PMC syndrome is replaced by a recognition of diverse PMC whose subtypes should be delineated and well-defined, the door is open to change the assumption that a single variable is responsible for "a premenstrual tension syndrome." It is highly unlikely that such diverse changes with evidence of differential correlates have the same pathophysiology. The diversity of PMC should lead to the assumption of multivariate etiology of these changes. Furthermore, the division of PMC into specific subtypes facilitates study of different, partially overlapping, mechanisms of pathophysiology of each subtype.

An imbalance between some hormones, especially estrogen and progesterone, has been previously suggested as a causative factor of PMC (Review: Rausch & Janowski 1982). Furthermore, there is indirect evidence that a high estrogen/progesterone ratio may be associated with irritability-anxiety-hostility PMC as opposed to predominantly depressive PMC (Bäckström & Mattsson 1975; Cullberg 1972).

From the other side, an imbalance between neurotransmitters (e.g., norepinephrine and acetylcholine) has been suggested in mental disorders with similar syndromes (Review: Pradhan & Bose 1978). Brain monoamines and other transmitters not only participate in the regulation of gonadal hormones, but there are feedback mechanisms, influence on metabolic enzymes, and effects on postsynaptic sensitivity through which the ovarian steroids actively interact with neurotransmitters (Rausch & Janowski 1982). In humans and animals, there are several reports that plasma, urine, and brain levels of neurotransmitters or their metabolites fluctuate along the menstrual cycle (Weiner & Elmadjian 1962; Deleon-Jones et al. 1978; Greengrass & Toung 1971).

It is reasonable to assume, with high likelihood, that changes in ovarian hormones and several neurotransmitters are involved in an intricate interactive balance whose impairment may be part of the pathophysiology of PMC. Moreover, there has recently been a substantial accumulation of data suggesting that various functions of the central nervous system are modulated by, or at least involve, a growing number of recently discovered substances, various endogenous opioids, prostaglandins, i.e., trace amines. A possible role of some of these substances in PMC has been hypothesized (Halbreich & Endicott 1981; Reid & Yen 1981; Horrobin 1979). These hypotheses were based on the fluctuations of the relevant substances along the menstrual cycle, their possible involvement in phenomenology that resembles PMC, and their interaction with gonadal hormones and neurotransmitters.

---

[1] Supported in part by NIMH Grants MH-36186 and MH-30906 and the New York State Department of Mental Hygiene.

[2] Department of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461.

[3] New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY 10032.

One may hypothesize that multiple interactions exist among all the above-mentioned systems (and probably some others) which influence each other. Such an interaction may be in an imbalance during the premenstrual period. The imbalance may be triggered by a succession of events which take place prior to, and during, the premenstrual period. This period may be defined as a period of *change*. Indeed, a premenstrual change in plasma levels or activity may be the only common denominator for the numerous substances whose involvement in the PMC has been hypothesized. In most cases premenstrual changes in levels of hormones and other substances, by themselves are normal, but the magnitude and pace of change vary substantially among women.

One may assume that when levels of several hormones (and other substances) change simultaneously, but at differing pace and magnitude, the homeostasis between hormones, modulators, and neurotransmitters may be temporarily impaired. As a consequence of this impaired homeostasis, vulnerability to external and internal stimuli are increased and greater imbalance may ensue. The imbalanced system is also susceptible to wide fluctuations which may be caused by minor changes in one or several of its components.

Such a model may provide an explanation for the diversity of premenstrual changes. Specific symptoms may be caused by a) changed activity of a single compound in the system; b) a change in an entire system (e.g., renin-angiotensin-aldesterone) which c) may be amplified by a simultaneous change in other compounds or systems (e.g., water retention may be caused by increased activity of the renin-angiotensin-aldesterone axis which may be further aggravated by increased acetylcholine activity which by itself causes increased secretion of antidiuretic hormone). Increase in other variables like prolactin may also contribute to the severity of the same results, namely, water retention; or d) impaired balance between two or more systems (e.g., various monoamines, endorphins, ovarian hormones, etc.) may cause change by itself.

A shift from a conceptual framework of a single causative factor to a multivariate imbalance hypothesis has immediate implications for future studies of PMC. Different strategies of research should be implemented.

The search for different biological mechanisms underlying the various clusters of PMC is self-explanatory. Women with different subtypes of PMC should be compared to each other; comparisons should not be limited to those with no changes at all. Determination of fluctuations in endogenous levels of hypothetical participating variables during the premenstrual period are interesting, but the yield is questionable (especially in plasma) unless the dynamic multiple balance between them is measured. Repeated measurement of dynamic multiple balance and its relationship to mental and behavioral changes in the same women during sequential premenstrual periods and under different environmental conditions may yield valuable information on the interaction among biological changes, vulnerability, and the environment. Dynamic intervention studies (which will not be listed here) may also result in more sophisticated information.

Indeed, a successful approach to the testing of a multivariate imbalance hypothesis of the pathophysiology of PMC necessitates a multidisciplinary team which will completely depart — conceptually and operationally — from the outdated dichotomy between "psychological" and "biological" changes. A multivariate time-sequence statistical analysis should be applied to the data. It is needless to say that an objective, nonbiased (to both sides) investigation should replace the highly prejudiced approach that is still so prevalent in menstrually related research.

References

Bäckström, T., and Mattsson, B. Correlation of symptoms of premenstrual tension to estrogen and progesterone concentrations in blood plasma. *Neuropsychobiology,* 1:80-86, 1975.

Cullberg, G. Mood changes and menstrual symptoms with different gestagen/estrogen combination. *Acta Psychiatr. Scand. (Suppl.),* 236:1-86, 1972.

Deleon-Jones, F.A., Steinburg, G., Dekirmenjian, H., and Garver, D. MHPG excretion during the menstrual cycle of women. *Commun. Psychopharmacol.,* 2:267-274, 1978.

Endicott, J., Halbreich, U., and Schacht, S. Premenstrual changes and affective disorders. *Psychosom. Med.,* 43:519-529, 1981.

Greengrass, P.M., and Toung, S.R. Changes in brain monoamine concentrations during the oestrus cycle in the mouse: Possible pharmacologic implications. *J. Pharm. Pharmacol.,* 23:897-898, 1971.

Halbreich, U., and Endicott, J. A possible involvement of endorphins in premenstrual syndromes and postpartum depression. *Med. Hypotheses,* 7:1045-1058, 1981.

Halbreich, U., and Endicott, J. The classification of the premenstrual changes. In: Friedman, R. (ed.), *Behavior and the Menstrual Cycle.* New York: Marcel Dekker, 1982, pp. 243-265.

Halbreich, U., Endicott, J., and Schacht, S. Premenstrual syndromes: A new instrument for their assessment. *J. Psychiatr. Treat. Eval.* 4:161-164, 1982a.

Halbreich U., Endicott, J , Schacht, S., and Nee, J. The diversity of premenstrual changes as reflected in the Premenstrual Assessment Form. *Acta Psychiatr. Scand.* 65:46-65, 1982b.

Halbreich, U., Endicott, J., Schacht, S., and Nee, J. Premenstrual depressive changes: Value of differentiation *Arch. Gen. Psychiatry.* (In press)

Horrobin, D.F. Cellular basis of prolactin action: Involvement of cyclic nucleotides, polyamines, prostaglandins, steroids, thyroid hormones, Na/K ATPases and calcium: Relevance to breast cancer and the menstrual cycle. *Med. Hypotheses,* 5:599-620, 1979.

Moos, R., and Leiderman, D. Toward a menstrual cycle typology. *J. Psychosom. Res.,* 22:31-40, 1978.

Pradhan, S.M., and Bose, S. Interactions among central neurotransmitters. In: Lipton, M.A., DiMascio, A., and Killan, K.F. (eds.), *Psychopharmacology: A Generation of Progress.* New York: Raven Press, 1978, pp. 271-281.

Rausch, J.L., and Janowski, D.S. Premenstrual tension: Etiology. In: Friedman, R. (ed.), *Behavior and the Menstrual Cycle.* New York: Marcel Dekker. (In press)

Reid, R.L., and Yen, S.S.C. Premenstrual syndrome. *Am. J. Obstet. Gynecol.,* 139:85-103, 1981.

Weiner, M.S., and Elmadjian, F. Excretion of epinephrine and norepinephrine in premenstrual tension. *Fed. Proc.,* 21:184, 1962.

Child Psychopharmacology

Chair: Rachel Gittelman, Ph.D.
New York State Psychiatric Institute
New York, N.Y.

Methylphenidate in Adults with MBD Symptomatology

Jeffrey A. Mattes, M.D.,[1] Lane Boswell, B.A.,[2] and Herman Oliver, M.D.[2]

The fate of children with minimal brain dysfunction (MBD) is uncertain. Until recently, it was believed that children outgrow the symptoms of MBD around the time of puberty (Eisenberg 1966). Recent studies, however, indicate that the outcome of children with MBD is not universally positive. Family (Cantwell 1975) and followup (Weiss et al. 1971) studies suggest that hyperactive children are at risk for behavioral difficulties, including alcoholism and sociopathy, past puberty; though the symptom of hyperactivity may decrease, distractibility, impulsivity, excitability, low self-esteem, poor academic achievement, and interpersonal difficulties may continue into later life. There are also preliminary data suggesting that stimulant medication may be effective in adult conditions possibly related to childhood MBD (Wood et al. 1976; Wender et al. 1981). However, these studies did not include a control group, and so were not able to determine the specificity of drug effect.

The objectives of this study were to evaluate whether methylphenidate (Ritalin), a standard treatment for childhood MBD, is effective in adults with symptoms considered related to MBD, and to evaluate the specificity of drug response. The overall goal was to determine if MBD is a specific diagnostic entity in adulthood with a specific treatment, i.e., stimulant medication.

Method

All patients applying to an adult psychiatric outpatient clinic (approximately 3,000 patients during the course of this study) were screened by questionnaires and interviews to determine eligibility. Two groups of patients were identified: 1) an experimental patient group with adult symptoms of MBD (restlessness, poor concentration, emotional lability, and impulsivity) and retrospective diagnoses of childhood MBD (more specifically, MBD with hyperactive symptomatology), and 2) a control group with similar adult symptoms but with no childhood histories of MBD (this controlled for the possibility that methylphenidate is helpful for certain adult symptoms regardless of childhood history).

It was assumed that the control group would manifest adult MBD-like symptomatology as a result of anxiety or depression; however, severe depressives (major depressive episodes of greater than mild severity), schizophrenics, and manic depressives were excluded. All patients were entered into a double-blind, crossover design, and given 3-week trials of methylphenidate (up to 60 mg/day; the actual mean dosage was 48 mg/day) and placebo.

Baseline evaluation included ratings by patients, psychiatrists, and significant others, on MBD-related and other symptomatology. In addition, old school records were obtained, and parents were asked to retrospectively rate the patient's childhood MBD symptomatology and neuropsychological testing. Evaluation of drug effect included ratings by patients, psychiatrists, and significant others.

---

[1] Psychiatric Ambulatory Care, Bronx Veterans Administration Medical Center, Bronx, NY 10468.

[2] Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 11004.

Results

Final results, with an *N* of 63 (approximately 30 in each group) are as follows:

The Diagnostic and Statistical Manual-III (DSM-III) diagnoses of the two groups did not differ significantly except, as expected, that the experimental group much more frequently met the criteria for attention deficit disorder, residual type. The most common diagnoses were major depressive disorder (mild in severity; $N = 19$), alcohol abuse ($N = 17$), drug abuse ($N = 16$), borderline personality disorder ($N = 16$), generalized anxiety disorder ($N = 7$), and antisocial personality disorder ($N = 5$).

A number of baseline measures differentiated the two groups. The experimental group (with childhood hyperactivity) began drinking heavily at an earlier age. Those who did drink heavily had histories of more drug abuse, had missed more time from work, had more conflicts with others, had more childhood antisocial symptoms, and did worse on the Tactual Perception Test. These differences were in the expected direction and indicate that we were successful in identifying relatively distinct groups.

Unfortunately, however, the groups did not differ significantly in response to medication (the principal analyses were four-way analyses of variance: drug x group x order x sex). There was a slight tendency for the experimental group to be judged as having improved more on methylphenidate than the control group, but statistically significant differences were rare.

Attempts to identify predictors of drug response were generally unsuccessful. Correlations between the baseline measures and improvement on methylphenidate were, for the most part, nonsignificant; of the few significant correlations with greater improvement, some were in the expected direction (e.g., more drug abuse and more childhood vandalism), but others were in the opposite-than-expected direction (e.g., fewer temper outbursts and less retrospective parent-rated childhood hyperactivity). Analyses comparing "improvers" on methylphenidate vs. "non-improvers" were also generally unsuccessful in identifying predictors of drug response. In particular, retrospective parent ratings of childhood hyperactivity, reported by Wender et al. (1981) to predict stimulant responsiveness, did not predict response in our sample. Subdividing patients according to the certainty of childhood diagnosis of hyperactivity, or according to the presence or absence of significant depression or anxiety, did not assist in the attempt to identify a homogeneous group of methylphenidate responders. Of the suggestive positive findings, history of drug abuse (polydrug) seemed to be the best predictor of positive methylphenidate response; also, psychiatrist ratings of hyperactive symptomatology tended to predict stimulant response (in the expected direction) more frequently than did ratings by patients, parents, or "significant others."

Despite the generally negative results, we were impressed that a few patients (about 10 in the total sample) did appear to obtain clinically meaningful benefit from the methylphenidate (but not from placebo); these patients had a variety of DSM-III diagnoses. For these patients methylphenidate was recommended clinically following this study, and several of these patients followed this recommendation and continued to benefit from methylphenidate (periodic trials off mediation confirmed this benefit). The response to methylphenidate in some of these cases was as dramatic as in the case histories reported by Wood et al. (1976) and Wender et al. (1981).

Discussion

This study failed to find evidence of methylphenidate response among adults with symptomatology suggestive of MBD. No baseline measure, including history of childhood MBD, predicted methylphenidate response. The clinical evidence of response in certain patients was not evident statistically, and is therefore basically anecdotal. It appears that further work should be done to identify predictors of stimulant response among adults with MBD symptomatology.

References

Cantwell, D.P. Familial-genetic research with hyperactive children. In: Cantwell, D.P. (ed.), *The Hyperactive Child.* New York: Spectrum Publications, 1975, pp. 93-105.

Eisenberg, L. The management of the hyperactive child. *Develop. Med. Child. Neurol.*, 8(10):593-598, 1966.

Weiss, B., Minde, K., Werry, J.S., and Nemeth, E. Studies on the hyperactive child, VII. Five year follow-up. *Arch. Gen. Psychiatry,* 24(5):409-414, 1971.

Wender, P.H., Reimherr, F.W., and Wood, D.R. Attention deficit disorder in adults. *Arch. Gen. Psychiatry,* 38(4):49-456, 1981.

Wood, D.R., Reimherr, F.W., Wender, P.H., and Johnson, G.E. Diagnosis and treatment of minimal brain dysfunction in adults. *Arch. Gen. Psychiatry,* 33(12):1453-1460, 1976.

Lithium and Haloperidol in Hospitalized Aggressive Children[1]

Magda Campbell, M.D.,[2] Arthur M. Small, M.D.,[2] Wayne H. Green, M.D.,[2] Susan J. Jennings, M.A.,[2] Richard Perry, M.D.,[2] Walter G. Bennett, M.D.,[2] Maria Padron-Gayol, M.D.,[2] and Lillian Anderson, R.N.[2]

The purpose of this clinical trial was to assess critically the relative efficacy of haloperidol and lithium in children diagnosed as conduct disorder with a behavioral profile of aggressiveness and explosiveness.

Both lithium and haloperidol have antiaggressive properties in adult psychiatric patients with symptoms of aggressiveness and explosiveness (Shopsin et al. 1975; Sheard et al. 1976; Tupin et al. 1973).

There has been little if any systematic investigation of the efficacy of psychoactive drugs involving large samples of aggressive children (for review, *see* Campbell et al. 1978, 1982). This is in spite of the fact that the most frequent reason for admitting children into psychiatric hospitals is repeated occurrences of disruptive and highly explosive behaviors. These children often fail to respond to psychosocial types of interventions and require placement into residential treatment centers.

Method

Sixty-one (57 males, 4 females) hospitalized children, ages 5.2 to 12.9 years (mean, 8.97) who met the Diagnostic and Statistical Manual (DSM-III, 1980) criteria of conduct disorder, undersocialized, aggressive, completed this double-blind, placebo-controlled study. The following criteria were used for patient selection: 1) a behavioral profile which consisted of severe aggressiveness, explosiveness, and disruptiveness unresponsive to various outpatient treatments including pharmacotherapy and which resulted in the current psychiatric hospitalization; 2) no evidence of psychosis; and 3) no evidence of mental retardation. In addition, the child had to have 1) laboratory values within normal limits; 2) no history of medical illness or no current medical illness contraindicating administration of psychoactive drugs; 3) no seizure disorder or administration of antiepileptic drugs; 4) no need for concurrent administration of any type of drugs; 5) discontinuation of any psychoactive drug for a minimum of 2 weeks prior to the beginning of administration of study medication; 6) meeting the criteria of the Aggression Checklist developed by Hardesty and Shopsin (unpublished); and 7) written informed consent from the child's parents or legal guardians.

On admission to the hospital various examinations, including physical and laboratory tests, were performed on the children. Birth and hospital records were obtained whenever feasible. Family history of psychiatric illness and pre- and perinatal complications were recorded on a scale developed in the authors' unit (Campbell 1977); in addition, the Rochester Research Obstetrical Rating Scale (ROS) (Zax et al. 1977) was completed.

The experiment lasted 6 weeks. All children were placed on placebo for 2 weeks in order to 1) carry out baseline assessments, and 2) eliminate the placebo responders. Children who were suitable for the study were randomly assigned to one of the three treatment conditions: haloperidol, lithium, or placebo. Throughout the study, starting with the first day of the 2-week placebo baseline period, children received three capsules t.i.d. or nine capsules daily. All capsules contained 0.5 mg or 2.0 mg of haloperidol, or 250 mg of lithium carbonate, or placebo. All capsules

---

[1] This study was supported in part by USPHS Grants MH-04665 and MH-32212 from the National Institute of Mental Health.

[2] Department of Psychiatry, New York Medical Center, New York, NY 10016.

Reprint requests to Dr. Magda Campbell, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016.

were identical in appearance. The medication was administered by the research nurse at 8 a.m., 12 noon, and 4 p.m.

Increments in drug dosages were carried out according to a fixed and coded schedule. Haloperidol dosage began at 1.0 mg/day; increments were gradual over a period of 2 weeks until a maximum of 16.0 mg/day was reached or until the development of untoward effects required reduction or stabilization of dosage. Lithium dosage began at 250 mg/day; increments were made in a similar fashion. The maximum dosage was not to exceed 2,000 mg/day and/or a blood level of 1.8 mEq/l. Dosage was individually regulated over a period of 2 weeks and was followed by a 2-week period on optimal dose. Lithium levels in saliva (Shopsin et al. 1969) were monitored twice a week throughout the study and in blood at termination.

Behavioral symptoms, cognitive functioning, untoward effects and electroencephalograms (EEGs) were assessed on baseline and during treatment at fixed points. Ratings were carried out under several rating conditions by multiple rates using multiple rating scales.

The following measures from the Early Clinical Drug Evaluation Unit (EDCEU) Assessment Battery (*Psychopharmacol. Bull.*, 1973) were used: The Children's Psychiatric Rating Scale (CPRS), Clinical Global Impressions (CGI), Conners Teacher Questionnaire (CTQ), Conners Parent-Teacher Questionnaire (PTQ), Dosage Record and Treatment Emergent Symptoms (DOTES), and the Treatment Emergent Symptom Scale-Write In, using a checklist of untoward effects. In addition, two scales developed by the authors and their staff were employed: a Timed Aggression Behavioral Checklist (ABC), and Global Clinical Judgment.

Results

Several demographic variables were examined to reveal possible influences on drug effectiveness, optimal dose, and outcome. These demographic variables were: socio-economic status (Hollinshead 1965), weight, age, sex, IQs (full scale, verbal, and performance), race, and total score from the ROS. The three treatment groups were compared using chi-square and one-way analyses of variance, which showed no differences between treatment groups at baseline on any of the measures. This precludes the possibility that drug related differences were confounded by these variables among treatment groups.

For children who received haloperidol the optimal doses ranged from 1.0 to 6.0 mg/day (mean, 2.95), or 0.04 mg/kg/day to 0.21 mg/kg/day (mean, 0.096). The maximum dose given during the regulation period ranged from 1.5 to 12.0 mg/day. The optimal doses of lithium ranged from 500 to 2,000 mg/day (mean 1,166). On these doses, lithium level in saliva ranged from 0.81 to 5.05 mEq/l (mean, 2.515); this corresponded to 0.32 to 1.51 mEq/l (mean 0.993) in serum. The maximum doses of lithium given during the regulation period ranged from 750 to 2,000 mg/-day (mean 1,452).

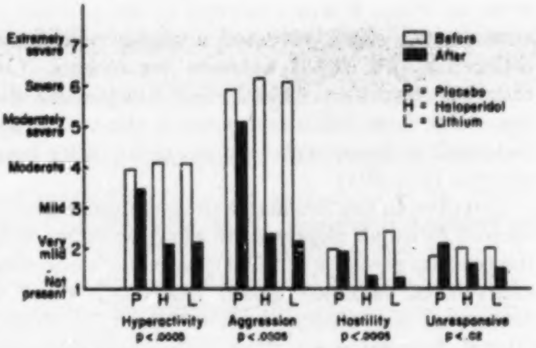


FIGURE 1. Ratings of two child psychiatrists on the Children's Psychiatric Rating Scale, before and after treatment.

Twenty-three CPRS items were entered into an average-linkage clustering analysis which yielded five clusters: Aggression, Hyperactivity, Unresponsive, Hostility, and Speech Problem. In addition, the items tension and bedwetting were also included in subsequent analyses. The details of the cluster analyses will be reported elsewhere. Week 6 ratings for the five clusters and two items were analyzed by an analysis of covariance to determine whether drug significantly affected these areas of behavior. The results are shown in Figure 1. The Hyperactivity cluster (which contained symptoms of hyperactivity, fidgetiness, and distractibility), Aggression cluster (fighting with peers, temper outbursts, and bullying), and Hostility cluster (negative-uncooperative, angry affect, loud voice, and lability of affect) showed highly significant drug effecs ($p < .0005$); the Unresponsive cluster (underproductive speech, and unspontaneous relation to examiner also showed a significant drug effect ($p < .02$). Speech Problem (level of speech development and mispronunciations), tension, and bedwetting, however, did not show significant drug effects.

Orthogonal contrasts used to compare haloperidol with lithium and to compare haloperidol and lithium with placebo on the four clusters yielded significant differences from baseline to treatment. In each case the two drugs did not differ from each other, but did differ from placebo for the Hyperactivity, Hostility, Aggression ($p < .001$), and Unresponsive clusters ($p < .01$).

The first item of the CGI scale, severity of illness, at Week 6 was analyzed by an analysis of covariance, which revealed a highly significant difference ($p < .0005$) between treatments. Orthogonal contrasts showed that haloperidol did not differ from lithium; however, the two drugs did result in improved ratings and did differ from placebo ($p < .001$).

Children in the two active drug conditions were viewed as much improved in contrast to those in the placebo group ($p < .0005$), based on a one-way analysis of variance which examined Week 6 ratings of the second item of the CGI Scale, Global Improvement. The differences between the two active drug conditions and placebo condition were significant ($p < .001$), but there were no significant differences between the active drugs.

The Efficacy Index is two dimensional, requiring an assessment of both therapeutic effects and side effects. The therapeutic effect differed significantly across conditions ($p < .00005$). Haloperidol did not differ from lithium, but these two differed from placebo ($p < .001$) by orthogonal contrasts. There was also a significant difference among treatment conditions for side effects ($p < .03$) due to the fact that haloperidol has (on optimal dose) more side effects than placebo or lithium which do not differ from each other.

The 39 items of the CTQ were rated by three teachers. Analysis of covariance showed no significant differences among treatment groups for any cluster or individual item. However, only 30 percent of the behaviors improved on placebo while 80 percent improved on haloperidol or lithium.

The PTQ scale was completed by the head nurse of the ward. The Week 6 data were analyzed by an analysis of covariance. Although no significant differences were found, there was a tendency for lithium to be more effective than haloperidol which in turn was more effective than placebo. Behavior actually worsened or remained the same on placebo, but improved in the two drug conditions.

The ABC scale yielded no significant results.

After each child completed the study he was rated on the Global Clinical Judgment Scale as unchanged or worse, minimal, moderate, or marked improvement. This rating was a result of a joint agreement of all staff, while still blind to the child's actual treatment condition. A highly significant difference ($p < .00005$) resulted from a one-way analysis of variance of these scores, as shown in Figure 2, indicating that children treated with haloperidol or lithium improved moderately in contrast to children who received placebo. Orthogonal contrasts confirmed that haloperidol does not differ significantly from lithium, but both lithium and haloperidol differed significantly from placebo ($p < .001$).

Untoward effects were recorded both during dosage regulation and optimal dose (*see* Table). All 20 children who were receiving haloperidol have shown untoward effects at some point: excessive sedation (15; 4 of these on optimal dose), acute dystonic reaction (10; none on optimal), drooling (6; one of these on optimal), and tremor

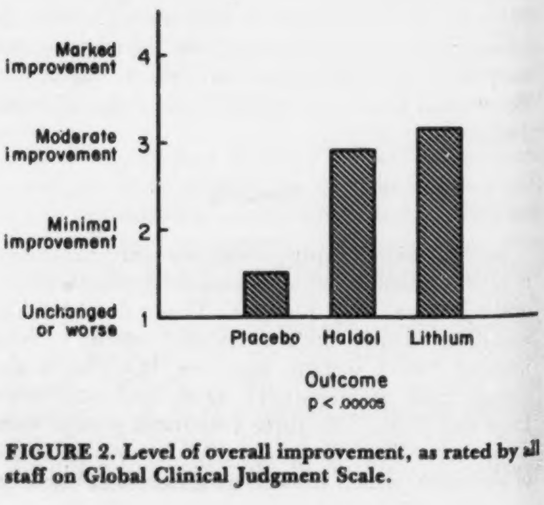


FIGURE 2. Level of overall improvement, as rated by all staff on Global Clinical Judgment Scale.

Table

Incidence of Untoward Effects* by Drug in 61 Patients

Untoward Effects	Haloperidol	Lithium	Placebo	Total
Excessive Sedation	15 (4)	–	4 (3)	19 (7)
Acute Dystonic Reaction	10	–	1 (1)	11 (1)
Tremor	5	5 (3)	1 (1)	11 (4)
Stomachache	–	7 (3)	2	9 (3)
Headache	–	6 (2)	–	6 (2)
Drooling	6 (1)	–	–	6 (1)
Other	18 (4)	25 (5)	6 (4)	49 (13)
TOTAL**	54 (9)	43 (13)	14 (9)	111 (31)
No. of Patients	20	21	20	61
No. of Patients with Untoward Effects	20	17	10	47

*On optimal dose in parenthesis

**Total number of occurrences of different untoward effects

(5; none of these on optimal) were most commonly observed. Of the 21 children assigned to lithium, 17 had untoward effects: pains in the stomach (7; 3 of these on optimal), headache (6; 2 of these on optimal), and tremor (5; 3 of these on optimal dose) were most frequent. In the 20 children who were receiving placebo, 10 patients had some type of untoward effect: excessive sedation (4; 3 of these on optimal dose) and worsening of aggressiveness (4; 3 on optimal) were most common.

During the optimal dose period the average number of untoward effects per child in each of the three treatment conditions did not differ significantly. However, the untoward effects of haloperidol during optimal dose seemed to interfere more with the child's daily functioning than those seen with lithium or placebo. The number of untoward effects on optimal dosage decreased with age on haloperidol ($r = -.40$, $p = .039$), but not lithium.

The cognitive battery and EEG data are currently being analyzed.

In summary, both lithium and haloperidol were superior to placebo in reducing target behaviors in hospitalized aggressive and explosive conduct disorder children on certain measures. The therapeutic effect of these drugs is not only statistically significant but also clinically meaningful.

However, these findings should be replicated. Further research is required to assess the long-term efficacy and safety of these drugs in children.

Acknowledgment: The authors wish to thank Miss Camille Petty, R.N., ward staff, teachers of P.S. 106, and Dr. Juanita Shell for their contribution, and Rowell Laboratories and McNeil Pharmaceutical for supplying the lithium, and placebo and haloperidol, respectively.

References

Campbell, M. Demographic parameters of disturbed children: A template to the CPDI and CSH, its rationale and significance. *Psychopharmacol. Bull.*, 13(2):30-33, 1977.

Campbell, M., Cohen, I.L., and Small, A.M. Drugs in aggressive behavior. *J. Am. Acad. Child Psychiatry,* 21:107-117, 1982.

Campbell M., Schulman, D., and Rapoport, J. The current status of lithium therapy in child and adolescent psychiatry. *J. Am. Acad. Child Psychiatry,* 17:717-720, 1978.

Diagnostic and Statistical Manual of Mental Disorders (DSM-III), 3d ed. Washington, D.C.: The American Psychiatric Association, 1980.

Hollingshead, A.B. *Two-Factor Index of Social Position (1957).* New Haven, Conn.: privately printed, 1965.

Pharmacotherapy of Children, Special Issue. *Psycopharmacol. Bull.*, 1973.

Sheard, M.H., Marini, J.L., Bridges, C.I., and Wagner, E. The effect of lithium on impulsive aggressive behavior in man. *Am. J. Psychiatry,* 133(12):1409-1413, 1976.

Shopsin, B., Gershon, S., and Pinckney, L. The secretion of lithium in human mixed saliva: Effects of ingested lithium on electrolyte distribution in saliva and serum. *Int. Pharmacopsychiatry,* 2:148-169, 1969.

Shopsin, B., Gershon, S., Thompson, H., and Collins, P. Psychoactive drugs in mania. A controlled comparison of lithium carbonate, chlorpromazine, and haloperidol. *Arch. Gen. Psychiatry,* 32(1):34-42, 1975.

Tupin, J.P., Smith, T.L., Clanon, L.I., Kim, A., and Groupe, A. The long-term use of lithium in aggressive prisoners. *Compr. Psychiatry,* 14(4):311-317, 1973.

Zax, M., Sameroff, A.J., and Babigian, H.M. Birth outcomes in the offspring of mentally disordered women. *Am. J. Orthopsychiatry,* 47:218-230, 1977.

Monoamine Receptor Sensitivity and the Mechanism of Action of Antidepressant Treatment

Chair: George R. Heninger, M.D.
Department of Psychiatry
Yale University School of Medicine
New Haven, Connecticutt

The Monoamine Receptor Sensitivity Hypothesis of Antidepressant Drug Action[1]

George R. Heninger, M.D.,[2] and Dennis S. Charney, M.D.[2]

The generalized monoamine receptor sensitivity hypothesis of antidepressant drug action is based on the premise that the therapeutic action of antidepressant treatments (ADT) results from changes in the sensitivity of several monoamine receptors. The overall net effect of these changes is to increase neurotransmission in several monoamine systems. This hypothesis was stimulated by the findings that the electrophysiological sensitivity of single cells to both norepinephrine (NE) and serotonin (5-HT) was increased following long-term antidepressant treatment (Aghajanian 1981), and it is based on the review of a large number of recent studies which have elucidated many of the complex effects of long-term antidepressant treatment (ADT) on monoamine receptor function (Charney et al. 1981a). Similar earlier hypotheses have usually focused on only one monoamine system (Sulser et al. 1978).

The original monoamine deficiency hypothesis of depression (Schildkraut 1965; Bunney & Davis 1965) and its more recent modifications (Maas 1975) were based on the premise that the therapeutic action of drugs is the consequence of an increased availability of synaptic norepinephrine (NE) or serotonin (5- HT) secondary to high affinity reuptake inhibition and/or decreased catabolism. This hypothesis has been questioned on two grounds: a) Some clinically effective antidepressant drugs, such as iprindole and mianserin do not inhibit amine uptake or metabolism (Gluckman & Baum 1969; Goodlet, et al. 1977), and some reuptake inhibitors, such as amphetamine, femoxetine, or cocaine are not effective antidepressant treatments (Overall et al. 1962; Post et al. 1974; Ghose et al. 1977). b) There is an obvious temporal discrepancy between the rapid drug-induced biochemical effects on amine uptake and catabolism, which occur within hours, and the clinical antidepressant response which occurs only after 7-14 days of treatment (Oswald et al. 1972). In addition, studies of NE and 5-HT turnover in animals

---

[1] This study was supported in part by USPHS Grants MH-36229, MH-30929, and MH-25642 from the National Institute of Mental Health and by the State of Connecticut.

[2] Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, CT 06519.

Address correspondence to: George R. Heninger, M.D., Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06519

following long-term ADT treatment show no consistent changes across the wide spectrum of antidepressant compounds or ECT (Charney et al. 1981a).

Since changes in amine uptake or catabolism do not easily explain the effects of long-term ADT on the behavior of animals or patients, current research has focused on the effects of ADT on monoamine receptor function. Major advances elucidating the complex effects of long-term ADT on NE, dopamine (DA), 5-HT, and histamine (H) receptor function have been facilitated by new developments in radioligand receptor binding, single unit electrophysiological recordings, pharmacologic characterization of cyclic adenosine 3′5′ monophosphate (cAMP) production, and neurotransmitter behavioral paradigms. All of these methods are capable of assessing receptor regulation and function, and they have led to an improved understanding of the effects of long-term ADT.

Receptor Sensitivity in Animals on Long-Term Antidepressant Treatment

Table 1 presents a general summary of the effects of long-term ADT on measures of monoamine receptor sensitivity measured by biochemical, physiologic, and behavioral methods across the receptors for these four monoamine neurotransmitters. (*See* Charney et al. 1981a for a detailed review of this area.) Following long-term ADT there is a decrease in beta receptor binding and a decrease in beta receptor stimulated increase of cAMP. Physiologic studies have, in general, tended to confirm this, but behavioral models for assessing beta receptors are not available.

Long-term ADT produces an increase in alpha-1 receptor sensitivity as indicated by electrophysiologic and behavioral measures. In contrast, no consistent changes in alpha-1 receptor binding have been observed. Alpha-2 sensitivity is decreased or unchanged depending on the drugs studied and the paradigm used. However, changes in alpha-2 sensitivity may reflect an important mechanism of action of some antidepressant drugs, and further studies are necessary to fully evaluate this possibility.

In the dopaminergic system, receptor binding studies demonstrate no change or possibly an increased binding assumed to occur on post synaptic receptors. Electrophysiologic and behavioral studies of the DA system demonstrate presynaptic subsensitivity and a postsynaptic supersensitivity. Thus, chronic ADT treatment appears to augment overall transmission in the dopaminergic system.

Table 1

Effects of Long-Term Antidepressant Treatment on Monoamine Receptor Sensitivity

Monoamine Receptor Type	Measures of Monoamine Receptor Sensitivity		
	Receptor Binding or cAMP Production	Sinble Unit Electrophysiology	Behavioral
Noradrenergic			
Beta	↓	0↓	—
Alpha 1	0	↑	↑
Alpha 2	↓↑	0↓	0↓
Dopaminergic			
Presynaptic	—	↓	↓
Postsynaptic	0↑	—	↑
Serotonergic	0↓	↑	↑
Histaminergic	0	↑	—

↑ = increase, ↓ = decrease, 0 = no change, — = not tested

Receptor binding in the serotonergic system has generally been found to be decreased, although it was increased following ECT. The increase in serotonergic receptor sensitivity assessed with electrophysiologic measures is consistent with the behavioral studies demonstrating increased sensitivity in this system.

A recent study in the histaminergic system has shown that changes in the sensitivity for cAMP production are not altered by chronic ADT, but that physiologic sensitivity is increased (Olianas et al. 1981). To date, histaminergic behavioral responses have not been studied following chronic ADT.

A careful examination of the studies mentioned above indicates that, particularly in the case of the alpha-1 and serotonin receptor systems, there is either no correlation or an inverse correlation between changes in receptor number determined by ligand binding and functional sensitivity assessed by electrophysiologic or behavioral techniques. It should be emphasized that changes in receptor number represent only one of several ways that sensitivity to a hormone or neurotransmitter may be regulated. It is possible that the sensitization of NE or 5-HT responses could result from antidepressant-induced changes in the coupling of alpha-adrenergic or 5-HT receptors to effector mechanisms or to changes in the effector mechanism itself. In this regard it is important to note that whereas antidepressant treatment has been shown to increase behavioral alpha-1 adrenergic sensitivity in the spinal cord without any increase in alpha-1 receptor binding, denervation with 6-hydroxydopamine does cause both increased alpha-1 sensitivity and alpha-1 binding (Davis et al. 1981).

A summary of the animal studies indicates that following long-term ADTs there is reduced beta adrenergic sensitivity while overall responsivity to alpha-1 adrenergic, postsynaptic, dopaminergic, serotonergic, and histaminergic stimulation appears to be increased. These changes in sensitivity occur with a time course that is similar to the 7- to 14-day delay in ADT effects observed in patients. Receptor sensitivity changes have usually been shown to occur following long-term administration of all effective antidepressive treatments (i.e., tricyclic antidepressants, 'atypical drugs,' monoamine oxidase inhibitors, and ECT). Thus, the receptor changes are observed irrespective of the markedly divergent pharmacologic profiles of the ADTs that induce them.

Receptor Sensitivity in Patients and Effects of Antidepressant Treatment

In rats, invasive procedures and pharmacologic experiments are conducted to verify that the neurotransmitter agonists and antagonists are indeed affecting the neurotransmitter system under study. Since this is not possible in humans, an alternative strategy has been utilized where a clinically safe neurotransmitter agonist or antagonist is administered. The changes in biochemical and physiological measures produced by the action of the agonist or antagonist on the putative receptor are used as a measure of that receptor's sensitivity. Using this paradigm, human studies have been conducted which support the hypothesis that changes in receptor sensitivity are relevant to the treatment of depressed patients.

A summary of the findings on noradrenergic receptor sensitivity in depressed patients is presented in Table 2. The alpha-2 agonist, clonidine, has been utilized to test the sensitivity of the presynaptic alpha-2 receptor. The dependent measures have been plasma MHPG and blood pressure (BP), both of which are reduced secondary to stimulation of brain alpha-2 adrenergic receptors. As can be seen in Table 2, the effect of clonidine on plasma MHPG and BP is not abnormal in depression (Charney et al. 1982). Treatment with desipramine produced a subsensitivity to clonidine, as measured by both plasma MHPG and BP (Charney et al. 1981b).

Table 2

Noradrenergic Receptor Sensitivity in Depressed Patients

Location	Type	Stimulus	Variable Measured	Level of Sensitivity (Patients vs. Controls)
Presynaptic	α_2	clonidine	plasma MHPG	normal
		clonidine	blood pressure	normal
Postsynaptic	α_2	clonidine	growth hormone	decreased
	α?	amphetamine	corticosteroid	decreased
	α?	dexamethasone	cortisol	decreased
	β	light	melatonin	decreased

Clonidine has been postulated to release growth hormone (GH) via direct action on adrenergic postsynaptic receptors. In depressed patients the GH response to clonidine is decreased (Matussek et al. 1980; Checkley et al. 1981; Charney et al. 1982). At present, it does not appear that this subsensitivity to clonidine is normalized following effective antidepressive treatment (Charney & Heninger 1982). However, there is still the possibility that this test will normalize when patients recover from their illness, i.e., when they can remain symptom-free off medication. Depressed patients have been found to have an impaired release of corticosteroids following stimulation by methylamphetamine. This response was normalized when patients were recovered and retested off medication (Checkley 1979). The resistance of plasma cortisol to dexamethasone suppression occurs in approximately 50 percent of patients and has been found to normalize with effective clinical treatment (Greden et al. 1980). The neurotransmitter receptors involved in the Dexamethasone Suppression Test have not been clearly established, although there is some evidence that an abnormal test could reflect subsensitive alpha adrenergic receptors.

The biochemical and neurophysiologic studies indicate that beta adrenergic receptors are decreased in sensitivity following chronic antidepressant treatment. No animal behavioral model has been found to adequately test the sensitivity of this receptor. It is of some interest that manic depressive patients have an increased sensitivity to light when plasma melatonin has been assayed (Lewy et al. 1981). Melatonin production is inhibited by light and increased by stimulation of beta receptors on the pineal. If the sensitivity of the other synapses in the neural chain between the retina and the superior cervical ganglia is unchanged and if the sensitivity of the beta receptor on the pineal is increased, the effects of light would not reduce melatonin secretion so readily. Thus, this very preliminary data would suggest that in manic depressive patients the sensitivity of the beta adrenergic system on the pineal is decreased. A decrease in beta receptor sensitivity following ADT would obviously not correct an abnormality in depression if beta receptors were already decreased before ADT was started.

Paradigms assessing central 5-HT receptors have not been well developed. The prolactin response following thyrotropin releasing hormone appears to be mediated by a central 5-HT mechanism. This response was potentiated in patients treated with ECT, which is consistent with the animal studies mentioned above (Coppen et al. 1980). Currently, there is considerable research activity in this area and data from additional studies should soon be available (Charney & Heninger 1982).

Discussion

The generalized monoamine receptor sensitivity hypothesis of antidepressant drug action is supported by three lines of evidence:

1. In animals long-term ADT produces changes in receptor sensitivity of at least four monoamine systems, i.e., decreased sensitivity at NE beta and increased sensitivity at NE alpha-1, DA, 5-HT, and H postsynaptic receptors with little evidence of change in acetylcholine, GABA, or glutamate sensitivity.
2. Similar changes in monoamine receptor sensitivity are seen following long-term treatment with very dissimilar drugs, i.e., drugs with very different pharmacologic profiles appear to have a common mechanism of action after long-term administration.
3. The changes in monoamine receptor sensitivity only occur following longer term administration, i.e., 7-14 days, a time course which is consistent with the delayed therapeutic effects of these treatments.

The eventual proof of this hypothesis must await clinical confirmation since the therapeutic mechanisms of action in depressed humans could be quite different than those seen in healthy young rats given larger relative doses of drug treatments. Therefore, it is important that clinical researchers be able to take advantage of the increasing number of methods available for evaluating this hypothesis in patients.

The data from studies of long-term ADTs on receptor sensitivity indicate that the original monoamine deficiency hypothesis requires modification and expansion. The enhancement of sensitivity by ADT of alpha adrenergic and serotonergic postsynaptic receptors is consistent with the original hypothesis that depressed patients have subnormal NE and/or 5-HT functional activity. Thus, the discovery of atypical agents, such as iprindol or mianserin, which were originally thought to weaken this hypothesis, may actually support it if the chronic effects of these agents on monoamine receptor sensitivity are taken into account. As mentioned, the induction of beta-adrenoceptor subsensitivity by ADT has prompted proposals (tantamount to a reversal of the monoamine deficiency hypothesis) that depression is the result of increased noradrenergic activity, at least in the beta noradrenergic system (Sulser et al. 1978). The opposite effects of long-term ADT on alpha and beta receptors do not necessarily have to be interpreted as incompatible. The reciprocal regulation of these adrenergic receptors observed in many studies may be an important mechanism for the homeostatic control of central noradrenergic activity. Thus, the effects induced by chronic antidepressant treatment on the relative sensitivity of alpha and beta adrenoceptors may serve to correct a disorder of adrenergic regulation in affective illness, where the balance between alpha and beta receptor sensitivity is more important than just the absolute effect in either system.

One of the most fundamental and far-reaching implications of the receptor sensitivity hypothesis is the opportunity that it allows for study of the mechanism of action of ADTs at the molecular level. If the induction of increased monoamine receptor sensitivity is an important common mechanism of action of ADTs, then the molecular mechanisms involved in the genesis of this process should allow for the development of much more specific, definitive, and efficacious treatments.

Summary

The generalized monoamine receptor sensitivity hypothesis of antidepressant drug action is based on the evidence that all ADTs produce changes in monoamine receptor sensitivity and that the time course of these changes is similar to the delayed therapeutic actions of these treatments. Long-term ADT has been found to reduce beta-adrenergic sensitivity while enhancing responses to alpha-adrenergic, dopaminergic, serotonergic, and histaminergic stimulation. The initial data from clinical studies suggest that postsynaptic adrenergic alpha receptors may be subsensitive in depression. This would support the hypothesis that depression is a result of decreased monoamine receptor sensitivity and that effective antidepressant treatment may reverse this abnormality.

Acknowledgment: Appreciation is extended to Grace M. Billings and Stella Rek for excellent secretarial help.

References

Aghajanian, G.K. Tricyclic antidepressants and single cell responses to serotonin and norepinephrine: A review of chronic studies. In: Usdin, E., Bunney, W.E., and Davis, J.M. (eds.), *Neuroreceptors: Basic and Clinical Aspects,* New York: Wiley & Sons, 1981, pp. 27-35.

Bunney, W.E., and Davis, J.M. Norepinephrine in depressive reactions. A review. *Arch. Gen. Psychiatry,* 13:483-494, 1965.

Charney, D.S., and Heninger, G.R. Assessment of adrenergic and serotonergic receptor function: Implications for the etiology and treatment of depression. *Psychopharmacol. Bull.,* 18(3):151-155, 1982.

Charney, D.E., Menkes, D., and Heninger, G. Receptor sensitivity and the mechanism of action of antidepressant treatment: Implications for the etiology and therapy of depression. *Arch. Gen. Psychiatry,* 38:1160-1180, 1981a.

Charney, D.S., Heninger, G.R., Sternberg, D.E., Redmond, D.E., Leckman, J.F., Maas, J.W., and Roth, R.H. Presynaptic adrenergic receptor sensitivity in depression: The effect of chronic desipramine treatment. *Arch. Gen. Psychiatry,* 38:1334-1340, 1981b.

Charney, D.S., Heninger, G.R., Sternberg, D.E., Hafstad, K.M., Giddings, S., and Landis, D.H. Adrenergic receptor sensitivity in depression: Effects of clonidine in depressed patients and healthy subjects. *Arch. Gen. Psychiatry,* 39:290-294, 1982.

Checkley, S.A. Corticosteroid and growth hormone responses to methylamphetamine in depressive illness. *Psychol. Med.,* 9:107-115, 1979.

Checkley, S.A., Slade, A.P., and Shur, E. Growth hormone and other responses to clonidine in patients with endogenous depression. *Br. J. Psychiatry,* 138:51-55, 1981.

Coppen, A., Rama Rao, V.A., Bishop, M., Abou-Salah, M.T., and Wood, K. Neuroendocrine studies in affective disorders. Part 1. Plasma prolactin response to thyrotropin-releasing hormone in affective disorders: Effect of ECT. *J. Affect. Disord.,* 2:311-315, 1980.

Davis, M., Menkes, D.B., Kehne, J.H., Gallager, D.W., and Aghajanian, G.K. Chronic tricyclic antidepressants alter α_1- and α_2-adrenoceptor responsivity as measured by the effects of selective agonists on the acoustic startle reflex. *Neurosci. Abstr.,* 7:817, 1981.

Ghose, K., Gupta, R., Coppen, A., and Lund, P. Antidepressant evaluation and the pharmacological actions of FG-4963 in depressive patients. *Eur. J. Pharmacol.,* 41:31-37, 1977.

Gluckman, M.I., and Baum, T. The pharmacology of iprindole, a new antidepressant. *Psychopharmacologia (Berlin)*, 15:169-183, 1969.

Goodlet, F., Mireylees, S.E., and Sugrue, M.F. Effects of mianserin, a new antidepressant, on the in vitro and in vivo uptake of monoamines. *Br. J. Pharmacol.*, 61:307-313, 1977.

Greden, J.F., Tarika, J.S., Devigne, J.P., Kronfol, Z., and Carroll, B.C. Dexamethasone test predicts treatment response (abstr.). Presented at 133rd Annual Meeting of the American Psychiatric Association, May 1980.

Lewy, A.J., Wehr, T.A., Goodwin, F.K., Newsome, D.A., and Rosenthal, N.E. Manic-depressive patients may be supersensitive to light. *The Lancet*, pp. 383-384, 1981.

Maas, J.W. Biogenic amines and depression: Biochemical and pharmacological separation of two types of depression. *Arch. Gen. Psychiatry*, 32:1357-1361, 1975.

Matussek, N., Ackenheil, M., Hippius, H., Muller, F., Schroeder, H.Th., Schultes, H., and Wasilewski, R. Effect of clonidine on growth hormone release in psychiatric patients and controls. *Psychiatry Res.*, 2:25-36, 1980.

Olianas, M.C., Oliver, A.P., and Neff, N.H. Chronic antidepressant treatment produces supersensitivity to the electrophysiological response of histamine in guinea pig hippocampus without a change in the sensitivity of the histamine sensitive adenylate cyclase. *Abstr. Soc. Neurosci.*, 7:818, 1981.

Oswald, I., Brezinova, V., and Dunleavy, D.L.F. On the slowness of action of tricyclic antidepressant drugs. *Br. J. Psychiatry*, 120:673-677, 1972.

Overall, J.E., Hollister, L.E., Pokorny, A.D., Casey, J.F., and Katz, G. Drug therapy in depressions. Controlled evaluation of imipramine, isocarboxazid, dextroamphetamine, amobarbital, and placebo. *Clin. Pharmacol. Ther.*, 3:16-22, 1962.

Post, R.M., Kopin, J., and Goodwin, F.K. The effects of cocaine on depressed patients. *Am. J. Psychiatry*, 131:511-517, 1974.

Schildkraut, J.J. The catecholamine hypothesis of affective disorders: A review of supporting evidence. *Am. J. Psychiatry*, 122:509-522, 1965.

Sulser, F., Vetulani, J., and Mobley, P.L. Mode of action of antidepressant drugs. *Biochem. Pharmacol.*, 27:257-261, 1978.

Catecholamine-Stimulated Production of Melatonin After Administration of Antidepressants

William E. Heydorn,[1] Stanley Caroff, M.D.,[2] and Alan Frazer, Ph.D.[3]

It is now established that repeated treatment with antidepressant drugs produces effects different from those observed after their acute administration. For example, repeated, but not acute, administration of either the tricyclic antidepressants or the monoamine oxidase inhibitors produces a decrease in the number of β-adrenergic receptors and a reduced ability to generate adenosine 3′, 5′-monophosphate (cyclic AMP) in response to catecholamine (*see* Frazer 1981a,b). What remains unclear is whether such effects have any impact on the overall response of the tissue to catecholamine. To assess this, we examined the effect of repeated administration of antidepressant drugs to rats on catecholamine-elicited production of N-acetyl-5-methoxytryptamine (melatonin) by the pineal gland. The pineal gland contains a high density of β-adrenergic receptors (Greenberg & Weiss 1979) coupled to a catecholamine-sensitive adenylate cyclase receptor that generates cyclic AMP (Weiss & Costa 1968). The β-adrenergic receptors of the pineal gland are activated either pharmacologically by exogenous administration of catecholamine or physiologically by the onset of darkness. Darkness, acting through a multisynaptic pathway, causes the release of norepinephrine from sympathetic nerve terminals innervating the pineal gland (Brownstein & Axelrod 1974). The resultant increase in the glandular content of cyclic AMP (Heydorn et al. 1980) initiates a cascade of processes resulting in the production of melatonin (*see* Klein 1979). Thus, melatonin levels are indicative of the activity of the β-adrenergic receptor/adenylate cyclase/cyclic AMP complex of the pineal gland.

---

[1] Department of Pharmacology, University of Pennsylvania, Philadelphia, PA 19104.

[2] Department of Psychiatry, University of Pennsylvania and Veterans Administration Hospital, Philadelphia, PA 19104.

[3] Departments of Pharmacology and Psychiatry, University of Pennsylvania and Veterans Adminstration Hospital, Philadelphia, PA 19104.

Male Sprague-Dawley rats, housed on a 12-hour light/dark cycle (lights on at 0700 hr), were used in these experiments. Animals received intraperitoneal injections of the tricyclic antidepressant desmethylimipramine (DMI) (10 mg/kg), or the monoamine oxidase inhibitor nialamide (40 mg/kg), either acutely or twice daily for 7 days. Control animals received 0.9 percent NaCl. Rats treated repeatedly were killed 24 hours after the last injection. It was found that such treatments reduced the number of β-adrenergic receptors of the pineal gland at this time. Rats treated acutely were decapitated 5 hours after drug adminstration.

The first series of experiments examined the effect of repeated antidepressant administration on the melatonin concentration of pineal gland and serum over a 24-hour cycle. Rats were treated as described above and killed at 1000, 1600, 2200, 2400, 0200, 0400, or 0600 hours. Pineal glands and serum were collected and, after extraction with chloroform and washing with petroleum ether, assayed for melatonin by a radioimmunoassay procedure (Pang et al. 1977). The data obtained were analyzed by analysis of variance and Duncan's Multiple Range Test.

The onset of darkness caused a marked elevation of the melatonin concentration in both pineal gland and serum of control rats. Pineal gland melatonin levels rose from approximately 200 picograms/gland during the day to a peak of 4000 picograms/gland at night. Serum melatonin values also rose significantly, from a daytime concentration of 7 picograms/ml to a nighttime level of 45 picograms/ml. Repeated treatment of rats with DMI produced a significant decrease in the nighttime rise of melatonin in both the pineal gland ($p<0.05$) and in serum ($p<0.01$). Similar results were obtained when rats were treated repeatedly with nialamide (pineal gland, $p<0.01$; serum, $p<0.05$). The extent of the inhibition of the nighttime rise of melatonin produced by repeated administration of these antidepressant drugs was about 25 percent. By contrast, if either DMI or nialamide were administered acutely at 1900 hours and the rats killed at midnight, there was no difference in pineal gland or serum melatonin levels in drug-treated rats as compared to that measured in control animals.

In a second series of experiments, melatonin production in the pineal gland was stimulated pharmacologically by the subcutaneous administration of L-isoproterenol. Rats were treated repeatedly with DMI, nialamide, or 0.9 percent NaCl as described above and then, 21 hours after the last injection, were administered either 0.5 mg/kg or 1 mg/kg L-isoproterenol. Three hours later the rats were killed and the pineal glands removed and assayed for melatonin. In control rats, administration of L-isoproterenol caused a marked elevation of pineal gland melatonin concentrations above baseline, about 15-fold with the lower dose of the catecholamine and about 20-fold with the higher dose. Repeated administration of DMI reduced significantly (by about 50%) the ability of either dose of L-isoproterenol to increase melatonin concentrations in the pineal gland ($p<0.01$). Similar results were seen upon repeated administration of nialamide to rats. However, if rats were treated acutely with either DMI or nialamide, the stimulatory effect of L-isoproterenol on melatonin levels in the pineal gland was essentially identical to that seen in control animals.

Therefore, in the pineal gland it appears that antidepressant drug-induced subsensitivity of β-adrenergic receptors with concomitant reduced responsiveness of the adenylate cyclase/cyclic AMP system results in a significant decrease in the ability of catecholamines to raise the concentration of melatonin in the gland.

Since this inhibitory effect of melatonin production after repeated antidepressant administration was detected in serum, we wanted to examine whether depressed patients treated with DMI would also show a blunted nighttime rise of melatonin while treated with the tricyclic drug. To date, one patient has been studied. This male unipolar depressed inpatient, aged 34, had a good clinical response to DMI, as shown by Hamilton Depression Scale scores decreasing from 22 prior to treatment to 6 after 4 weeks of treatment. Serum was obtained for melatonin analysis every 1.5 hours between 1730-0600 hours, with lights turned off at 2200 hours. This was done prior to treatment and after 4 weeks of treatment with DMI. Prior to treatment, the patient showed markedly elevated serum concentrations of melatonin during the night (about 115 pg/ml) as compared to those measured in the daytime (about 30 pg/ml). After treatment with DMI, the serum concentration of melatonin rose shortly after the lights were turned off, but then fell during the course of the night. As a consequence, while the patient was treated with DMI the mean nighttime concentration of melatonin in the serum of this patient (58 ± 11 pg/ml; average of the five values taken between midnight and 6:00 am) was significantly lower than those measured over the corresponding times prior to treatment (114 ± 9 pg/ml; $p<0.005$). Such data are consistent with the belief that antidepressant treatments produce β-adrenergic receptor subsensitivity in patients, although other interpretations of the data are possible also. Further work will be needed to determine whether this approach can provide an index of β-adrenergic subsensitivity in patients. If it can, then the possible clinical importance of the β-receptor subsensitivity produced by antidepressant treatments can be evaluated.

References

Brownstein, M., and Axelrod, J. Pineal gland: 24-hour rhythm in norepinephrine turnover. *Science*, 184:163-165, 1974.

Frazer, A. Antidepressant drugs: Effect on adrenergic responsiveness and monoamine receptors. In: Usdin, E., Bunney, W.E., and Davis, J.M. (eds.), *Neuroreceptors — Basic and Clinical Aspects*. New York: John Wiley & Sons Ltd, 1981a, pp. 85-98.

Frazer, A. Tricyclic antidepressants — Basic considerations. In: Palmer, G. (ed.), *Neuropharmacology of Central Nervous System and Behavioral Disorders*. New York: Academic Press, 1981b, pp. 73-91.

Greenberg, L., and Weiss, B. Ability of aged rats to alter beta-adrenergic receptors of brain in response to repeated administration of reserpine and desmethylimipramine. *J. Pharmacol. Exp. Ther.*, 211:309-316, 1979.

Heydorn, W., Mendels, J., and Frazer, A. Effects of darkness and of desmethylimipramine on pineal gland concentrations of adenosine 3′,5′-monophosphate. *Biochem. Pharmacol.*, 29:1341-1346, 1980.

Klein, D.C. Circadian rhythms in the pineal gland. In: Krieger, D.T. (ed.), *Endocrine Rhythms*. New York: Raven Press, 1979, pp. 203-223.

Pang, S.F., Brown, G.M., Grota, L.J., Chambers, J.W., and Rodman, R.L. Determination of N-acetylserotonin and melatonin activities in the pineal gland, brain, and serum of rats and chickens. *Neuroendocrinology*, 23:1-13, 1977.

Weiss, B., and Costa, E. Selective stimulation of adenylate cyclase of rat pineal gland by pharmacologically active catecholamines. *J. Pharmacol. Exp. Ther.*, 161:310-319, 1968.

Agonist-Induced Changes in Behavior as a Measure of Functional Changes in Receptor Sensitivity Following Chronic Antidepressant Treatments[1]

Michael Davis, Ph.D.[2]

Introduction

Therapeutic effects of antidepressant drugs typically do not appear until 2 or more weeks after treatment initiation (Oswald et al. 1972; Klein et al. 1980). Hence, the neuropharmacological actions of antidepressant treatments that accompany chronic as opposed to acute administration should be the ones most relevant to their therapeutic effects. In recognition of this, an increasing number of biochemical and electrophysiological studies are being done to determine changes in neural transmission following chronic antidepressant treatments. However, as elegant as these studies might be, it is important to emphasize that changes in behavior ultimately have to be used to determine functional changes in neural transmission. In general, two broad classes of behavior could be brought to bear on this question. One would include "animal models of depression" in which the behavior of the animal bears some resemblance to human depression. Paradigms such as learned helplessness, the swimming despair test, or social behavior of nonhuman primates following early isolation would be examples. Paradigms such as these have already proved to be important for screening prospective antidepressant drugs and ultimately will be very important for analyzing the etiology of depression. At the present time, however, the complexity of these paradigms makes them difficult to use as behavioral tests to deduce changes in specific transmitter systems following antidepressant treatments.

Behavioral tests of the second class are ones that have been shown to be modulated by specific central neurotransmitter systems judged by their response to selective pharmacological agonists. These tests are not used as model systems of depression, but as model behavioral systems for deducing functional changes in specific neurotransmitter systems. For example, it is well documented that the drug apomorphine elicits stereotyped behavior via activation of dopamine systems in the brain. Thus, changes in the ability of apomorphine to elicit stereotyped behavior following antidepressant treatments can be used to infer how antidepressants alter functional dopamine transmission.

---

[1] This research was supported by National Science Foundation Grant BNS-78-04170, NIMH Grants MH-25642 and MH-18949, Research Scientist Development Award MH-00004 to M.D., and the State of Connecticut.

[2] Yale University School of Medicine, New Haven, CT 06508.

In the present paper, experiments will be reviewed that use changes in behavioral output induced by selective agonists to assess functional changes in receptor sensitivity following chronic as compared to acute antidepressant treatments. Recent studies in the author's own laboratory will then be reviewed which show that the acoustic startle reflex may be an especially good test system to analyze functional changes in different neurotransmitter systems. Finally, changes in alpha-1 and alpha-2 adrenergic receptor sensitivity following chronic vs. acute treatment with selected tricyclic antidepressant drugs using acoustic startle will be presented.

Table 1

Functional Changes in Dopamine Transmission Based on Behavioral Measures

Treatment	Treatment Test Interval	Probe Drug	Behavior	Treatment Effect	Authors
ECS (× 10)	24 hrs	Methamphetamine	Activity Increase	Enhance	Green et al. 1977
ECS (× 10)	24 hrs	Tranylcypromine L-DOPA	Activity Increase	Enhance	Green et al. 1977
ECS (× 10)	24 hrs	Apomorphine	Turning after Unilateral 6-OHDA	Enhance	Green et al. 1977
ECS (× 5)	24 hrs	Apomorphine	Activity Increase	Enhance—Blocked by Prior NE Depletion	Green & Deakin 1980
ECS (× 8)	24-96 hrs	Apomorphine	Stereotyped Behavior	Enhance	Serra et al. 1981
10 Days of Imipramine or Amitriptyline or Mianserin or ECS (× 8)	48-96 hrs	Low Dose of Apomorphine	Activity Decrease	Blunt—Therefore Net Increase in DA Transmission	Serra et al. 1979
ECS (× 3)	48 hrs	Amphetamine or Apomorphine	Drug Discrimination	Enhance	White & Barrett 1981
Desipramine × 14	24-48 hrs	---	Self-Stimulation	Enhance	Fibiger & Phillips 1981
Amitriptyline Imipramine Desipramine Mianserin Danitracen Iprindole × 14	2 hrs	Apomorphine	Stereotyped Behavior	No Change	Maj et al. 1979b
Amitriptyline Clomipramine Maprotiline Imipramine × 7	½ hr	Apomorphine	Stereotyped Behavior	No Change or Blockade	Delini-Stula & Vassout 1979

Functional Changes in Receptor Sensitivity Following Antidepressant Treatments

Table 1 summarizes studies that have assessed functional changes in dopamine (DA) transmission following chronic antidepressant treatments. In this and all subsequent tables, only studies in which chronic treatments have been used will be included. In general, the effects to be reported only occur after chronic and not acute treatment, although this comparison has not been included in every study.

Table 1 shows that chronic antidepressant treatments tend to enhance DA transmission when behavioral testing occurs at least 24 hours after the final treatment. Repeated applications of electroconvulsive shocks (ECS) enhance the ability of DA agonists such as amphetamine, L-DOPA, or apomorphine to increase locomotor activity (Green et al. 1977; Green & Deakin 1980) or of apomorphine to increase turning in 6-OHDA lesioned rats (Green et al. 1977); or to produce stereotyped behavior (Serra et al. 1981). Repeated ECS or chronic treatment with different antidepressant drugs blunts the ability of low doses of apomorphine to depress locomotor activity, suggesting a net increase in DA transmission (Serra et al. 1979, 1981). Three ECS treatments

Table 2

Functional Changes in Serotonin Transmission Based on Behavioral Measures

Treatment	Treatment Test Interval	Probe Drug	Behavior	Treatment Effect	Authors
ECS (× 10)	24-72 hrs	Tranylcypromine + L-tryptophan	Activity	Enhance	Green et al. 1977 Costain et al. 1979
ECS (× 10)	24 hrs	5-MeODMT	Activity	Enhance	Evans et al. 1976
ECS (× 10)	24 hrs	Tranylcypromine + 5-HTP	Head Twitch	Enhance	Lebrecht & Nowack 1980
ECS (× 10)	24 hrs	Tranylcypromine + L-tryptophan or Quipazine or 5-MeODMT	Activity	Enhance—Blocked by PCPA or Metergoline or NE Depletion but not Haloperidol	Green et al. 1980
Amitriptyline Mianserin Danitracen ×10	48-72 hrs	5-HTP	"Wet Dog Shakes"	Enhance	Moglinicka & Klimek 1979
Amitriptyline Imipramine ×28	48 hrs	5-MeODMT	Head Twitch	Enhance	Friedman & Dallob 1979
Zimelidine ×14	24 hrs	5-MeODMT (low dose)	Head Twitch	Enhance	Fuxe et al. 1981
		5-MeODMT (high dose)		Depress	
Mianserin Imipramine Amitriptyline Desipramine ×8	12 hrs	5-HTP	Sleep Time in Chicks	Enhance	Jones 1980
ECS (×10)	1 hr	Tranylcypromine + L-tryptophan	Head Twitch	No Change	Lebrecht & Nowack 1980
Amitriptyline Imipramine ×28	1 hr	5-MeODMT	Head Twitch	Block	Friedman & Dallob 1979
Fluoxetine Zimelidine Trazodone Amitriptyline ×14	2 hrs	Tranylcypromine + L-tryptophan	"Serotonin Syndrome"	No Change	Hwang & Van Woert 1980

improve the ability of rats to discriminate amphetamine or apomorphine from saline in a drug discrimination paradigm (White & Barrett 1981). Finally, 2 weeks' administration of desipramine increased rates of intracranial brain stimulation in areas of the midbrain that contain DA cells (Fibiger & Phillips 1981). The results of the last two studies would again point to an enhancement of DA transmission. On the other hand, Table 1 also shows that when testing occurs shortly after the last injection of an antidepressant drug, no increase in apomorphine's effect can be demonstrated (Maj et al. 1979b; Delini-Stula & Vassout 1979).

Table 2 shows that chronic antidepressant treatments also increase functional serotonin (5-HT) transmission, provided that testing occurs at least 12-24 hours after the last treatment. Repeated ECS enhances the ability of various 5-HT agonists to increase locomotor activity (Green et al. 1977, 1980; Costain et al. 1979; Evans et al. 1976) or behaviors associated with heightened 5-HT transmission such as head twitches (Lebrecht & Nowack 1980). Repeated administration of different antidepressant drugs also enhances the ability of 5-HT agonists to increase head twitches (Friedman & Dallob 1971; Fuxe et al. 1981), wet dog shakes (Moglinicka & Klimek 1979) or sleep time in young chicks (Jones 1980), although in some cases this enhancement may only occur with certain doses of 5-HT agonists with reversed effects at other doses (Fuxe et al. 1981). Again, the interval between testing and the last antidepressant treatment is critical, since comparable increases in the effects of 5-HT agonists are not seen at short intervals (Lebrecht & Nowack 1980; Friedman & Dallob 1979; Huang & VanWoert 1980).

Table 3 suggests that chronic antidepressant treatments may increase functional alpha-1 adrenergic transmission. However, the data here are less clear, since the pharmacological mechanisms underlying changes in these behaviors induced by the drugs that were used is

Table 3

Functional Changes in α_1-Adrenergic Transmission Based on Behavioral Studies

Treatment	Treatment Test Interval	Probe Drug	Behavior	Treatment Effect	Authors
Imipramine Amitriptyline Danitracen × 10	24-72 hrs	High-Dose Clonidine	Activity	Increase Activity in TCA-Treated Animals	Maj et al. 1979a
Amitriptyline Imipramine Desipramine Clomipramine Mianserin Danitracen Iprindole × 14	2 hrs	High-Dose Apomorphine	Aggression	Enhance	Maj et al. 1979b
Imipramine Mianserin Iprindole × 10	2 hrs	Very High-Dose Clonidine	Aggression	Enhance	Maj et al. 1980
ECS ×7	24 hrs	Reserpine + Apomorphine + Clonidine+	Activity	Enhance	Modigh 1975
Imipramine Amitryptyline ×21	20 hrs	Yohimbine or Clonidine	Cessation of Swimming in "Despair Test"	Yohimbine Potentiates Effects of TCAs Clonidine Blocks Effects of TCAs	Zebrowska-Lupina 1980

not well documented. Chronic antidepressant drugs or ECS increase the ability of high doses of clonidine to increase locomotor activity alone (Maj et al. 1979a) or in combination with reserpine plus apomorphine (Modigh 1975). Antidepressants also increase apomorphine or clonidine-induced aggression, which can be blocked by the alpha-1 antagonist phenoxybenzamine (Maj et al. 1979b, 1980). Clearly, these data are only suggestive for an enhancement of alpha-1 adrenergic transmission, but they assume greater interest in view of other findings. First, Tables 1 and 2 indicate that the enhancement by ECS of the ability of either DA or 5-HT agonists to increase locomotor activity can be blocked by prior norepinephrine (NE) depletion via administration of 6-OHDA (Green & Deakin 1980). Second, Table 3 shows that the therapeutic effect of chronic imipramine or amitriptyline in the swimming despair test is potentiated by the drug yohimbine and blocked by the drug clonidine (Zebrowska-Lupina 1980). Since these drugs increase and decrease NE transmission, respectively, the data support a role for NE in mediating the effects of these tricyclic antidepressant compounds in this test.

Finally, Table 4 indicates that chronic treatment with desipramine blunts the ability of a low dose of clonidine to decrease locomotor activity when testing occurs 48 hours after the last antidepressant treatment (Spyraki & Fibiger 1980) but not when testing occurs shortly after 7 days of imipramine (VonVoightlander et al. 1980). These data suggest that chronic desipramine may decrease functional sensitivity of alpha-2 receptors, although it is not known if this would occur if other antidepressant treatments were used as well.

Table 4

Functional Changes in α_2-Adrenergic Transmission Based on Behavioral Measures

Treatment	Treatment Test Interval	Probe Drug	Behavior	Treatment Effect	Authors
Desipramine × 15	48 hrs	Low-Dose Clonidine	Activity Decrease	Blunt	Spyraki & Fibiger 1980
Imipramine × 7	3.5 hrs	Clonidine	Activity Decrease	No Change	Von Voightlander et al. 1978

Table 5

Acoustic Startle as a Behavioral Test for Analyzing Functional Changes in Receptor Sensitivity Following Agonist Challenge

Receptor System	Agonist	Route	Dose Range	Effect on Startle
Norepinephrine				
Alpha-1	Phenylephrine	Intrathecal	6-50 μg	Increase
Alpha-2	Clonidine	Intraperitoneal	10-40 μg/kg	Decrease
Serotonin				
Forebrain-Inhibitory	Serotonin	Intraventricular	3-50 μg	Decrease
Spinal-Excitatory	Serotonin	Intrathecal	12-100 μg	Increase
	5-MeODMT	Intraperitoneal	0.5-4 mg/kg	Increase
Dopamine	Apomorphine	Intraperitoneal	0.2-3 mg/kg	Increase

Acoustic Startle as a Behavioral Test for Analyzing Functional Changes in Receptor Sensitivity Following Agonist Challenge

Over the last several years our laboratory has been investigating how various neurotransmitter systems modulate the acoustic startle reflex. Acoustic startle is a brainstem reflex that has a latency of only 8 msec in the rat measured electromyographically. Startle is sensitive to a variety of environmental variables and shows habituation, sensitization, pre-pulse inhibition, and modification by prior classical conditioning (cf., Davis 1980). Recently it has been determined that the neural circuit that mediates startle may consist of the ventral cochlear nucleus, the dorsal and ventral nuclei of the lateral lemniscus, a ventral region of the pontine reticular formation, and lower motor neurons in the spinal cord (Davis et al., in press). The simplicity of the reflex allows one to determine, therefore, where in the central nervous system various neurotransmitters might act in its modulation.

Table 5 summarizes specific data to indicate that startle could be used as a single test system to analyze changes in the sensitivity of NE, 5-HT, and DA systems following antidepressant treatments. Startle is increased via stimulation of alpha-1 receptors in the spinal cord. Thus, direct infusion of NE itself or the alpha-1 agonist phenylephrine into the subarachnoid space (intrathecal administration) increases acoustic startle. This effect is blocked by the alpha-1 antagonist WB-4101, but not by the 5-HT antagonist cyproheptadine or the DA antagonist haloperidol or the beta-adrenergic antagonist propranolol (Astrachan & Davis 1981). Moreover, the phenylephrine effect can be enhanced by prior selective depletion of spinal NE following intrathecal administration of 6-OHDA (Astrachan, Davis, and Gallager, in preparation).

In contrast, acoustic startle is markedly depressed by the alpha-2 adrenergic agonist clonidine (Davis et al. 1977). This effect can be blocked by the alpha-2 antagonists piperoxane or yohimbine (Davis et al. 1977; Davis & Astrachan 1981).

Serotonin has opposite effects on startle depending on whether it acts in the forebrain or spinal cord. Direct infusion of 5-HT itself or 5-HT agonists intraventricularly depresses startle (Davis et al. 1980b; Commissaris & Davis 1982). On the other hand, direct infusion of 5-HT or 5-HT agonists into the spinal subarachnoid space increases acoustic startle (Davis et al. 1980a, b).

Finally, startle is increased by DA, since systemic administration of the DA agonists apomorphine or *d*-amphetamine increases acoustic startle (Davis & Aghajanian 1976; Davis et al. 1977). These effects can be blocked by the DA antagonists haloperidol or pimozide (Davis & Aghajanian 1976; Kehne & Sorenson 1978).

Changes in Functional Alpha-1 and Alpha-2 Adrenergic Receptor Sensitivity Following Tricyclic Antidepressant Drugs

Studies are now underway to use startle as a test system to determine changes in functional receptor sensitivity following antidepressant treatments. Thus far the work has focused on changes in functional NE transmission, since other behavioral data suggest that such effects on NE might interact with changes in 5-HT and DA transmission following chronic antidepressant treatments, as well as being important by themselves.

Changes in Alpha-2 Sensitivity

In the first experiment the effects of three tricyclic antidepressant (TCA) drugs on functional changes in alpha-2 adrenergic transmission were assessed by measuring the degree to which clonidine would depress startle following chronic treatment with antidepressants or saline (Davis & Menkes, in press). Four groups of 20 rats each were used. Animals in each group were injected intraperitoneally (i.p.) once a day for 14 days with saline, desipramine HCl (DMI, 10 mg/kg, USV Pharmaceuticals), amitriptyline (AMI, 10 mg/kg, Merck Sharpe and Dohme), or iprindole (IPR, 5 mg/kg, Wyeth Labs). All drug weights are based on the weight of the salt. Twenty-four hours after the last injection five rats in each group were injected with saline and five with clonidine (20 µg/kg). Immediately afterward they were placed into the startle test cages described elsewhere

(Davis et al. 1980b) and presented with a total of 90 noise bursts (110 db) at a 20-second interburst interval, creating a 30-minute test session. Twenty-four hours later the same procedure was repeated except rats previously given saline were now given clonidine (20 μg/kg) and vice versa. The other rats in each of the groups were tested identically with the exception that the dose of clonidine was 40 μg/kg.

To determine if any of the tricyclics might alter the effect of clonidine on startle after acute administration, an additional 4 groups of 10 rats each were given saline, 10 mg/kg DMI, 10 mg/kg AMI, or 5 mg/kg IPR. One hour later, half the rats in each group were injected with saline and half with clonidine (40 μg/kg) and then tested for startle over the next 30 minutes as described earlier. Twenty-four hours later the same tricyclic treatments were repeated, and 1 hour later the rats were given clonidine or saline. In this case, however, rats previously given clonidine were given saline and vice versa.

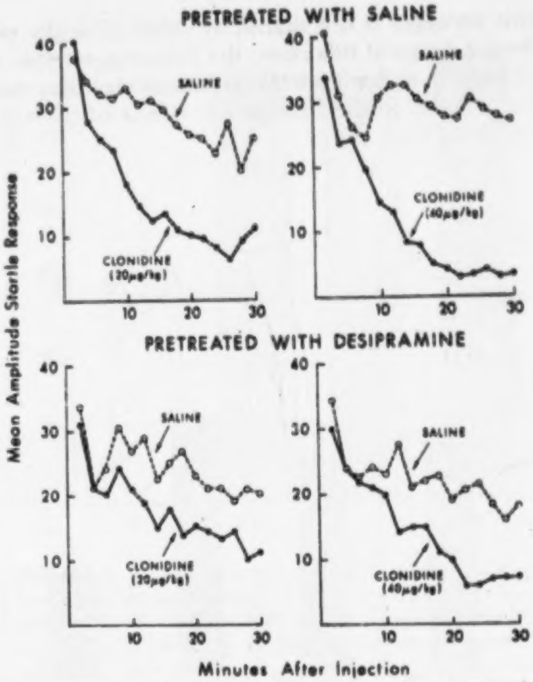


FIGURE 1. Mean amplitude startle response at various times after injection of saline or 20 or 40 μg/kg clonidine in rats pretreated for 14 days with either saline (top) or 10 mg/kg desipramine (bottom).

Figure 1 illustrates that chronic DMI treatment attenuated the depressant effect of either 20 or 40 μg/kg clonidine on acoustic startle. Thus, in the saline-treated rats, clonidine markedly depressed startle within about 10 minutes after injection after either 20 or 40 μg/kg, $t = 7.09$, $p < .001$ and $t = 10.19$, $p < .001$, respectively. Clonidine also depressed startle in the rats treated chronically with DMI, $t = 4.27$, $p < .001$; $t = 6.83$, $p < .001$ for doses of 20 or 40 μg/kg, respectively. However, the magnitude of the depressant effect was less in the DMI-treated rats at both of the test doses of clonidine. For example, from 10 to 20 minutes after injection clonidine depressed startle in rats pretreated with saline by about 55 percent after 20 μg/kg and about 75 percent after 40 μg/kg. In contrast, the same doses of clonidine depressed startle by about 30 and 45 percent in the rats pretreated with DMI, and the difference in the magnitude of depression between saline and DMI pretreated rats was significant at each test dose of clonidine, $t = 2.79$, $p < .01$ for 20 μg/kg; $t = 3.29$, $p < .01$ for 40 μg/kg. The attenuated response to clonidine after DMI occurred in both replications and was significant in each case.

On the other hand, chronic treatment with either AMI or IPR did not alter the depressant effect of clonidine on acoustic startle (Figure 2). After these tricyclics, the percentage changes in startle after either 20 or 40 μg/kg of clonidine were essentially identical to that after saline and significantly greater than the percent changes after DMI ($p < .01$ at each dose when DMI was compared with AMI or DMI was compared with IPR). Finally, none of the tricyclics significantly altered baseline startle levels after chronic administration.

In contrast to chronic DMI treatment, acute treatment with DMI or the other tricyclics did not significantly affect the response to 40 μg/kg clonidine relative to that observed after acute saline (percentage decreases = 80.0, 94.3, 88.9, and 77.4 after IPR, AMI, DMI, or SAL, respectively). Finally, none of the tricyclics significantly altered baseline startle levels at these doses (baseline means = 32.4, 29.8, 30.7, or 32.4 for IPR, AMI, DMI, and SAL, respectively).

These results indicate that chronic but not acute treatment with DMI attenuates the depressant effect of clonidine on acoustic startle. Since this property is not shared by other clinically effective drugs of this class, the data suggest that a change in alpha-2 adrenergic sensitivity may not be relevant to the therapeutic effects of tricyclic antidepressant drugs.

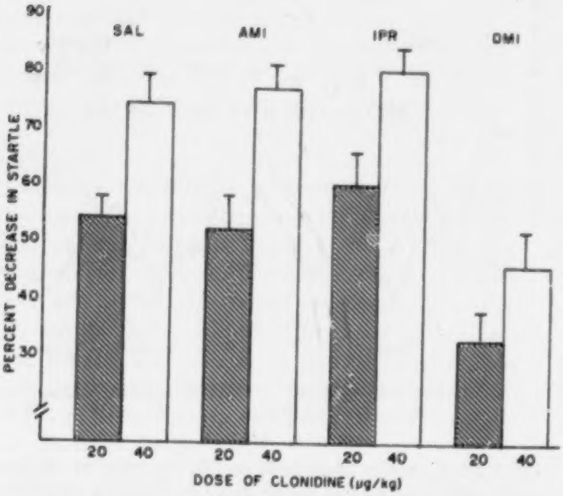


FIGURE 2. Percent decrease in startle after injection of either 20 or 40 µg/kg clonidine in rats pretreated for 14 days with either saline, amitriptyline (10 mg/kg), iprindole (5 mg/kg), or desipramine (10 mg/kg). Baseline means were unchanged by the chronic treatments (29.6, 28.8, 33.0, and 23.9 for the chronic saline, AMI, IPR, and DMI groups, respectively. *f* = 0.24, N.S.).

The next experiment sought to determine how chronic administration of tricyclic antidepressant drugs would alter alpha-1 adrenergic transmission (Menkes, Kehne, Gallager, Aghajanian, & Davis, in preparation). The same rats used for the study on clonidine were placed back on their respective saline or tricyclic drugs for another 7 days. The rats were then implanted with intrathecal catheters (Davis et al. 1980b) and 1 day later tested for startle by presenting noise bursts once every 20 seconds for 15 minutes. Following this pre-test, the rats were removed from the test cages and infused intrathecally with 25 µg of the alpha-1 adrenergic agonist phenylephrine in a volume of 10 µl at a rate of about 5 µl/minute. The rats were than tested for startle over the next 30 minutes by presenting 90 noise bursts every 20 seconds.

Figure 3 shows the mean amplitude startle prior to and following the infusion of phenylephrine in rats treated chronically for 21 days with either saline or amitriptyline. At this dose, phenylephrine had only a slight excitatory effect in rats chronically treated with saline. However, the magnitude of this effect was considerably larger in rats chronically treated with amitriptyline ($t = 2.35$, $p < .05$). Figure 4 summarizes data obtained after chronic treatment with other drugs. Consistent with the desipramine results, amitriptyline and iprindole also enhanced the effect of phenylephrine. Other experiments showed that this enhanced response to phenylephrine did not occur when testing was carried out 1 hour after a single dose of the tricyclics, a time when brain levels of the tricyclics are known to be higher than 24 hours after a chronic sequence (Vetulani et al. 1976).

Taken together, these data suggest that chronic but not acute treatment with three clinically effective antidepressant drugs increased functional alpha-1 adrenergic transmission. To determine if the enhanced behavioral response to phenylephrine might reflect an increase in the number of alpha-1 adrenergic receptor sites, the

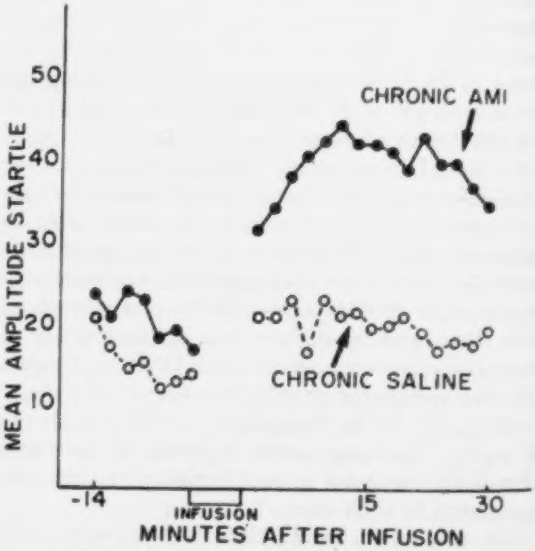


FIGURE 3. Change in startle amplitude before and after intrathecal administration of 25 µg phenylephrine in rats pretreated for 21 days with either saline or amitriptyline.

lumbar portions of the spinal cords from these rats were removed and prepared for 3H-prazosin binding according to the methods of Greengrass and Bremmer (1979). For comparison, rats pretreated 1 week earlier with intrathecal 6-OHDA were also included, since this treatment produces an enhancement of phenylephrine excitation or startle comparable in magnitude to that seen after 3 weeks' treatment of the antidepressant drugs. Figure 5 shows that prior 6-OHDA treatment increased the number of ^{3}H-prazosin binding sites, whereas pretreatment with the antidepressant drugs did not. Other experiments indicated that ^{3}H-prazosin also did not change in rats that were simply pretreated for 21 days with these same tricyclic compounds without getting the clonidine or phenylephrine tests on startle.

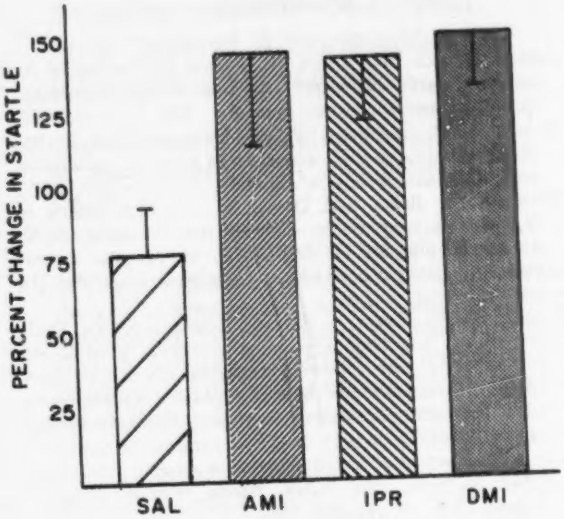


FIGURE 4. Percent change in startle from 0-30 min after intrathecal administration of 25 μg phenylephrine in rats pretreated for 21 days with either saline, amitriptyline (10 mg/kg), iprindole (5 mg/kg), or desipramine (10 mg/kg).

Discussion

To date, the available literature indicates that chronic compared to acute antidepressant treatments produce a pattern of functional changes in receptor sensitivity that includes an enhancement of central DA, 5-HT, and alpha-1 adrenergic sensitivity. These behavioral effects are consistent with enhanced electrophysiological responses to local application of 5-HT, NE, or DA in selected brain regions (cf., Charney et al. 1981). In contrast, changes in functional receptor sensitivity have not correlated with traditional receptor binding techniques, even when these have been done on parts of the nervous system that are known to mediate the behavioral effect (e.g., the present study). Future research should focus on mechanisms that might be common to 5-HT, DA, and NE at a level of neural transmission other than the receptor.

Acknowledgments: The work on chronic antidepressants was done in collaboration with Dr. Dorothy Gallager, John Kehne, and David Menkes. Our sincere thanks are extended to Lee Schlesinger for running the startle tests.

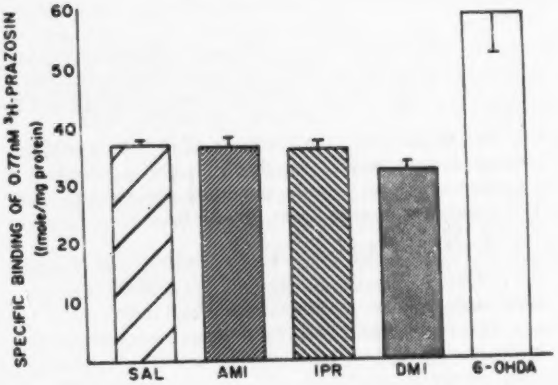


FIGURE 5. Specific binding of ^{3}H-prazosin (0.77 nM) to rat lumbar spinal cord membranes from rats tested for acoustic startle. Animals were killed 3 days after intrathecal injection of phenylephrine and 24 hours after their final chronic antidepressant or saline injection. Non-specific binding was determined by the addition of 1 μM WB-4101. Binding in individual animals was determined by quadruplicate determinations and each value plotted is the mean ± S.E.M. of at least eight treated animals.

References

Astrachan, D.I., and Davis, M. Spinal modulation of the acoustic startle response: The role of norepinephrine, serotonin, and dopamine. *Brain Res.*, 206: 223-228, 1981.

Charney, D.S., Menkes, D.B., and Heninger, G.R. Receptor sensitivity and the mechanism of action of antidepressant treatment. *Arch. Gen. Psychiatry*, 38:1160-1180, 1981.

Commissaris, R.L., and Davis, M. Opposite effects of N,N-dimethyltryptamine (DMT) and 5-methoxy-N,N-dimethyltryptamine (5-MeODMT) on acoustic startle: Spinal vs. brain sites of action. *Neurosci. Biobehav. Rev.* (In press)

Costain, D.W., Green, A.R., and Grahame-Smith, D.G. Enhanced 5-hydroxytryptamine-mediated behavioural responses in rats following repeated electroconvulsive shock: Relevance to the mechanism of the antidepressant effect of electroconvulsive therapy. *Psychopharmacology (Berlin)*, 61:1979.

Davis, M. Neurochemical modulation of sensory-motor reactivity: acoustic and tactile startle reflexes. *Neurosci. Biobehav. Rev.*, 4: 241-263, 1980.

Davis, M., and Aghajanian, G.K. Effects of apomorphine and haloperidol on the acoustic startle response in rats. *Psychopharmacology (Berlin)*, 47: 217-223, 1976.

Davis, M., and Astrachan, D.I. Spinal modulation of acoustic startle: Opposite effects of clonidine and *d*-amphetamine. *Psychopharmacology (Berlin)*, 75: 219-225, 1981.

Davis, M., Astrachan, D.I., Gendelman, P.M., and Gendelman, D.S. 5-Methoxy-N,N-dimethyltryptamine: Spinal cord and brainstem mediation of excitatory effects on acoustic startle. *Psychopharmacology (Berlin)*, 70:123-130, 1980a.

Davis, M., Astrachan, D.I., and Kass, E. Excitatory and inhibitory effects of serotonin on sensorimotor reactivity measured with acoustic startle. *Science*, 209: 521-523, 1980b.

Davis, M., Cedarbaum, J.M., Aghajanian, G.K., and Gendelman, D.S. Effects of clonidine on habituation and sensitization of acoustic startle in normal, decerebrate, and locus coeruleus lesioned rats. *Psychopharmacology (Berlin)*, 51:243-253, 1977.

Davis, M., Gendelman, D.S., Tischler, M.D., and Gendelman, P.M. A primary acoustic startle circuit: Lesion and stimulation studies. *J. Neurosci.* (In press)

Davis, M., and Menkes, D.B. Tricyclic antidepressants vary in decreasing alpha-2 adrenergic sensitivity: Assessment with clonidine inhibition of acoustic startle. *Br. J. Psychiatry.* (In press)

Davis, M., Svensson, T.H., and Aghajanian, G.K. Effects of *d*- and *l*-amphetamine on habituation and sensitization of the acoustic startle response in rats. *Psychopharmacologia (Berlin)*, 43:1-11, 1975.

Delini-Stula, A., and Vassout, A. Modulation of dopamine-mediated behavioral responses by antidepressants: Effects of single and repeated treatment. *Eur. J. Pharmacol.*, 58: 443-451, 1979.

Evans, J.P., Grahame-Smith, D.G., Green, A.R., and Tordoff, A.F.C. Electroconvulsive shock increases the behavioural responses of rats to brain 5-hydroxytryptamine accumulation and central nervous system stimulant drugs. *Br. J. Pharmacol.*, 56: 193-199, 1976.

Fibiger, H.C., and Phillips, A.G. Increased intracranial self-stimulation in rats after long-term administration of desipramine. *Science*, 214:683-684, 1981.

Friedman, E., and Dallob, A. Enhanced serotonin receptor activity after chronic treatment with imipramine or amitriptyline. *Commun. Psychopharmacol.*, 3:89-92, 1979.

Fuxe, K., Ogren, S.O., Agnati, L.F., Eneroth, P., Holm, A.C., and Andersson, K. Long-term treatment with zimelidine leads to a reduction in 5-hydroxytryptamine neurotransmission within the central nervous system of the mouse and rat. *Neurosci. Lett.*, 21:57-62, 1981.

Green, A.R., and Deakin, J.F.W. Brain noradrenaline depletion prevents ECS-induced enhancement of serotonin and dopamine-mediated behavior. *Nature*, 285: 232-233, 1980.

Green, A.R., Heal, D.J., and Grahame-Smith, D.G. Further observations on the effect of repeated electroconvulsive shock on the behavioural responses of rats produced by increases in the functional activity of brain 5-hydroxytryptamine and dopamine. *Psychopharmacology (Berlin)*, 52:195-200, 1977.

Greengrass, P., and Bremmer, R. Binding characteristics of ^{3}H-prazosin to rat brain α-adrenergic receptors. *Eur. J. Pharmacol.*, 55: 323-326, 1979.

Huang, E.C., and VanWoert, M.H. Acute versus chronic effects of serotonin uptake blockers on potentiation of the "serotonin syndrome." *Commun. Psychopharmacol.*, 4: 161-167, 1980.

Jones, R.S.G. Enhancement of 5-hydroxytryptamine induced behavioral effects following chronic administration of antidepressant drugs. *Psychopharmacology (Berlin)*, 69: 307-311, 1980.

Kehne, J.H., and Sorenson, C.A. The effects of pimozide and phenoxybenzamine pretreatments on amphetamine and apomorphine potentiation of the acoustic startle response in rats. *Psychopharmacology (Berlin)*, 58:137-144, 1978.

Klein, D.F., Gittelman, R., Quitkin, F., and Rifkin, A. *Diagnosis and Drug Treatment of Psychiatric Disorders: Adults and Children.* Baltimore: Williams and Wilkins Co., 1980.

Lebrecht, U., and Nowak, J.Z. Effect of single and repeated electroconvulsive shock on serotonergic system in rat brain. II. Behavioral studies. *Neuropharmacology*, 19:1055-1061, 1980b.

Maj. J., Mogilnicka, E., and Klimek, V. The effect of repeated administration of antidepressant drugs on the responsiveness of rats to catecholamine agonists. *J. Neural Trans.*, 44: 221-235, 1979a.

Maj, J., Mogilnicka, E., and Kordecka, A. Chronic treatment with antidepressant drugs: Potentiation of apomorphine-induced aggressive behavior in rats. *Neurosci. Lett.*, 13: 337-341, 1979b.

Maj, J., Mogilnicka, E., and Kordecka-Magiera, A. Effects of chronic administration of antidepressant drugs on aggressive behavior induced by clonidine in mice. *Pharmacol. Biochem. Behav.*, 13:153-154, 1980.

Modigh, K. Electroconvulsive shock and postsynaptic catecholamine effects: Increased psychomotor stimulant action of apomorphine and clonidine in reserpine pretreated mice by repeated ECS. *J. Neural Trans.*, 36: 19-32, 1975.

Mogilnicka, E., and Klimek, V. Mianserin, danitracen, and amitriptyline withdrawal increases the behavioural responses of rats to L-5-HTP. *J. Pharm. Pharmacol.*, 31: 704-705, 1979.

Oswald, I., Brezinova, V., and Dunleavy, D.L.F. On the slowness of action of tricyclic antidepressant drugs. *Br. J. Psychiatry*, 120: 673-677, 1972.

Serra, G., Argiolas, A., Fadda, F., Melis, M.R., and Gessa, G.L. Repeated electroconvulsive shock prevents the sedative effect of small doses of apomorphine. *Psychopharmacology (Berlin)*, 73: 194-196, 1981.

Serra, G., Argiolas, A., Klimek, V., Fadda, F., and Gessa, G.L. Chronic treatment with antidepressants prevents the inhibitory effect of small doses of apomorphine on dopamine synthesis and motor activity. *Life Sci.*, 25:415-424, 1979.

Spyraki, C., and Fibiger, H.C. Functional evidence for subsensitivity of noradrenergic α_2-receptors after chronic desipramine treatment. *Life Sci.*, 27: 1863-1867, 1980.

Vetulani, J., Stawarz, R.J., Dingell, J.V., and Sulser, F. A possible common mechanism of action of antidepressant treatments. *Naunyn-Schmied. Arch. Pharmacol.*, 293: 109-114, 1976.

VonVoigtlander, P.F., Triezenberg, H.J., and Losey, E.G. Interactions between clonidine and antidepressant drugs: A method for identifying antidepressant-like agents. *Neuropharmacology*, 17:375-381, 1978.

White, D.K., and Barrett, R.J. The effects of electroconvulsive shock on the discriminative stimulus properties of *d*-amphetamine and apomorphine: Evidence for dopamine receptor alteration subsequent to ECS. *Psychopharmacology (Berlin)*, 73: 211-214, 1981.

Zebrowska-Lupina, I. Presynaptic α-adrenoceptors and the action of tricyclic antidepressant drugs in behavioural despair in rats. *Psychopharmacology (Berlin)*, 71: 169-172, 1980.

Antidepressant Treatment and Central Adrenergic and Histamine Receptors

Ghanshyam N. Pandey, Ph.D.,[1] P. Sudershan, Ph.D.[1] and John M. Davis, M.D.[1]

The presumed mode of action of antidepressant drugs has been related to their ability to increase postsynaptic concentrations of neurotransmitters such as norepinephrine (NE) or serotonin, either by inhibiting the uptake of such neurotransmitters by inhibiting their metabolism, or by causing increased release. Thus tricyclic antidepressants, like imipramine (IMI) and amitriptyline (AMI) and their metabolites inhibit amine uptake. Monoamine oxidase inhibitors (MAOI), like phenelzine (PHZ) and parnate (PAR), inhibit amine metabolism, and treatment with electroconvulsive therapy (ECT) causes increased release of such amines. The antidepressant drugs thus increase the postsynaptic concentrations of amines and potentiate transmitter function. This presumed mode of action of antidepressant drugs does not explain, however, the delayed onset of clinical effects after the initiation of antidepressant therapy and the antidepressant properties of such drugs as iprindole and Wellbatrin (WB) which do not alter amine uptake or metabolism.

The effect of treatment with antidepressant drugs on beta adrenergic receptor sensitivity has been widely studied, and it has been reported that most antidepressant drugs cause down regulation of the NE-coupled adenylate cyclase system (Vetulani et al. 1976) and beta adrenergic receptor sensitivity (Frazer et al. 1974) after chronic treatment. These effects have been related to the antidepressant properties of these drugs.

In order to further examine the role of beta adrenergic receptors in the mode of action of antidepressant drugs, the authors have studied the effect of treatment with some antidepressant drugs and neuroleptics on ^{3}H-dihydroalprenolol (^{3}H-DHA) binding in rat brain. Since it has been reported that certain antidepressant drugs block histamine receptors, the authors have also studied the effect of antidepressant treatment on histamine receptor mediated cyclic AMP accumulation in guinea pig cortex.

---

[1] Illinois State Psychiatric Institute and University of Illinois College of Medicine, Chicago, IL 60612.

Antidepressant Treatment and Beta Adrenergic Receptors

It was first reported by Banerjee et al. (1977) that treatment with antidepressants caused a decrease in beta adrenergic receptor binding sites in rat brain as determined by ^{3}H-DHA binding. The authors in the current investigation examined the effect of chronic treatment with several other antidepressants on beta adrenergic receptor sensitivity in rat cortex by studying the binding of ligand ^{3}H-DHA. The experimental conditions and the results are listed in the Table. It was observed that treatment with desipramine (DMI) caused a significant reduction of the maximum number of ^{3}H-DHA binding sites (receptor density). These results are similar to those reported by Banerjee et al. (1977). Chronic treatment with ECT also caused a significant reduction in the maximum number of ^{3}H-DHA binding sites as previously reported by the authors (Pandey et al. 1979).

The authors examined the specificity of the effects of various antidepressant drugs on ^{3}H-DHA binding to the rat brain by studying the effect of some other classes of antidepressants such as IMI, the MAO inhibitor PHZ, the antidepressant WB, lithium (Li^+), and the neuroleptics, chlorpromazine (CPZ) and haloperidol (HP) (Pandey & Davis 1981). The antidepressant drugs IMI, PHZ, and WB, but not Li^+, caused a significant reduction in the maximum number of ^{3}H-DHA binding sites. Treatment with Li^+ produced a small reduction (14%) in ^{3}H-DHA binding, but this was not significantly different from the binding in control rats ($p < 0.07$, *t*-test, two-tailed just below level of significance).

To examine whether this reduction in receptor density caused by antidepressant treatment is related to a change in the affinity of ^{3}H-DHA binding, the authors calculated the apparent dissociation constant (K_d) of ^{3}H-DHA binding, as summarized in the Table. There was no significant change in the K_d of ^{3}H-DHA binding in

Table

Effect of Chronic Treatment with Antidepressants on Receptor Density (Maximum ^{3}H-DHA Bound) and Apparent Dissociation (^{3}H-DHA Binding) in Rat Brain

Treatment	Receptor Density ^{3}H-DHA Bound, (fmole mg Protein^{-1})	Percent of Control	*p* Values as Compared With Control	Dissociation Constant (nM)
Control (1)	119 ± 8.8	100		1.06
Desipramine	84 ± 3.5	71	<0.001	1.19
Imipramine	66 ± 9.0	56	<0.001	0.90
ECT	87 ± 3.5	73	<0.001	1.14
Phenelzine	87 ± 4.6	73	<0.001	1.19
Control (2)	—	100	—	0.90
Lithium	—	86	<0.07	0.97
Wellbatrin	—	74	<0.05	1.06
Cocaine	—	97	NS	
Haloperidol	—	97	NS	
Chlorpromazine	—	88	NS	

Groups of male Sprague-Dawley rats (100-150 g) were given one of the following treatments for 12-14 days: Desipramine (10 mg/kg), imipramine (20 mg/kg), phenelzine (10 mg/kg), WB (60 mg/kg), cocaine (10 mg/kg), haloperidol (5 mg/kg), or chlorpromazine (10 mg/kg) were administered once daily b.i.p. injection and lithium chloride (4 m Eq/kg) twice daily. Control rats received normal saline ECT (75 MA for 1 sec) was administered through transcorneal electrodes once daily for 12 days and controls were treated similarly but did not receive the shock. The rats were killed 1 hr after the last treatment, and the cortices were removed, homogenized in 50 volumes (w/v) of Tris buffer (0.05 M, pH 7.4), and spun at 49,000 g for 10 min. This process was repeated, and the pellet was finally suspended in Tris buffer. Binding of ^{3}H-DHA was carried out in triplicate by incubation of an aliquot of the suspension (0.3-0.5 mg protein) with ^{3}H-DHA at three concentrations (between 0.4 and 4 nM) in Tris buffer in a final volume of 1 ml, with or without 1 μM (−) propranolol, at 23 °C for 15 min. ^{3}H-DHA bound to the memurane was separated by filtration through a Whatman (GF/F) filter and washed three times with 4 ml buffer. The filter was placed in a BBS cocktail and counted in a Nuclear Chicago scintillation spectrometer. Specific binding is defined as the difference between total binding and the binding observed in the presence of 1 μM (−) propranolol. Receptor density and K_d values were calculated by Scatchard analysis: *p* values were obtained by paired *t*-test (two-tail). Each group of treatment consisted of 6-8 rats.

animals streated with antidepressants as compared to the control group, indicating that a reduction in the maximum number of ^{3}H-DHA binding sites is not attributable to a change in the affinity of these binding sites.

In order to examine if a decrease in ^{3}H-DHA binding is specific to treatment with antidepressant drugs, the authors examined the effect of treatment with neuroleptic drugs HP and CPZ and the psychomotor stimulant cocaine which, like tricyclic antidepressant drugs, is a potent inhibitor of amine uptake. Neither treatment with HP and CPZ nor with cocaine caused any significant changes in ^{3}H-DHA binding as shown in the Table. These results thus indicated that antidepressant drugs may share a common property of reducing beta adrenergic receptor sensitivity after chronic treatment.

Antidepressant Treatment and Histamine Receptors

Treatment with antidepressant drugs causes alterations in several of the monoamine receptors. It was reported by Green and Mayaani (1977) and Kanof and Greengard (1978) that antidepressant drugs are potent blockers of histamine receptors in the brain under *in vitro* conditions. In order to examine if treatment with antidepressant drugs causes changes in histamine receptor sensitivity, the authors studied the effects of treatment with antidepressant drugs on histamine receptor mediated cyclic AMP accumulation in guinea pig cortex.

Groups of male guinea pigs were injected intraperitoneally (i.p.) with the drugs as indicated (Figure 1) or with normal saline either once daily for 15 days for chronic studies or once for acute studies. The animals were then sacrificed either 1 hour or 24 hours after the last treatment. Histamine-stimulated accumulation of ^{3}H-cyclic AMP in slices of guinea pig cortex that had been prelabelled with ^{3}H-adenine was used as an index of adenylate cyclase-coupled histamine receptor sensitivity by the procedure described by Pandey et al. (1982).

The effects of chronic treatment (15 days) with antidepressant drugs on histamine-stimulated accumulation of ^{3}H-cyclic AMP in the guinea pig cortex obtained when the animals were killed 1 hour after the last injection are shown in Figure 1. For the purpose of graphical display, histamine stimulated ^{3}H-cyclic AMP accumulation in treated animals has been expressed as percent of ^{3}H-cyclic AMP accumulation of control animals. The differences between control and treated animals were not significant in the basal accumulation of ^{3}H-cyclic AMP (without histamine), although it tended to be lower in treated animals. Histamine (10^{-5}M, 10^{-4})-stimulated accumulation of ^{3}H-cyclic AMP in the cortical slices obtained from guinea pigs that were chronically treated with AMI, DMI, or PHZ was significantly lower than that in the control animals. However, histamine-stimulated accumulation of ^{3}H-cyclic AMP in the slices obtained from guinea pigs treated with CPZ, which has been shown to be a potent blocker of histamine H_2 receptors *in vitro* (Kanof & Greengard 1978), was not significantly different from that in the control animals. Similar results

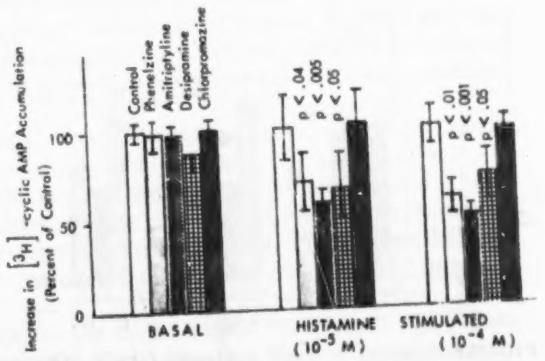


FIGURE 1. Effect of chronic treatment with antidepressants on ^{3}H-cyclic AMP accumulation in cortical slices obtained from guinea pigs sacrificed 1 hour after last injection. Groups of guinea pigs ($N = 7$ in each group) were injected i.p. with amitriptyline (8 mg/kg), phenelzine (15 mg/kg), desipramine (10 mg/kg), chlorpromazine (10 mg/kg), or normal saline (equal volume once daily for 15 days). One hour after the last treatment the animals were killed, and the cerebral cortex was immediately removed from the brain. Accumulation of ^{3}H-cyclic AMP in the absence (basal) or presence of histamine was then determined for each animal. In each set of experiments, treated guinea pigs were paired with control giunea pigs. Since the experiments were conducted in different sets, the results for treated animals have been expressed as percent of ^{3}H-cyclic AMP accumulation relative to controls. The data were analyzed by a *t*-test for two independent groups; *p* values (two-tailed) expressed above are those compared to control animals.

were obtained when animals treated for 15 days were sacrificed 24 hours after the last treatment, thus indicating that the effects persist at least up to 24 hours after the termination of the treatment as reported earlier (Pandey et al. 1982).

For acute studies, animals were given single administration of the drugs as indicated and were sacrificed 1 hour after treatment for cyclic AMP accumulation studies. The basal accumulation of ^{3}H-cyclic AMP in the slices obtained from guinea pigs treated acutely with antidepressants was similar to that in control animals, as shown in Figure 2. The accumulation of ^{3}H-cyclic AMP in the presence of histamine (10^{-5}M, 10^{-4}M) was significantly lower in the slices obtained from the animals acutely treated with AMI and DMI, but not in animals treated with PHZ, indicating that the effect of acute treatment with PHZ differs form its effect under chronic conditions.

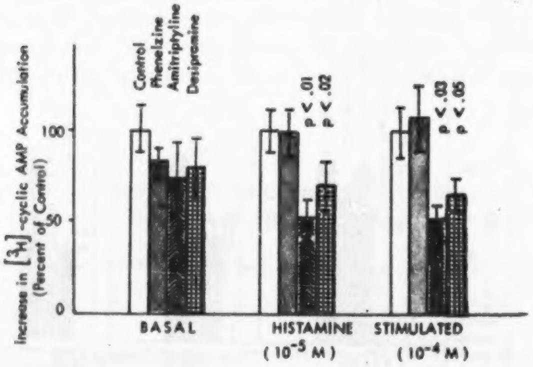


FIGURE 2. Effect of acute treatment (single injection) with antidepressants on ^{3}H-cyclic AMP accumulation in guinea pig cortical slices.

These studies thus indicate that treatment with antidepressant drugs causes a decrease in histamine receptor response in guinea pig cortex. The decrease observed after acute treatment with tricyclic antidepressants may be related to the histamine receptor-blocking properties of these drugs. The effects observed after chronic treatment appears to be related to adaptive changes in the histamine receptor-adenylate cyclase system because PHZ, which is a weak inhibitor of histamine receptors *in vitro*, produces a decrease in histamine-stimulated ^{3}H-cyclic AMP accumulation after chronic but not acute treatment. It therefore appears that at least two different mechanisms may be associated in decreasing histamine sensitive accumulation of ^{3}H-cyclic AMP accumulation in guinea pig cortex.

In summary, the results reported in this paper indicate that chronic treatment with antidepressant drugs causes a decrease in beta adrenergic receptor sensitivity in rat brain and histamine receptor mediated cyclic AMP accumulation in guinea pig cortex. Whereas the role of the histamine receptor in the mode of action of antidepressant drugs remains unclear, the results reported by the authors and other groups of investigators indicate a close relationship between changes in central beta adrenergic receptor sensitivity and antidepressant effects of these drugs. Further work is obviously needed for a better understanding of the molecular mechanisms associated with the mode of action of antidepressant drugs.

References

Banerjee, S.P., Kung, L.S., Riggi, S.J., and Chanda, S.K. Development of beta-adrenergic receptor subsensitivity by antidepressants. *Nature*, 268:455-456, 1977.

Frazer, A., Pandey, G., Mendels, J., Neeley, S., Kane, M., and Hess, M.E. The effect of tri-iodothyronine in combination with imipramine on ^{3}H-cyclic AMP production in slices of rat cerebral cortex. *Neuropharmacology*, 13:1131-1140, 1974.

Green, J.P., and Maayani, S. Tricyclic antidepressant drugs block histamine H_2 receptor in brain. *Nature*, 269:163-169, 1977.

Kanof, P.D., and Greengard, P. Brain histamine receptors as targets for antidepressant drugs. *Nature*, 272:329-333, 1978.

Pandey, G.N., and Davis, J.M. Treatment with antidepressants, sensitivity of beta-adrenergic receptors and affective illness. In: Usdin, E., Bunney, W.E., and Davis, J.M. (eds.), *Neuroreceptors — Basic and Clinical Aspects*. New York: John Wiley & Sons, Ltd., 1981, pp. 99-120.

Pandey, G.N., Heinze, W.J., Brown, B.D., and Davis, J.M. Electroconvulsive shock treatment decreases beta-adrenergic receptor sensitivity in rat brain. *Nature*, 280:234-235, 1979.

Pandey, G.N., Krueger, A., Sudershan, P., and Davis, J.M. Treatment with antidepressants and histamine receptor mediated ^{3}H-cyclic AMP formation in guinea pig cortex. *Life Sci.*, 30:921-927, 1982.

Vetulani, J., Stawarz, R.J., Dingell, J.V., and Sulser, F. A possible common mechanism of action of antidepressant treatment. *Naunyn-Schmiedeberg's Arch. Pharmacol.*, 293:109-114, 1976.

Assessment of Adrenergic and Serotonergic Receptor Function: Implications for the Etiology and Treatment of Depression[1]

Dennis S. Charney, M.D.,[2] and George R. Heninger, M.D.[2]

Recent studies conducted in laboratory animals have provided the basis for several hypotheses relating alterations in adrenergic and serotonergic receptor function to the etiology and treatment of affective illness. Long-term antidepressant (AD) treatment has been shown to decrease the functional sensitivity of alpha-2 and beta adrenergic receptors and to increase the functional sensitivity of alpha-1 adrenergic receptors and serotonergic (5-HT) receptors. (For review, *see* Charney et al. 1981b).

Although it is not possible in human studies to utilize the invasive electrophysiologic and pharmacologic strategies used in animals to develop such hypotheses, several useful methods to assess the clinical relevance of serotonin and noradrenergic receptor function have recently been developed. One method is to design and determine the efficacy of treatment approaches which, based on preclinical investigations, have specific effects on adrenergic and serotonergic receptor function. Another is to use "receptor challenge" paradigms to assess the physiological, biochemical, and behavioral effects of centrally active neurotransmitter receptor agonists and antagonists in healthy controls and depressed patients before and during long-term AD treatment. Recent data obtained from a series of investigations indicate that use of these strategies allows testing of specific receptor hypotheses developed from laboratory animal studies and facilitates the development of improved treatments for patients refractory to standard treatments.

Receptor Challenge Paradigms

Presynaptic Alpha-2 Adrenergic Receptors

This receptor is located both presynaptically and postsynaptically. There is considerable evidence that the presynaptic alpha-2 adrenergic receptor plays a major role in the modulation of central noradrenergic activity by regulating the release of norepinephrine (NE) through a negative feedback mechanism (Cedarbaum & Aghaajanian 1977; Langer et al. 1980; Nyback et al. 1975). Activation of this receptor by alpha-2 adrenergic receptor agonists, such as clonidine, decreases NE impulse flow and turnover (Anden et al. 1976; Cedarbaum & Aghajanian 1977; Svensson & Usdin 1978). Conversely, the alpha-2 adrenergic antagonists, yohimbine and piperoxane, increase NE impulse flow and turnover (Cedarbaum & Aghajanian 1976; Scatton et al. 1980). Consequently, measurement of the effect of alpha-2 adrenergic receptor agonists and antagonists on NE turnover may provide an index of presynaptic alpha-2 adrenergic receptor sensitivity.

The effects of clonidine on behavior, blood pressure, and plasma free 3-methoxy-4-hydroxyphenylethylene glycol (MHPG) in healthy subjects have recently been determined in two separate investigations. Plasma-free MHPG was used as an index of central NE turnover because it has been shown to reflect brain MHPG, the major metabolite of brain NE (Maas et al. 1979; Elsworth et al. 1982). In the first study of 11 male subjects (mean age 28 yrs., range 21-34), oral clonidine (5 μg/kg) produced a 22 percent decrease in plasma-free MHPG 3½, 4, and 5 hours after the dose in comparison to placebo ($p < .01$) (Leckman et al. 1980, unpublished data). In a second sample of 6 male and 6 female subjects (mean age 40 yrs., range 27-57), clonidine (5 μg/kg) produced a 19 percent decrease in mean plasma-free MHPG 3-½, 4, and 5 hours following the dose in comparison to placebo ($p < .05$) (Charney et al. 1982b). In both studies, clonidine also significantly decreased blood pressure and produced behavioral sedation. Thus, the results of the second healthy subject investigation replicated the findings of the original study and supported the reliability of this test as a possible measure of the presynaptic alpha-2

---

[1] The studies reported in this paper were supported in part by USPHS Grants MH-18949, MH-14276, MH-30929, and MH-25642 and by the State of Connecticut.

[2] Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, CT 06508.

Address correspondence to: Dr. Dennis S. Charney, M.D., Department of Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508.

adrenergic receptor system.

A study assessing the effects of oral yohimbine on plasma-free MHPG, cardiovascular function, and behavior in eight healthy subjects has recently been completed. Administration of three doses of oral yohimbine (10, 15, and 20 mg) produced significant increases in mean plasma-free MHPG levels of 33, 33, and 66 percent, respectively, 3 and 4 hours after the dose compared to placebo (Charney et al. 1982a). The 15 and 20 mg yohimbine doses induced significant but clinically safe increases in systolic blood pressure and autonomic symptoms such as piloerection and rhinorrhea. The 20 mg yohimbine dose produced a modest but significant increase in self-rated anxiety. Taken together, the results of these studies indicated that determination of the effects of clonidine and yohimbine on plasma-free MHPG may be a useful method to examine the functional sensitivity of presynaptic alpha-2 adrenergic receptors in depressed patients.

The ability of antidepressant drugs, such as desipramine (DMI), to induce a subsensitivity of the alpha-2 adrenergic receptor may have important implications regarding the mechanism of action of antidepressant drugs and the catecholamine hypothesis of depression (Charney et al. 1981b). To determine whether desipramine induces a subsensitivity in alpha-2 adrenergic receptor sensitivity in depressed patients, the effect of clonidine and clonidine placebo on plasma MHPG in 10 depressed patients was evaluated before and during long-term DMI treatment (Charney et al. 1981a). Long-term DMI treatment significantly attenuated the effects of clonidine on plasma-free MHPG. Prior to DMI treatment, clonidine decreased plasma-free MHPG by 25 percent compared to placebo ($p < .05$). During desipramine treatment, the clonidine-induced decrease in MHPG was only 11 percent and was significantly less than the comparable decrease in MHPG levels observed prior to treatment ($p < .05$). DMI treatment also produced a 36 percent decrease in baseline plasma-free MHPG compared to pretreatment levels ($p < .01$). In the 10 patients studied, there was no association among therapeutic response, pretreatment MHPG level, and clonidine effects on MHPG and blood pressure either prior to or during DMI treatment.

The findings of the study are consistent with the results of previous animal studies that central alpha-2 receptor subsensitivity develops with long-term DMI treatment. However, what is left unanswered and requires further investigation is whether DMI's ability to reduce alpha-2 adrenergic receptor sensitivity is a necessary condition for antidepressant efficacy. The decreased plasma MHPG level during DMI treatment suggests that the reduced NE turnover in the depressed patients studied may reflect the relative balance between the inhibition of NE neuronal firing rate and enhancement of NE released per impulse induced by long-term desipramine treatment. The development of the alpha-2 adrenergic receptor subsensitivity and consequent increased NE release per impulse may be insufficient to overcome the persistently decreased impulse flow.

It has been suggested that a subgroup of depressed patients may have hypersensitive presynaptic alpha-2 adrenergic receptors resulting in decreased synaptic NE and neuronal transmission (Leckman et al. 1980; Charney et al. 1981a). To evaluate this hypothesis, the effects of clonidine on plasma-free MHPG and blood pressure were evaluated in 15 depressed patients and 12 healthy subjects of similar age and sex (Charney et al. 1982b). Following placebo clonidine, the increase in plasma-free MHPG in the controls was significantly greater than the small decrease in the patients (+0.7 vs. −0.1 ng/ml, $p < .05$). In addition, the decrease in plasma-free MHPG in the patients following active clonidine was significantly greater than the response to active clonidine in the controls (−0.9 vs. +0.1 ng/ml, $p < .01$). However, of central importance is the finding that there was no significant difference between the patients and the controls in the overall "net" effect of clonidine on plasma-free MHPG (i.e., when the effect of placebo clonidine is subtracted from the active clonidine effect the controls had a "net" clonidine induced decrease of 0.6 ng/ml while in the patients there was a "net" decrease of 0.8 ng/ml, a nonsignificant difference). The decreases in blood pressure induced by clonidine were not different between the healthy subjects and the depressed patients.

The findings of this study did not provide support for the hypothesis that depressed patients have hypersensitive presynaptic alpha-2 adrenergic receptors. The ability of clonidine to decrease NE turnover was not different in depressed patients and healthy controls similar in age and sex.

In addition, clonidine induced similar decreases in blood pressure in both groups. This study did reveal several potentially important differences in NE function between the depressed patients and the healthy controls. When considered separately, the plasma-free MHPG response to placebo clonidine and active clonidine were significantly different between the two groups. One explanation for the different MHPG responses of depressed patients and healthy subjects to placebo and clonidine are that the two groups differ in the circadian secretion of MHPG. Wehr et al. (1980) reported that depressed patients were phase advanced in their urinary MHPG circadian rhythm compared to normal subjects. Therefore, in the present investigation, while the plasma MHPG levels of the healthy subjects are rising during the time period of the test day (8 a.m. to 3 p.m.), the MHPG levels of the patients may have peaked earlier and then remained stable. Clonidine simply lowered plasma MHPG an equal amount in both groups. The differences in diurnal MHPG secretion may reflect abnormalities in NE synthesis or metabolism or in the sensitivity of other receptors aside from the presynaptic alpha-2 adrenergic receptor.

Studies are now in progress in healthy subjects and depressed patients before and during AD treatment to determine whether the same assessment of alpha-2 adrenergic receptor sensitivity obtained with clonidine is also observed with yohimbine.

Postsynaptic Alpha-2 Adrenergic Receptors

The ability of clonidine to increase growth hormone secretion appears to be due to stimulation of postsynaptic alpha-2 adrenergic receptors in the hypothalamus (Terry & Martin 1981). Several groups of investigators (Charney et al. 1982b; Checkley et al. 1981; Mattusek et al. 1980) have demonstrated that oral and intravenous clonidine results in significant increases in growth hormone secretion in healthy subjects. These findings indicate that this effect of clonidine may be used as an index of postsynaptic alpha-2 adrenergic receptor function. The growth hormone response to clonidine has been shown to be blunted in drug-free depressed patients compared to healthy subjects, suggesting that the sensitivity of postsynaptic alpha-2 adrenergic receptors may be decreased (Charney et al. 1982b; Checkley et al. 1981; Mattusek et al. 1980). The effect of DMI and amitriptyline on the growth hormone response to clonidine was studied in 12 depressed patients to determine whether the blunted pretreatment response normalized following long-term treatment (Charney, et al., in press-b). The AD treatments did not alter the growth hormone response to clonidine in either treatment responders or nonresponders. Thus, while the etiologic significance of the blunted pretreatment growth hormone response remains to be determined, it does not appear that the efficacy of AD agents is dependent upon increasing the sensitivity of the postsynaptic alpha-2 adrenergic receptors.

Postsynaptic Serotonin Receptors

Despite the evidence that serotonin (5-HT) containing neurons in the central nervous system are involved in the regulation of a variety of brain functions, few paradigms have been developed that are capable of assessing brain 5-HT function in human subjects. In order to develop a method capable of evaluating central 5-HT function, the effects of intravenous tryptophan (6-7 grams) administered over 20 minutes on the secretion of prolactin, growth hormone, and mood state were studied in 10 healthy subjects (Charney et al. in press-a). The tryptophan infusion induced robust increase in prolactin in all 10 subjects with a peak occurring 60 minutes after the start of the infusion. Prolactin levels increased from a baseline of 9.6 +/− 1.4 ng/ml to a peak of 32.6 +/− 6.3 ng/ml ($p < .01$). A significant but variable increase in growth hormone concentration was observed, with the peak increase also occurring 60 minutes following the infusion (1.0 +/− .3 to 12.1 +/− 6.0 ng/ml, $p < .01$). The subjects reported feeling significantly more 'high,' 'mellow,' and 'drowsy' following the infusion in comparison to placebo ($p < .01$). These results, considered in conjunction with animal studies demonstrating that the ability of 5-HT to increase prolactin is potentiated by treatments which increase postsynaptic 5-HT sensitivity (Kuhn et al. 1981), suggest that study of the effects of intravenous tryptophan may be a means of assessing central postsynaptic 5-HT receptor function in depressed humans. Studies are now in progress in patients to determine the effects of a variety of AD treatments on the actions of intravenous tryptophan.

Treatment Approaches Based Upon the Receptor Sensitivity Model of Antidepressant Action

The identification of changes in postsynaptic beta, alpha-1, and 5-HT receptor function has proven useful in the development of new treatment strategies (Table). It has been suggested that the decrease in beta adrenergic receptor density induced by long-term AD administration may be a good screening test for AD activity. Two recent reports indicate an accelerated development of beta adrenergic receptor subsensitivity when desipramine is combined with the alpha adrenergic antagonists phenoxybenzamine and yohimbine (Paul & Crews 1980; Ursillo et al. 1980). If beta receptor binding alterations are related to AD efficacy, one might expect the clinical response to such a combination to be accelerated. To test this hypothesis, an ongoing investigation is evaluating the therapeutic effects of a yohimbine-desipramine and a yohimbine-amitriptyline combination in depressed patients. The preliminary findings of this study indicate that these combinations can be given safely to human subjects and should provide a valid assessment of the role of beta adrenergic receptor changes in the therapeutic actions of AD agents.

Table

Therapeutic Implications of Receptor Sensitivity Model

Antidepressant-induced Receptor Alteration	Treatment Strategy*
Decreased beta adrenergic receptor sensitivity	Yohimbine-antidepressant combination
Increased alpha-1 adrenergic receptor sensitivity	Thyroid hormone-antidepressant combination
Increased 5-HT receptor sensitivity	Lithium-antidepressant combination

*See text for details.

A similar approach of attempting to enhance the AD-induced receptor changes has recently been exploited. In a recent report, deMontigny et al. (1981) described eight patients with major unipolar depressions who failed to respond to AD treatment. All eight patients had a marked reduction in symptoms within 48 hours after lithium carbonate was added to their AD regimen. The remarkable improvement in the eight patients was attributed to an enhancement by lithium of central 5-HT systems that acted synergistically with the AD-induced sensitization of 5-HT postsynaptic receptors. To replicate and extend these findings, a placebo-controlled, double-blind investigation of the ability of lithium to potentiate the effects of a variety of AD drugs in treatment refractory patients has recently been conducted (Heninger & Charney, submitted for publication). The results of this study, while strongly supporting the original findings of deMontigny et al. (1981), indicate the therapeutic activity of lithium is not universal, and in some patients this effect may begin to appear only after a minimum of 4 to 7 days of lithium treatment. Clearly, more studies are needed to answer the questions: What type of patients respond most favorably to lithium potentiation? When is the best time to add lithium to an ongoing AD regimen? How long must lithium be continued to maintain a therapeutic response?

The ability of thyroid hormone to accelerate and potentiate the effects of a variety of tricyclic antidepressants has recently received renewed attention (Goodwin et al. 1982). This effect of thyroid hormone may be due to increased sensitivity of alpha-1 adrenergic receptors. Recent animal investigations indicate that thyroid hormone increases the number of alpha-1 adrenergic receptor binding sites in the cerebral cortex (Grob et al. 1981) and the behavioral responses to central postsynaptic alpha adrenergic receptor stimulation (Strombom et al. 1977).

The monoamine receptor sensitivity hypothesis provides a heuristic framework from which to develop clinical research strategies in depressed patients that may generate new insights into the pathophysiologic processes of depressive illness and to the development of improved therapeutic agents. The results decribed above are evidence of this and illustrate the benefits that occur when findings from basic neuroscience are applied to clinical treatment.

Acknowledgment: We wish to thank Grace M. Billings for her excellent secretarial help.

References

Anden, N.E., Grabowski, M., and Strombom, U. Different alpha-adrenoceptors in the central nervous system mediating biochemical and functional effects of clonidine and receptor blocking agents. *Naunyn Schmiedebergs Arch. Pharmacol.*, 292:43-52, 1976.

Cedarbaum, J.M., and Aghjanian, G.K. Catecholamine receptors on locus coeruleus neurons: Pharmacological characterization. *Eur. J. Pharmacol.*, 44:375-385, 1977.

Cedarbaum, J.M., and Aghajanian, G.K. Noradrenergic neurons of the locus coeruleus: Inhibition of epinephrine and activation by the alpha-antagonist piperoxane. *Brain Res.*, 112:413-419.

Charney, D.S., Heninger, G.R., Reinhard, J.F., Sternberg, D.E., and Hafstad, K.M. The effect of intravenous L-tryptophan on prolactin and growth hormone and mood in healthy subjects. *Psychopharmacology*. (In press-a)

Charney, D.S., Heninger, G.R., and Sternberg, D.E. Assessment of presynaptic alpha-2 adrenergic receptor function in humans: Effects of oral yohimbine. *Life Sci.*, 30:2033-2041, 1982a.

Charney, D.S., Heninger, G.R., and Sternberg, D.E. Failure of chronic antidepressant treatment to alter growth hormone response to clonidine. *Psychiatry Res.* (In press-b)

Charney, D.S., Heninger, G.R., and Sterngerg, D.E. Failure of chronic antidepressant treatment to alter growth hormone response to clonidine. *Psychiatry Res.* (In press-b)

Charney, D.S., Heninger, G.R., Sternberg, D.E., Hafstad, K.M., Giddings, S., and Landis, D.H. Adrenergic receptor sensitivity in depression: Effects of clonidine in depressed patients and healthy subjects. *Arch. Gen. Psychiatry*, 39:290-294, 1982b.

Charney, D.S., Heninger, G.R., Sternberg, D.E., Redmond, D.E., Leckman, J.F., Maas, J.W., and Roth, R.H. Presynaptic adrenergic receptor sensitivity in depression: The effect of long-term desipramine treatment. *Arch. Gen. Psychiatry*, 38:1334-1340, 1981a.

Charney, D.S., Menkes D.B., and Heninger, G.R. Receptor sensitivity and the mechanism of action of antidepressant treatment. *Arch. Gen. Psychiatry*, 38:1160-1180, 1981b.

Checkley, S.A., Slade, A.P., and Shur, E. Growth hormone and other responses to clonidine in patients with endogenous depession. *Br. J. Psychiatry*, 138:51-55, 1981.

deMontigny, C., Grunbey, F., Mayer, A., and Deschenes, J.P. Lithium induces a rapid relief of depression in tricyclic antidepressant drug nonresponders. *Br. J. Psychiatry*, 138:252-256, 1981.

Elsworth, J.D., Redmond, D.E., and Roth, R.H. Plasma and cerebrospinal fluid 3-methoxy-4-hydroxyphenylethylene glycol (MHGP) as indices of brain norepinephrine metabolism in primates. *Brain Res.*, 235:115-124, 1982.

Goodwin, F.K., Prange, A.J., Post, R.M., Muscettola, G., and Lipton, M. Potentiation of antidepressant effects by L-triiodothyronine in tricyclic nonresponders. *Am. J. Psychiatry*, 139:34-38, 1982.

Grob, G., Brodde, O.E., and Schumann, H.J. Regulation of alpha-1 adrenoceptors in the cerebral cortex of the rat by thyroid hormones. *Naun Schmiedeberg's Arch. Pharmacol.*, 316:46-50, 1981.

Kuhn, C.M., Vogel, R.A., Mailman, R.B., Schanberg, S.M., and Breese, G.R. Effect of 5,7-dihydroxytryptamine on serotonergic control of prolactin secretion and behavior in rats. *Psychopharmacology (Berlin)*, 73:188-193, 1981.

Langer, S.Z., Briley, M.S., and Raisman, R. Regulation of neurotransmission through presynaptic receptors and other mechanisms: Possible clinical relevance and therapeutic potential. In: Pepau, G., Kuhar, M.J., and Enna, S.J., (eds.), *Receptors for Neurotransmitters and Peptides*. New York: Raven Press, 1980, pp. 203-212.

Leckman, J.F., Maas, J.W., Redmond, D.E., and Heninger, G.R. Effects of oral clonidine on plasma 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) in man: Preliminary report. *Life Sci.*, 26:2179-2185, 1980.

Maas, J.W., Hattox, S.E., Greene, N.M., and Landis, D.H. MHPG production by human brain in vivo. *Science*, 205:1025-1027, 1979.

Matussek, N., Ackenheil, M., Hippius, H., Muller, F., Schroder, H-Th., Schultes, H., and Wasilewski, B. Effect of clonidine on growth hormone release in psychiatric patients and controls. *Psychiatry Res.* 2:25-36, 1980.

Nyback, H.V., Walters, J.R., Aghajanian, G.K., and Roth, R.H. Tricyclic antidepressants: Effects on the firing rate of brain noradrenergic neurons. *Eur. J. Pharmacol.*, 32:302-312, 1975.

Paul, S.M., and Crews, F.M. Rapid desensitization of cerebral cortical adrenergic receptors induced by desmethylimipramine and phenoxybenzamine. *Eur. J. Pharmacol.*, 62:349-350, 1980.

Scatton, B., Zivkovic, B., and Dedek, J. Antidopaminergic properties of yohimbine. *J. Pharmacol. Exp. Ther.*, 215:494-499, 1980.

Strombom, U., Svensson, T.H., and Jackson, D.M. Hyperthyroidism: Specifically increased response to central NA-(alpha) receptor stimulation and generally increased monoamine turnover in brain. *J. Neural Transm.*, 41:73-92, 1977.

Svensson, T.H., and Usdin, T. Feedback inhibition of brain noradrenaline neurons by tricyclic antidepressants: Alpha-receptor mediation. *Science*, 202:1089-1091, 1978.

Terry, L.C., and Martin, J.B. Evidence for alpha-adrenergic regulation of episodic growth hormone and prolactin secretion in the undisturbed male rat. *Endocrinology*, 108:1869-1973, 1981.

Ursillo, R.C., Wiech, N.L., Reisine, T.D., and Yamamura, H.I. Mechanisms of action of antidepressants. In: Yamamura, H.I., Olsen, R.W., Usdin, E. (eds.), *Psychopharmacology and Biochemistry of Neurotransmitter Receptors*. New York: Elsevier, North-Holland, 1980, pp. 189-202.

Wehr, T.A., Muscettola, G., and Goodwin, F.K. Urinary 3-methoxy-4-hydroxyphenylglycol circadian rhythm. *Arch. Gen. Psychiatry*, 37:257-263, 1980.

Protein Phosphorylation and Synaptic Mechanisms

Chair: Walter M. Lovenberg, Ph.D.
Hypertension Endocrine Branch
National Heart and Lung Institute
Bethesda, Maryland

Introductory Comments

Walter Lovenberg, Ph.D.[1]

Protein phosphorylations appear to play key roles in neurotransmission and the response of cells to neurotransmitters. A number of protein kinases have been identified in brain and these are known to phosphorylate proteins in several subcellular elements. There appear to be three basic types of protein kinases (cyclic nucleotide dependent, Ca^{+2}-calmodulin· dependent, and Ca^{++}-cyclic nucleotide independent) although each of these may exist in various molecular forms. The fact that at least some of the kinases appear to be activated by limited proteolysis tends to make exact characterization of these enzymes difficult. The second messengers cAMP and Ca^{++} are ideally suited for interneuronal communication, since Ca^{++} fluxes are an integral part of neuronal transmission and neuronal membranes are rich in adenylate cyclase. It would appear that at least in certain instances these adenylate cyclases are coupled to neurotransmitter receptors.

Phosphorylation of Cell Membranes. If one incubates synaptic plasma membranes purified from rat brain with Mg^{++} and adenosine triphosphate (ATP) labeled with ^{32}P, a number of protein bands resolved on slab gel electrophoresis are labeled. Autoradiographs of the proteins solubilized from such an incubation indicate that these proteins range in molecular weight from 40K to over 100K. Addition of cAMP to the phosphorylation reaction results in an increase in incorporation of PO_4 into selective bands. Particularly prominent are two bands with molecular weights in the range of about 80,000. These protein stubstrates have been extensively characterized be Greengard and his colleagues (Ueda & Greengard 1977) and were originally termed protein Ia and Ib. More recently they have been localized primarily to synaptic vesicles, and it has been suggested that they be called synapsin. Calcium also stimulates the incorporation of ^{32}P into a number of specific proteins in the presence of calmodulin. Protein I is also a substrate for the Ca^{++}-calmodulin dependent protein kinase. It would appear that each of the kinases act at specific sites (Huttner & Greengard 1979).

The physiologic role for phosphorylation of neuronal specific membrane proteins remains to be defined, although changes in ion permeability, receptor function, and neurotransmitter release are likely candidates.

Cytosolic Phosphorylation. Some of the functions of cytosolic protein kinases have been well defined. In many instances these kinases are involved in regulating the activity of cytosolic enzymes. The regulation of phosphorylase by protein kinase has been well studied. Studies in our laboratory and others indicate that the synthesis of the catecholamines and serotonin may be regulated by phosphorylation of their biosynthetic enzymes. Both Ca^{++} and cAMP-dependent kinases play important roles in these systems.

---

[1] Section on Biochemical Pharmacology, Hypertension-Endocrine Branch, National Heart, Lung, and Blood Institute, Bethesda, MD 20205.

With regard to tyrosine hydroxylase, we initially showed that the enzyme could be activated in the presence of a cAMP-dependent protein kinase and protein phosphorylating conditions. This activation at pH 6.0, the pH optimum of the enzymic reaction, appeared to be due to an increased affinity for the cosubstrate, tetrahydrobiopterin, and a decreased affinity for the end-product (dopamine). To understand whether protein phosphorylation represented a significant physiologic control mechanism, it seems important to know the relative concentration of tyrosine hydroxylase and its cosubstrates within the neuron. Also, knowledge of the kinetic properties of the enzyme at a physiological pH was necessary. By a variety of techniques with specific brain lesioning and enzyme kinetics we have been able to suggest a model for the regulation of dopamine synthesis in a dopamine neuron (Levine et al. 1981). By estimating the concentration of enzyme subunits and hydroxylase cofactor concentration in the terminal to be about 100 μM each, and by understanding the kinetics of the phosphorylated and non-phosphorylated enzyme at physiologic pH, we can conclude that a cyclic AMP-dependent phosphorylation of tyrosine hydroxylase converts an essentially inactive enzyme to a fully active form.

Protein phosphorylation may also play an important role in the regulation of tryptophan hydroxylase. We know far less about this system which is specifically present in serotonergic neurons. In contrast to tyrosine hydroxylase this enzyme can only be activated by Ca^{++} calmodulin-dependent protein kinase (Kuhn et al. 1980). At this stage little is known about the regulation of tryptophan hydroxylase *in vivo*, altough protein phosphorylation is likely involved.

References

Huttner, W.B., and Greengard, P. Multiple Phosphorylation sites in protein I and their differential regulation by cyclic AMP and calcium. *Proc. Natl. Acad. Sci. USA*, 76:5402-5406, 1979.

Kuhn, D.M., O'Callaghan, J.P., Juskevich, J., and Lovenberg. W. Activation of brain tryptophan hydroxylase by ATP-Mg^{2+}: Dependence on calmodulin. *Proc. Natl. Acad. Sci. USA*, 77:4688-4691, 1980.

Levine, R., Miller, L., and Lovenberg, W. Tetrahydrobiopterin in the striatum: Localization in dopamine nerve terminals and its role in catecholamine synthesis. *Science*, 214:919-921, 1981.

Ueda, T., and Greengard, P., Adenosine 3':5'-monophosphate-regulated phosphoprotein system or neuronal membrances. *J. Biol. Chem.*, 252:515-516, 1977.

The Possible Role of Phosphorylation of Tyrosine Hydroxylase in Catecholaminergic Neurons[1]

Mitchell A. Lazar, Ph.D., M.D.,[2] and
Jack D. Barchas, M.D.[2]

Tyrosine hydroxylase (TH) catalyzes the rate-determining step in the biosynthesis of catecholamines (Levitt et al. 1965). The regulation of TH activity is therefore a major determinant of the quantitative aspects of catecholaminergic neurotransmission. TH can be phosphorylated by cAMP-dependent (Edelman et al. 1981; Joh et al. 1978; Markey et al. 1980; Vulliet et al. 1980), and independent (Raese et al. 1979; Yamauchi & Fujisawa 1981), protein kinases, resulting in kinetic activation of the enzyme. It has been proposed that *in vivo* activation of TH during conditions of increased neuronal firing rate may be mediated by phosphorylation of the enzyme (Weiner et al. 1978; Lazar et al. 1981a). The adequacy of phosphorylation of TH for the short-term control of catecholamine synthesis is the subject of the present paper. A hypothesis concerning the role of TH phosphorylation in neuronal homeostasis is also presented.

Studies of purified bovine striatal TH have elucidated the kinetic properties of the non-phosphorylated and phosphorylated forms of the enzyme (Lazar et al. in press). At representative concentrations of dopamine and BH$_4$, K$_m$, K$_i$, and V$_{max}$ values of TH at pH 7.0 can be used to theoretically calculate the relative activities of nonphosphorylated and phosphorylated TH in a dopaminergic neuron (Lazar 1980). Such calculations are tabulated in the Table.

---

[1] This study was supported by USPHS Grant MH-23861 from the National Institute of Mental Health and the ONR (SRO-001). M.A.L. is a fellow of the Medical Scientist Training Progam.

[2] Nancy Pritzker Laboratory of Behavioral Neurochemistry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305.

Table

Calculations of TH Activity at Different Co-Factor and Inhibitor Concentrations

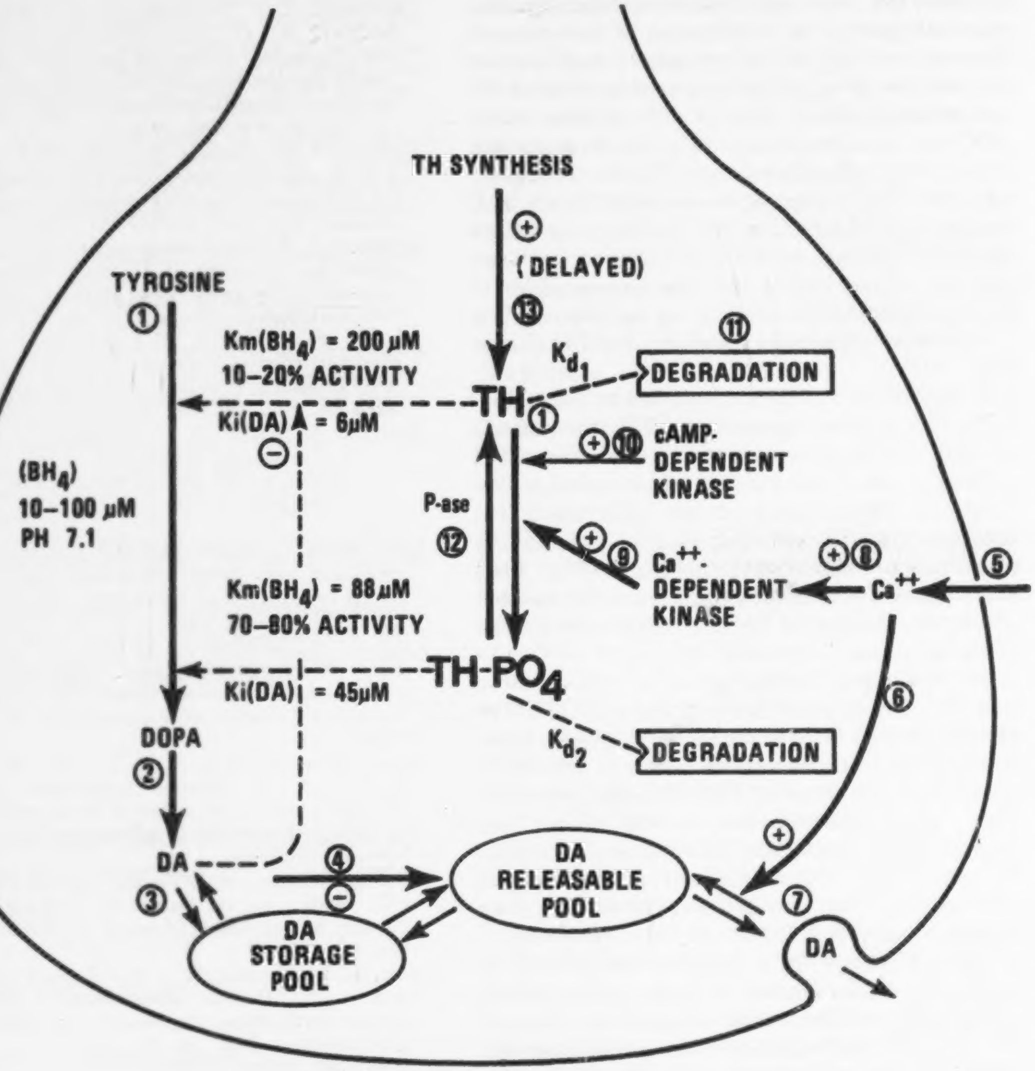
(BH$_4$)	(Dopamine)	V(Non-P)	V(Phos)	Fold Activation
1	5	0.01	0.15	15.0
10	5	0.11	1.36	12.8
100	5	0.86	7.32	8.5
1	20	0.005	0.11	23.9
10	20	0.05	1.07	21.4
100	20	0.41	6.38	15.6
1	40	0.003	0.09	33.8
10	40	0.03	0.83	27.7
100	40	0.24	5.45	22.7

(BH$_4$) and (Dopamine) are in μM. V(Velocity) is in nmoles DOPA formed per minute per milligram TH. V(Non-P) and V(Phos) refer to calculated rates of reactions catalyzed by nonphosphorylated and phosphorylated TH, respectively. Estimates of BH$_4$ concentration are from Lloyd and Weiner (1970) and Levine, Kuhn, and Lovenberg (1979). Estimates of dopamine concentration are from Mefford, Gilber, and Barchas (1980), and the range shown takes into account the fact that only about 40% of neuronal dopamine is bound to sedimentable material (Whittaker 1966). Intraneuronal pH has been estimated to be approximately 7.1 by Vigny, Hultorel, Henry, and Pantaloni (1980).

It can be seen that in the range of likely intracellular concentrations of dopamine and BH$_4$, activation of TH by phosphorylation would be on the order of 8-33 fold, if all TH molecules were phosphorylated. This would be expected to cause a major increase in the rate of catecholamine synthesis, but nevertheless some time would be necessary before the increase in catecholamine synthesis had an effect on the absolute concentration of dopamine concentration within the nerve ending. Thus it is doubtful that the function of increased dopamine synthesis is to replenish the cell with the amount of catecholamine lost during neurotransmission. Yet, it appears that short-term activation of TH occurs during periods of nerve firing, and that this activation is quantitatively similar to the activation induced by phosphorylation of the TH molecule (Masserano & Weiner 1979). The physiological relevance of TH phosphorylation may relate to the observations that newly synthesized catecholamines, including norepinephrine (Kopin et al. 1968) and dopamine (Glowinski 1970), are preferentially released during nerve stimulation.

A dopaminergic nerve terminal is schematically represented in the Figure. Numbers in parenthesis in the text refer to the correspondingly numbered steps in the Figure. Kinetic properties of purified bovine striatal TH, which were used to generate the calculation in the Table, are shown in the Figure (Lazar et al. 1982). It is proposed that phosphorylation would increase the rate of DOPA formation as discussed above (1). As TH is the rate-limiting step in catecholamine synthesis, immediate decarboxylation of DOPA (2) would result in an increased rate of dopamine synthesis. Dopamine exists in three intracellular forms, which may or may not be experimentally indistinguishable: a) cytoplasmic, which serves to inhibit TH, b) stored, not for immediate release (3), and c) available for release (4). Presumable in times of active nerve firing more newly synthesized dopamine is channeled to the releasable pool than in times of relative inactivity.

Intracellular calcium increases as a result of nerve stimulation (5). Calcium (6) is absolutely required for release of transmitter (7). In addition, calcium influx has also been shown to result in activation of a Ca^{+2}-dependent protein kinase (8), possibly via calmodulin (Schulman & Greengard 1978). Calcium-dependent protein phosphorylation has been speculated to play a role in transmitter release (DeLorenzo et al. 1979). It is hypothesized here that calcium-dependent phosphorylation may be involved in TH activation *in vivo* (9). Raese et al. (1979) have shown that cyclic AMP-independent protein kinase may also activate TH, and it has been recently suggested that calcium-dependent phosphorylation may also activate the enzyme (Yamauchi & Fujisawa 1980). If this were the case in vivo, calcium-dependent phosphorylation would promote both the increased release of neurotransmitter and the increased synthesis of transmitter available for release. Thus one intracellular event, the increase in calcium concentration, may rapidly result in neurotransmitter synthesis and neurotransmission, with little compromise of the cell's ability to respond to further stimuli. Phosphorylation of TH by cAMP-dependent protein kinase (10) may also serve a physiological role as a parallel method of increasing catecholamine synthesis.


TH SYNTHESIS
+
(DELAYED)
⑬
TYROSINE
①
Km(BH$_4$) = 200 µM
10–20% ACTIVITY
⑪
K$_{d_1}$
DEGRADATION
TH
①
Ki(DA) = 6µM
−
+ ⑩ cAMP-DEPENDENT KINASE
(BH$_4$)
10–100 µM
PH 7.1
P-ase
⑫
+ ⑨
Ca^{++}-DEPENDENT KINASE
+ ⑧
Ca^{++}
⑤
Km(BH$_4$) = 88µM
70–80% ACTIVITY
TH-PO$_4$
Ki(DA) = 45µM
⑥
DOPA
②
K$_{d_2}$
DEGRADATION
DA
③
④
−
DA RELEASABLE POOL
+
⑦
DA STORAGE POOL
DA

HYPOTHESIZED ROLE OF PHOSPHORYLATION IN THE REGULATION OF TYROSINE HYDROXYLASE ACTIVITY DURING STIMULI RESULTING IN INCREASED NEURONAL FIRING RATE

FIGURE. Schematic dopaminergic neuron. Numbered steps are referred to in text. Pluses and minuses refer to activating and inhibiting steps, respectively. The activities shown for phosphorylated (TH-PO$_4$) and non-phosphorylated TH refer to the ratio of TH activity at pH 7to that at pH 6.0, the *in vitro* pH optimum of non-phosphorylated TH. Estimates of dopamine, BH$_4$, and hydrogen ion concentrations are derived from the references to the Table.

Once TH is activated there are two hypothesized mechanism of inactivation of the enzyme. Thermal stability of the phosphorylated form of the enzyme is significantly less than that of the nonphosphorylated form of TH (Lazar et al. 1981b). If this correlates with *in vivo* turnover rate (Bond 1975), phosphorylated TH may be degraded faster than nonphosphorylated TH (11, Kd_2 greater than Kd_1). This could serve to time limit the activation process. In addition, phosphorylated TH may be susceptible to dephosphorylation (12), possibly by a phosphatase with some specificity for TH (Lazar et al. 1978).

If degradation of TH is involved in the regulation of levels of phosphorylated TH, then after a number of stimuli there might be depletion of TH molecules. However, there is ample evidence that long-term stimulation produces induction of TH synthesis in the cell body (13), possibly by transsynaptic induction (Thoenen 1975). Thus there exists a mechanism to increase the number of nonphosphorylated TH molecules after periods of sustained nerve stimulation.

In summary, phosphorylation produces a number of significant kinetic changes in TH. The phosphorylated form of the enzyme appears more suited to the intraneuronal milieu than is the nonphosphorylated form of TH. This magnifies the effect of phosphorylation of TH on *in vivo* catecholamine synthesis. The relative inhibition of nonphosphorylated TH under physiological constraints is what may enable the cell to regulate catecholamine synthesis quickly with relatively little overall change in the internal milieu. If, as suggested, calcium influx and calcium-dependent phosphorylation link nerve stimulation, transmitter release, and synthesis of transmitter for release, then the phosphorylation of tyrosine hydroxylase may play a crucial homeostatic role in the regulation of catecholaminergic neurons.

Acknowledgment: The authors thank Sue Poage for assistance in the preparation of the manuscript.

References

Bond, J. S. Correlations between *in vitro* turnover and *in vivo* inactivation of rat liver enzymes. In: Schimke, R. T., and Katunuma, N. (eds.), *Intracellular Protein Turnover.* New York:Academic Press, 1975, pp. 281-293.

DeLorenzo, R. J., Freedman, S. D., Yohe, W. B., and Maurer, S. C. Stimulation of Ca^{2+}-dependent neurotransmitter release and presynaptic nerve terminal protein phosphorylation by calmodulin and a calmodulin-like protein isolated from synaptic vesicles. *Proc. Natl. Acad. Sci. USA,* 76:1838-1842, 1979.

Edelman, A. M., Raese, J. D., Lazar, M. A., and Barchas, J. D. Tyrosine hydroxylase from brain: Phosphorylation of the enzyme by cyclic AMP-dependent protein kinase. *J. Pharmacol. Exp. Ther.,* 216:647-653, 1981.

Glowinski, J. Release of monoamines in the central nervous system. In: Schumann, H. J., and Kroneberg, G. (eds.), *New Aspects of Storage and Release Mechanisms of Catecholamines.* New York:Springer-Berlag, 1970, pp. 237-248.

Joh, T. H., Park, D. H., and Reis, D. J. Direct phosphorylation of brain tyrosine hydroxylase by cyclic AMP-dependent protein kinase: Mechanism of enzyme activation. *Proc. Natl. Acad. Sci. USA,* 75:4744-4748, 1978.

Kopin, I. J., Breese, G. R., Krauss, K. R., and Weise, V. K. Selective release of newly synthesized norepinephrine from the cat spleen during sympathetic nerve stimulation. *J. Pharmacol. Exp. Ther.,* 161:271-278, 1968.

Lazar, M. A. Characterization and properties of the phosphorylated and nonphosphorylated forms of purified bovine striatal tyrosine hydroxylase. Ph.D. Dissertation, Stanford University, 1980.

Lazar, M. A., Lockfeld, A., Mefford, I. N., and Barchas, J. D. Regulation of tyrosine hydroxylase activity by phosphorylation. Abstract, Proceedings of the Eighth International Congress of Pharmacology, Tokyo, Japan, 1981a.

Lazar, M. A., Lockfeld, A. J., Truscott, R. J. W., and Barchas, J. D. Tyrosine hydroxylase from bovine striatum: Catalytic properties of the phosphorylated and nonphosphorylated forms of the purified enzyme. *J. Neurochem.* (In press)

Lazar, M. A., Raese, J. D., Edelman, A. M., and Barchas, J.D. Studies on the enzymatic dephosphorylation of tyrosine hydroxylase. (Abstract) Neuroscience Annual Meeting, 1978.

Lazar, M. A., Truscott, R. J. W., Raese, J. D., and Barchas, J. D. Thermal denaturation of native striatal tyrosine hydroxylase: Increased thermolability of the phosphorylated form of the enzyme. *J. Neurochem.,* 36:677-682, 1981b.

Levitt, M., Spector, S., Sjoerdsma, A., and Undenfriend, A. Elucidation of the rate-limiting step in norepinephrine biosynthesis in the perfused guinea pig heart. *J. Pharmacol.,* 148:1-8, 1965.

Markey, K.A., Kondo, S., Shenkman, L., and Goldstein, M. Purification and characterization of tyrosine hydroxylase from a clonal pheochromocytoma line. *Mol. Pharmacol.,* 17:79-85, 1980.

Masserano, J., and Weiner, N. Similarities between the *in vivo* activation of adrenal tyrosine hydroxylase and the *in vitro* activation of the enzyme by an adenosine 3′, 5′-monophosphate dependent protein phosphorylating system. In: Usdin, E., Kopin, I., and Barchas, J. (eds.), *Catecholamines: Basic and Clinical Frontiers.* New York: Pergamon Press, 1979, pp. 100-102.

Mefford, I.N., Gilberg, M., and Barchas, J.D. Simultaneous determination of catecholamines and unconjugated 3-4-dihydroxyphenylacetic acid in brain tissue by ion-pairing reverse-phase high-performance liquid chromatography with electrochemical detection. *Arch. Biochem.*, 104:469-480, 1980.

Raese, J.D., Edelman, A.M., Makk, G., Bruckwick, E.A., Lovenberg, W., and Barchas, J.D. Brain striatal tyrosine hydroxylase: Activation of the enzyme by cyclic AMP-independent phosphorylation. *Commun. Psychopharmacol.*, 3:295-301, 1979.

Schulman, H., and Greengard, P. Ca^{+2}-dependent protein phosphorylation system in membranes from various tissues, and its activation by "calcium-dependent regulator." *Proc. Natl. Acad. Sci. USA*, 75:5432-5436, 1978.

Thoenen, H. Transsynaptic induction of neuronal enzyme synthesis. In: Iversen, L., Iversen, S., and Snyder, S. (eds.), *Handbook of Psychopharmacology*. New York: Plenum Press, 1975, pp. 443-475.

Vulliet, P.R., Langan, R.A., and Weiner, N. Tyrosine hydroxylase: A substrate of cyclic AMP-dependent protein kinase. *Proc. Natl. Acad. Sci. USA*, 77:92-96, 1980.

Weiner, N., Lee, F.L., Dreyer, E., and Barnes, E. The activation of tyrosine hydroxylase in noradrenergic neurons during acute nerve stimulation. *Life Sci.*, 22:1197-1216, 1978.

Yamauchi, T., and Fujisawa, H. Tyrosine 3-monooxygenase is phosphorylated by Ca^{+2}-dependent protein kinase followed by activation by activator protein. *Biochem. Biophys. Res. Commun.*, 100:807-813, 1981.

Calcium-Dependent Phosphorylation and the Regulation of Serotonin Synthesis

Donald M. Kuhn, Ph.D.[1]

Introduction

The brain is a major organ system which is comprised of over 10 billion heterogenous cells and driven by over 300 trillion connections and interconnections among these cells. Dysfunction of the brain presents a difficult problem in diagnosis and treatment. Not surprisingly, *brain* dysfunction manifests itself in many ways along a broad continuum of psychiatric disorders, most of which remain poorly understood. However, the results of a great deal of research are providing clues into the etiology of some psychiatric illnesses. A major focus for much research into psychiatric disorders centers on the chemistry of the neurotransmitter systems and one such neurotransmitter, serotonin (5-HT), is the subject of the present discussion. The reader only has to examine this volume to realize that 5-HT is still implicated in a variety of psychiatric disorders, not the least of which include depression and schizophrenia. This chapter will concentrate on the control of 5-HT synthesis and the role of phosphorylating mechanisms in this process.

The biosynthetic pathway for 5-HT begins with the conversion of the essential amino acid l-tryptophan (TRY) to 5-hydroxytryptophan (5-HTP) and is completed by the decarboxylation of 5-HTP (by l-aromatic amino acid decarboxylases) to 5-HT. The first step, TRY → 5-HTP, is catalyzed by tryptophan hydroxylase which is also the rate limiting step in 5-HT synthesis, and this reaction takes place exclusively in a very small proportion of cells in the brain. This is known as the 5-HT neuronal system. Since tryptophan hydroxylation is the initial and rate limiting step in 5-HT synthesis, the rate of this reaction can have a profound influence on the amount of 5-HT produced. Therefore, the present discussion will deal exclusively with the control of tryptophan hydroxylase activity. Furthermore, the role of phosphorylation in controlling 5-HT synthesis will focus, by necessity, on the rate-limiting hydroxylation step. These restrictions by no means lessen the importance of numerous other aspects of 5-HT synthesis and control (e.g., levels of substrates, release or uptake of 5-HT, 5-HT receptors) nor do they indicate that a phosphorylation reaction is the only means by which tryptophan hydroxylase is controlled.

Phosphorylation reactions are mediated by protein kinase enzymes which, in general, involve the transfer of the terminal phosphate from adenosine triphosphate (ATP) to some substrate (e.g., another enzyme or protein) via a covalent linkage. Perhaps the most extensively studied protein kinases are the ones which are dependent on cyclic nucleotides (cAMP or cGMP) for activity whereas, more recently, a number of protein kinases have been discovered to be dependent on calmodulin (CaM), the calcium-binding protein

---

[1] Section on Biochemical Pharmacology, Hypertension-Endocrine Branch, National Heart, Lung, and Blood Institute, Bethesda, MD 20205.

(*see* Cheung 1980), for expression of catalytic activity. Furthermore, it appears that tryptophan hydroxylase is a substrate for Ca^{2+}-CaM dependent proteins kinase and that phosphorylating conditions activate tryptophan hydroxylase.

Method

Tryptophan hydroxylase was measured in extracts from rat mesencephalic tegmentum, since this brain section contains the majority of all cerebral 5-HT cell bodies and is rich in tryptophan hydroxylase activity. The enzyme was assayed by the fluorometric method described by Baumgarten et al. (1973) which involves the measurement of 5-HTP fluorescence after termination of the enzyme reaction. In order to study the effects of phosphorylation on tryptophan hydroxylase, ATP, Mg^{2+}, and calcium were added to the assay mixture. All reactions were carried out for 15 minutes at 37°C. Additional details on methodology are given in the following sections.

Results and Discussion

Effects of Phosphorylating Conditions on Tryptophan Hydroxylase Activity

Hamon et al. (1978) first observed that tryptophan hydroxylase could be activated by phosphorylating conditions and almost simultaneously Kuhn et al. (1978) reported similar observations. In these studies the addition of 0.5 mM ATP and 5.0 mM Mg^{2+} to the enzyme reaction mixture resulted in increased tryptophan hydroxylase activity when the assays were carried out with subsaturating concentrations of the substrate 2-amino-4-hydroxy-6-methyl-5,6,7,8 tetrahydrobiopterin (6-MPH_4). Lineweaver-Burk plots of kinetic data revealed that phosphorylating conditions decreased the apparent Km of tryptophan hydroxylase for the pteridine cofactor (6-MPH_4) without changing the Km for tryptophan. In fact, the Km for 6-MPH_4 was reduced from 210 to approximately 90 μM by phosphorylating conditions (Kuhn et al. 1978).

The requirements for activation of tryptophan hydroxylase appeared quite simple initially (Hamon et al. 1978; Kuhn et al. 1978). In addition to ATP and Mg^{2+}, only Ca^{2+} was necessary to allow complete activation. The Ca^{2+} requirement is demonstrated in Figure 1. This curve was generated by using a Ca^{2+}-EGTA buffer to control the levels of free Ca^{2+} (which can be calculated) and zero Ca^{2+} simply indicates the addition of excess EGTA without added Ca^{2+}. It can be seen that the reaction is sensitive to low concentrations of Ca^{2+} (10^{-7}–10^{-5} M Ca^{2+}) and the activation reaches half maximum at approximately 7.5×10^{-7} M Ca^{2+}. A number of cyclic nucleotides including CAMP and cGMP were tested and found to be inactive. Thus, the activation of tryptophan hydroxylase by phosphorylating conditions was apparently mediated by a cyclic nucleotide-independent but Ca^{2+}-dependent protein kinase. This total dependency on Ca^{2+} suggested that CaM might also be involved and the remaining discussion will concentrate on results with CaM and the phosphorylation induced activation of tryptophan hydroxylase. The interested reader is referred to previous, more detailed discussions on this subject (Kuhn et al. 1980).

The role of calmodulin in the activation of tryptophan hydroxylase by phosphorylating conditions. Cheung (1980) has identified several criteria which are

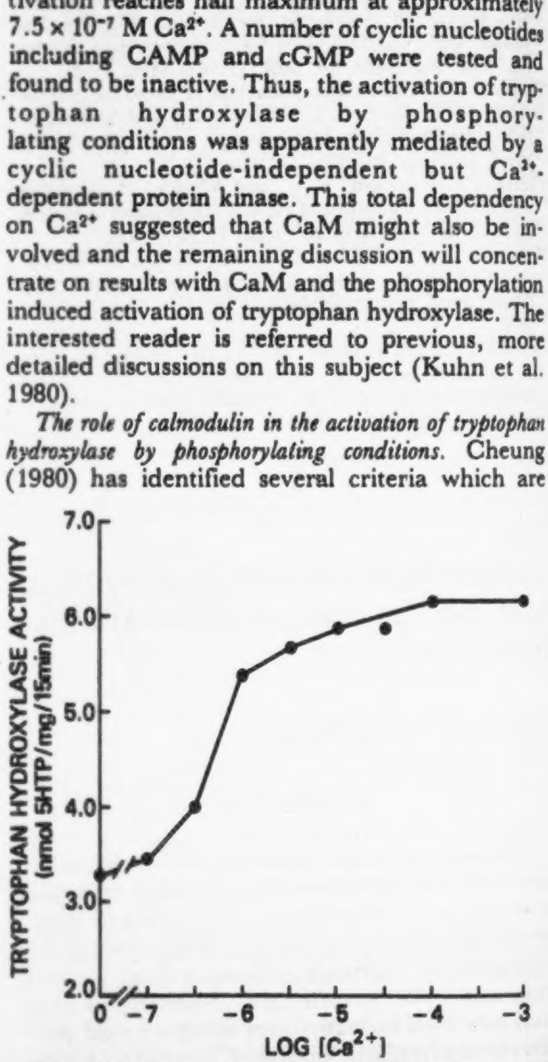


FIGURE 1. Calcium dependency of the activation of tryptophan hydroxylase by phosphorylating conditions. Ca^{2+} concentrations were adjusted to the indicated values by the use of Ca^{2+}-EGTA buffers. Zero Ca^{2+} refers to the use of excess EGTA.

useful in identifying CaM dependent biological reactions and previous studies (*see* above) satisfied one criterion, Ca^{2+} dependency. A second criterion demands that the removal of CaM from the tissue alters the reaction. To test this, tegmental extracts were chromatographed on an affinity matrix comprised of fluphenazine covalently attached to Sepharose 4B (*see* Charbonneau & Cormier, 1979, for a description) in order to remove endogenous CaM. The data in the Table indicate that removal of CaM rendered the hydroxylase unresponsive to phosphorylating conditions. The ability of exogenously added CaM to reinstate the activation in chromatographed brain extracts is also demonstrated in the Table, and these data satisfy another criterion, that CaM can be added back into the system from which it was removed and at the same time restore function to the system. Analysis of brain extracts by SDS-polyacrylamide slab gel electrophoresis both before and after affinity chromatography on fluphenazine Sepharose confirmed that CaM was indeed present in the brain under study (satisfying the fourth criterion of Cheung 1980) and that the affinity chromatography was quite efficient and selective in removing CaM. These results are shown in Figure 2.

A fifth criterion states that fluphenazine should inhibit the CaM-dependent reaction and is based on the observation that fluphenazine and a large number of other antipsychotic drugs bind with high affinity to CaM in a Ca^{2+}-dependent fashion (*see* Weiss et al. 1980). To test this criterion, a number of antipsychotic drugs were added to the tryptophan hydroxylase reaction mixture in the presence of phosphorylating conditions. The effects of three such drugs are shown in Figure 3. It can be seen that increasing concentrations of fluphenazine, trifluoperazine, and cis-flupenthixol produced inhibition of the phosphorylation-induced activation of tryptophan hydroxylase. Other antipsychotics including penfluridol, pimozide, haloperidol, and chlorpromazine were also effective in this regard, the inhibitory potencies for the inhibition of the activation of tryptophan hydroxylase by these drugs agreed precisely with the order of potency of the binding of these drugs to CaM (Weiss et al. 1980). Since these drugs are by no means completely specific in their *in vitro* actions, additional studies were carried out to assess the extent to which their inhibitory properties were related to CaM binding. The

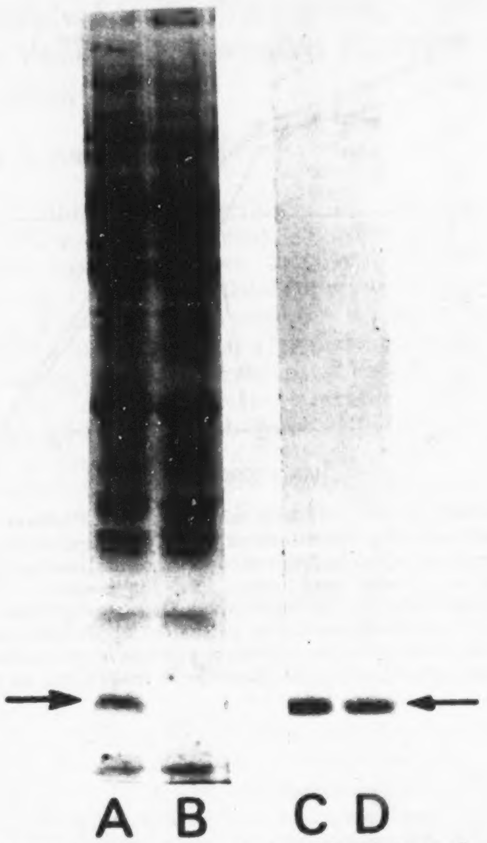


FIGURE 2. SDS-polyacrylamine slab gel electrophoresis of brain protein. Lane A, extract (100 μg of protein) before chromatography on fluphenazine-sepharose 4B; Lane B, effluent (100 μg of protein) from fluphenazine-sepharose 4B; Lane C. EGTA eluant (2 μg of protein) from affinity column after dialysis against 0.1 mM Ca^{2+}; Lane D, purified calmodulin (2 μg) from pig brain acetone powder prepared by the method of Klee (1977). Arrows indicate the position of calmodulin. Reprinted, with permission, from Kuhn et al. (1980).

Table

Phosphorylation Effects on Tryptophan Hydroxylase After Chromatography on Fluphenazine-Sepharose

		Assay Conditions	
Enzyme	Addition	Control	Phosphorylating
Control	-	5.21 ± 0.07	8.44 ± 0.40
Chromatographed	-	5.65 ± 0.21	5.72 ± 0.18
	Calmodulin	5.32 ± 0.04	9.22 ± 0.42
	Calmodulin + EGTA	5.20 ± 0.15	4.62 ± 0.19

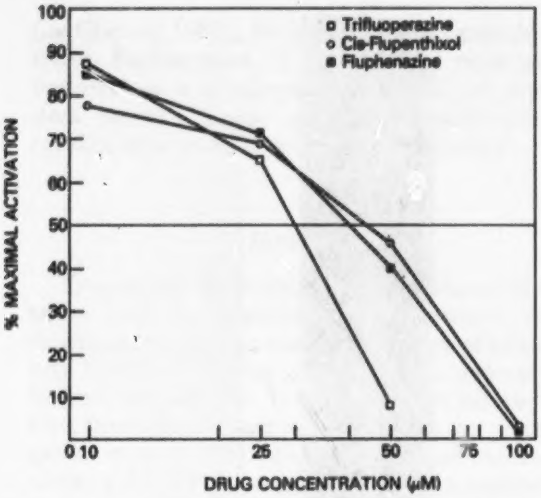


FIGURE 3. Drug-induced inhibition of the effects of phosphorylating conditions on tryptophan hydroxylase. Drugs were added in the final concentrations listed on the abscissa. Drugs used were: ■, fluphenazine; □, trifluoperazine; O, cis-flupenthixol. Data are expressed as percent maximal activation, calcualted by dividing the activity under phosphorylating conditions in the absence of drug. Reprinted, with permission, from Kuhn et al. 1980.

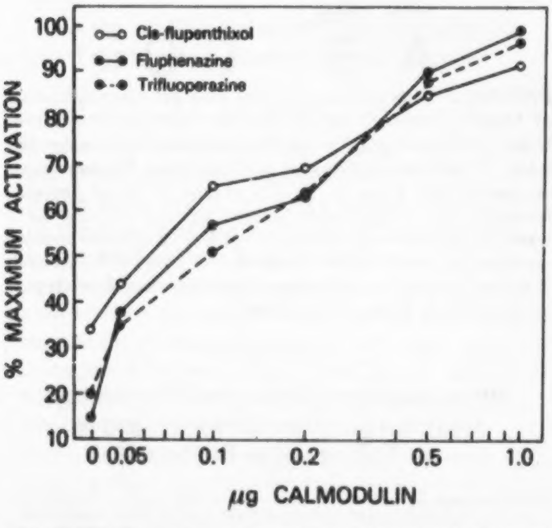


FIGURE 4. Protection against drug-induced inhibition of phosphorylation of tryptophan hydroxylase by calmodulin. Phosphorylation reaction mixtures were prepared and cis-flupenthixol (O-O), fluphenzaine (•—•) or trifluoperazine (•--•) was added to the reaction mixture. Reprinted, with permission, from Kuhn et al. (1980).

results in Figure 4 indicate that the addition of exogenous CaM to reaction mixtures containing fluphenazine, trifluoperazine, or cis-flupenthixol (50 μM for each) overcame the inhibitory effects of these drugs. Thus, it seems likely that the inhibitory effects of these drugs are mediated by their ability to bind to CaM.

A final criterion suggests that antibodies to CaM should prevent the CaM-dependent process but, unfortunately, this criterion has not yet been fulfilled. The assay for tryptophan hydroxylase requires the presence of a reducing agent, typically dithiothreitol (DTT), and DTT reduces the sulfhydryl bridge which retains structural integrity (and function) between the heavy and light chains of the IgG antibody raised against CaM. Experiments are continuing with various CaM antibody preparations to test their ability to block the CaM dependent activation of tryptophan hydroxylase.

In summary, the data suggest rather conclusively that CaM is an essential component in the activation of tryptophan hydroxylase by phosphorylating conditions. However, some very important questions have not yet been answered. For example, is tryptophan hydroxylase itself directly phosphorylated during activation or is some other protein intermediate the substrate for the CaM-dependent protein kinase? Only studies with highly purified preparations of tryptophan hydroxylase will allow this question to be answered and unfortunately, such a purified enzyme preparation is not yet available. Another question which must be answered is whether this phosphorylation-induced activation occurs *in vivo*. Fortunately, some data are available which are pertinent to this question. For example, tryptophan hydroxylase in brain slices is activated by neuronal depolarizing conditions in a Ca^{2+} dependent manner and this activation can be blocked by fluphenazine (Mestikevay et al. 1982; Boadle-Biber 1982). Furthermore, the cerebral distribution of the Ca^{2+} -CaM dependent protein kinase parallels that of tryptophan hydroxylase (Hamon et al. 1979), and selective destruction of 5-HT cells with the neurotoxin 5,7-dihydroxytryptamine also substantially reduces Ca^{2+} dependent protein kinase activity (Hamon et al. 1979). Finally, Yamauchi and Fujisawa (1980) have identified three different CaM-activated protein kinases in brain, and tryptophan hydroxylase is apparently a substrate for one of these enzymes. Although these data do not constitute conclusive proof, collectively they strongly indicate that a Ca^{2+}-CaM dependent protein kinase can phosphorylate tryptophan hydroxylase *in vivo,* and this mechanism could be closely coupled to neuronal depolarization and Ca^{2+} influx.

References

Baumgarten, H. G., Victor, S. J., and Lovenberg, W. Effects of intraventricular injection of 5,7-dihydroxytryptamine on regional tryptophan hydroxylase of rat brain. *J. Neurochem.*, 21:251-253, 1973.

Boadle-Biber, M. C. Ca^{2+} and calmodulin antagonists block activation of tryptophan hydroxylase. *Trans. Am. Soc. Neurochem.*, 13:141, 1982.

Charbonneau, H., and Cormier, M. J. Purification of plant calmodulin by fluphenazine-sepharose affinity chromatography. *Biochem. Biophys. Res. Comm.*, 90:1039-1047, 1979.

Cheung, W. Y. Calmodulin plays a pivotal role in cellular regulation. *Science*, 207:19-27, 1980.

Hamon, M., Bourgoin, S., Hery, F., and Simonnet, G. Activation of tryptophan hydroxylase by adenosine triphosphate, magnesium, and calcium. *Mol. Pharmacol.*, 14:99-110, 1978.

Hamon, M., Bourgoin, S., Artaud, F., and Glowinski, J. The role of intraneuronal 5-HT and of tryptophan hydroxylase activation in the control of 5-HT synthesis in rat brain slices incubated in K^+-enriched medium. *J. Neurochem.*, 33:1031-1042, 1979.

Klee, C.B. Conformational transition accompanying the binding of Ca^{2+} to the protein activator of 3′,5′ cyclic adenosine monophosphate phosphodiesterase. *Biochemistry*, 16:1017-1024, 1977.

Kuhn, D. M., Vogel, R. L., and Lovenberg, W. Calcium dependent activation of tryptophan hydroxylase by ATP and magnesium. *Biochem. Biophys. Res. Commun.*, 82:759-766, 1978.

Kuhn, D. M., O'Callaghan, J. P., Juskevich, J., and Lovenberg, W. Activation of brain tryptophan hydroxylase by ATP-Mg^{2+}-dependence on calmodulin. *Proc. Natl. Acad. Sci., USA*, 77:4688-4691, 1980.

Mestikevay, S. L., Buorgoin, S., Artaud, F., and Hamon, M. *In vitro* and *in vivo* activation of tryptophan hydroxylase in rat brain. In: Usdin, E., Weiner, N., and Youdim, M. (eds.), *Function and Regulation of Monoamine Enzymes: Basic and Clinical Aspects.* New York:Macmillan. (In press)

Weiss, B., Prozialeck, W., Cimino, M., Barnette, M. S., and Wallace, T. L. Pharmacological regulation of calmodulin. *Ann. NY Acad. Sci.*, 356:319-345, 1980.

Yamauchi, T., and Fujisawa. H. Evidence for three distinct forms of calmodulin-dependent protein kinases from rat brain. *FEBS Lett.*, 116:141-144, 1980.

Control of Phosphorylation of a Vesicle-Associated Protein, Synapsin 1[1]

Mary B. Kennedy, Ph.D.[2]

Reversible phosphorylation of proteins, catalyzed by a class of enzymes called protein kinases, has been shown to play a role in regulating a variety of cellular processes. For example, several hormones stimulate the synthesis of cAMP which then acts as a "second messenger," stimulating the phosphorylation of specific proteins by cAMP-dependent protein kinase (Greengard 1978; Krebs & Beavo 1979). In an attempt to understand the mechanism of action of neurotransmitters that have relatively long term effects on neurons, Paul Greengard's laboratory showed that some of these neurotransmitters stimulate the synthesis of cAMP (Greengard 1981). More recently, the same lab has described a protein doublet, initially termed protein I, that is found only in neural tissue, and is phosphorylated by cAMP-dependent protein kinase (Ueda & Greengard 1977). Studies on the location of protein I have shown that it is located specifically in most, if not all, synaptic terminals (Bloom et al. 1979; DeCamilli et al. 1979) where it is associated primarily with synaptic vesicles (Ueda et al. 1979; DeCamilli, Harris, Huttner and Greengard, in preparation). Because of its location, the protein has been renamed synapsin I (Huttner et al. 1981a).

More detailed studies on phosphorylation of synapsin I have shown that its phosphorylation can be regulated by free calcium levels in nerve terminals, as well as by cAMP (Krueger et al. 1977). This was demonstrated in an experiment in which brain synaptosomes were prelabeled with ^{32}P-phosphate, then transferred to depolarizing solutions containing either veratridine or high potassium, in the presence or absence of calcium. Following brief incubations, protein phosphorylation was assessed by SDS gel electrophoresis and

---

[1] The work described in this paper was carried out in the laboratory of P. Greengard and was supported by USPHS Grants MH-17387 and NS-08440 (to P. Greengard), a grant from the McKnight foundation (to P. Greengard), and a postdoctoral research fellowship from the Muscular Dystrophy Association awarded to M.B. Kennedy.

[2] Division of Biology 216-76, California Institute of Technology, Pasadena, CA 91125.

autoradiography. Depolarization in the presence of calcium, but not in its absence, increased the rate of phosphorylation of synapsin I (Krueger et al. 1977; Sieghart et al. 1979). Three lines of evidence indicate that the calcium-stimulated phosphorylation occurs by a pathway distinct from the cAMP-dependent pathway. First, depolarization of synaptosomes in the presence of calcium produces no measurable increase in cAMP (Krueger et al. 1977). Second, calcium-stimulated phosphorylation occurs at three distinct sites on the synapsin I molecule. One (site 1) is recovered in a 10 kdalton fragment after proteolysis with *Staph aureus* V8 protease and is the same site that is phosphorylated by cAMP-dependent kinase. The other two (sites 2 and 3) are recovered in a 30 kdalton fragment and are not phosphorylated by cAMP-dependent protein kinase under physiological conditions (Huttner & Greengard 1979; Huttner et al. 1981b). Finally, calcium and calmodulin-dependent protein kinase activity has been identified in synaptosomal lysates (Schulman & Greengard 1978a,b).

In order to purify and characterize the calcium-dependent protein kinase or kinases that phosphorylate synapsin I, a quantitative assay for such kinases was developed using purified synapsin I as a substrate (Kennedy & Greengard 1981; Figure). Under optimal conditions in this assay, the rate of phosphorylation of synapsin I by a crude brain homogenate is stimulated as much as 40-fold by calcium ion to a rate of about 5 nmoles/min/mg of protein. Both the soluble and particulate fractions of the homogenate contain calcium-stimulated synapsin I kinase (Figure). The soluble activity catalyzes the phosphorylation of all three sites on synapsin I, while the particulate activity phosphorylates primarily sites 2 and 3 (Kennedy & Greengard 1981). Fractionation of the soluble proteins by DEAE-chromatography revealed the presence of two distinct synapsin I kinases. One peak of activity phosphorylated site 1 ("10 k fragment kinase") while the other, larger, peak phosphorylated sites 2 and 3 ("30 k fragment kinase"). The 10 k fragment kinase is calcium-dependent, but does not at this stage of purification require exogenous calmodulin. It is, however, inhibited by 50 μM trifluoperazine which suggests that it may be calmodulin-dependent, and have a sufficiently high affinity for calmodulin that the two copurify through the DEAE fractionation. The 30 k fragment kinase is both calcium and calmodulin-dependent.

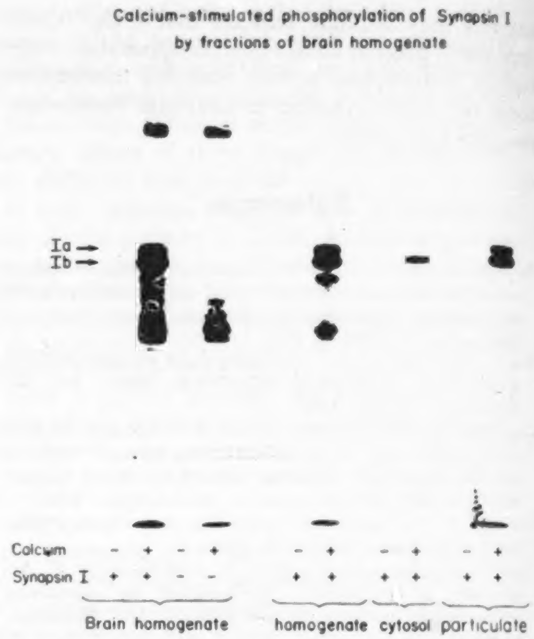

Calcium-stimulated phosphorylation of Synapsin I
by fractions of brain homogenate
Ia
Ib
Calcium - + - + - + - + - +
Synapsin I + + - - + + + + + +
Brain homogenate
homogenate
cytosol
particulate

FIGURE. The fractions of brain homogenate were prepared, and assays performed as described in Kennedy and Greengard, 1981.

This latter soluble synapsin I kinase activity is apparently closely related or identical to the particulate calmodulin-dependent synapsin I kinase (Kennedy, McGuinness, and Greengard, manuscript in preparation). Fifty to seventy percent of the particulate enzyme can be solubilized by prolonged incubation in dilute buffer, and can then be partially purified by DEAE-cellulose chromatography. The enzymes of both soluble and particulate origin have been further purified by calmodulin-sepharose affinity chromatography. At this stage of purification, the two enzymes are indistinguishable in their catalytic properties (substrate specificities, affinity for substrates, calcium requirement, optimum pH) and in their mobilities on DEAE-cellulose.

Both of the brain synapsin I kinases can be distinguished from the two previously described calmodulin-dependent protein kinases, myosin light chain kinase (Dabrowska et al. 1978; Yagi et al. 1978) and phosphorylase kinase (Cohen et al. 1978), by differences in their substrate specificities (*see* Table), in their mobilities on DEAE-cellulose, and in their tissue distributions

(Kennedy & Greengard 1981). The calcium-stimulated synapsin I kinase activities are three to ten times more highly concentrated in brain homogenates than in any other tissue homogenates assayed. The relationship of these enzymes to the endogenous particulate calmodulin-dependent protein kinase described by Schulman and Greengard is being investigated.

Table

Comparison of Substrate Specificities of Calmodulin-Dependent Protein Kinases

	Substrate		
Enzyme	Myosin Light Chain	Phosphorylase b	Synapsin I
	pmole/min	pmole/min	pmole/min
Myosin light chain kinase (M. Conti and R. Adelstein)	27	---	5.7 (10 k fragment)
Phosphorylase kinase (J. Wang)	---	14	1.3 (30 k fragment)
Crude synapsin I kinase 1.		<0.02	76
2.	0.08		89

Purified enzymes were obtained from the indicated investigators. Crude synapsin I kinase refers to the DEAE peak of enzyme activity described in Kennedy and Greengard, 1981. Myosin light chain was a gift of Dr. Angus Nairn. Phosphorylase b was purchased from Sigma Chemical Co. Assays were performed as described in Kennedy and Greengard, 1981. Mixing experiments indicated that the crude synapsin I kinase preparation did not contain substances that interferred with the measurement of either myosin light chain kinase or phosphorylase kinase.

The complex regulation of phosphorylation of synapsin I, together with its association with synaptic vesicles, suggests it is involved in a vesicle function that is regulated by events that alter either cyclic AMP levels or calcium levels. One such function is transmitter release. In some terminals, agents that alter cyclic AMP levels can cause facilitation, which is an increase in the number of quanta of transmitter released per impulse (e.g., Goldberg & Singer 1969; Kandel 1981). In addition, under some circumstances, calcium influx through voltage-dependent calcium channels can lead to post-tetanic potentiation which is a relatively long-lasting increase in the number of quanta released per impulse (Rosenthal 1969). Future experiments should elucidate whether synapsin I is involved in regulation of transmitter release, or in some other vesicle function.

Acknowledgment: The help of C. Hochenedel in preparing this manuscript is greatefully acknowledged.

References

Bloom, F.E., Ueda, T., Battenberg, E., and Greengard, P. Immunocytochemical localization, in synapses, of protein I, an endogenous substrate for protein kinases in mammalian brain. *Proc. Natl. Acad. Sci. USA*, 76:5982-5986, 1979.

Cohen, P., Burchell, A., Foulkes, J.G., Cohen, P.T.W., Vanaman, T.C., and Nairn, A.C. Identification of the Ca^{2+}-dependent modulator protein as the fourth subunit of rabbit skeletal muscle phosphorylase kinase. *FEBS Lett.*, 92:287-293, 1978.

Dabrowska, R., Sherry, J.M.F., Aromatorio, P.K., and Hartshorne, D.J. Modulator protein as a component of the myosin light chain kinase from chicken gizzard. *Biochemistry*, 17:253-258, 1978.

DeCamilli, P., Ueda, T., Bloom, F.E., Battenberg, E., and Greengard, P. Widespread distribution of protein I in the central and peripheral nervous systems. *Proc. Natl. Acad. Sci. USA*, 76:5977-5981, 1979.

Goldberg, A.L., and Singer, J.J. Evidence for a role of cyclic AMP in neuromuscular transmission. *Proc. Natl. Acad. Sci. USA*, 64:134-141, 1969.

Greengard, P. Phosphorylated proteins as physiological effectors. *Science*, 199:146-152, 1978.

Greengard, P. Intracellular signals in the brain. *Harvey Lectures*, 75:277-331, 1981.

Huttner, W.B., and Greengard, P. Multiple phosphorylation sites in protein I and their differential regulation by cyclic AMP and calcium. *Proc. Natl. Acad. Sci. USA*, 76:5402-5406, 1979.

Huttner, W.B., DeCamilli, P., Schiebler, W., and Greengard, P. Phosphorylation of synapsin I (protein I) in highly purified synaptic vesicles and other subcellular fractions from rat brain. *Soc. Neurosci. Abstr.*, 7:441, 1981a.

Huttner, W.B., De Gennaro, L.J., and Greengard, P. Differential phosphorylation of multiple sites in purified protein I by cyclic AMP-dependent and calcium-dependent protein kinases. *J. Biol. Chem.*, 256:1482-1488, 1981b.

Kandel, E.R. Calcium and the control of synaptic strength by learning. *Nature*, 293:697-700, 1981.

Kennedy, M.B., and Greengard, P. Two calcium/calmodulin-dependent protein kinases, which are highly concentrated in brain, phosphorylate protein I at distinct sites. *Proc. Natl. Acad. Sci. USA*, 78:1293-1297, 1981.

Krebs, E.G., and Beavo, J.A. Phosphorylation-dephosphorylation of enzymes. *Ann. Rev. Biochem.*, 48:923-960, 1979.

Krueger, B.K., Forn, J., and Greengard, P. Depolarization-induced phosphorylation of specific proteins, mediated by calcium ion influx, in rat brain synaptosomes. *J. Biol. Chem.*, 252:2764-2773, 1977.

Rosenthal, J. Post-tetanic potentiation at the neuromuscular junction of the frog. *J. Physiol. (Lond.)*, 203:121-133, 1969.

Schulman, H., and Greengard, P. Stimulation of brain membrane protein phosphorylation by calcium and an endogenous heat-stable protein. *Nature*, 271:478-479, 1978a.

Schulman, H., and Greengard, P. Ca^{2+}-dependent protein phosphorylation system in membranes from various tissues, and its activation by "calcium-dependent regulator." *Proc. Natl. Acad. Sci. USA*, 75:5432-5436, 1978b.

Sieghart, W., Forn, J, and Greengard, P. Ca^{2+} and cyclic AMP regulate phosphorylation of same two membrane-associated proteins specific to nerve tissue. *Proc. Natl. Acad. Sci. USA*, 76:2475-2479, 1979.

Ueda, T., and Greengard, P. Adenosine 3′:5′-monophosphate-regulated phosphoprotein system of neuronal membranes. I. Solubilization, purification, and some properties of an endogenous phosphoprotein. *J. Biol. Chem.*, 252:5155-5163, 1977.

Ueda, T., Greengard, P., Berzins, K., Cohen, R.S., Blomberg, F., Grab, D.J., and Siekevitz, P. Subcellular distribution in cerebral cortex of two proteins phosphorylated by a cAMP-dependent protein kinase. *J. Cell Biol.*, 83:308-319, 1979.

Yagi, K., Yazawa, M., Kakiuchi, M., Ohshima, M., and Uenishi, K. Identification of an activator protein for myosin light chain kinase as the Ca^{2+}-dependent modulator protein. *J. Biol. Chem.*, 253:1338-1340, 1978.

The Indole Hallucinogens—A New Look at Their Mechanisms of Action

Chair: **Herbert Y. Meltzer, M.D.**
Department of Psychiatry
University of Chicago
Pritzker School of Medicine
Chicago, Illinois

Action of Hallucinogenic Drugs at Postsynaptic Serotonergic Receptors[1]

Barry L. Jacobs, Ph.D.,[2] James Heym, Ph.D.,[2] and Kurt Rasmussen, B.S.[2]

Hallucinogenic drugs such as LSD, psilocin, 2,5-dimethoxy-4-methylamphetamine (DOM), mescaline, and N,N-dimethyltryptamine (DMT) appear to constitute a distinct drug class based on their similar phenomenological effects in humans and the fact that cross-tolerance can be demonstrated between many of them. Theories regarding the mechanism of action of these drugs have gone through several distinct phases, all of them focusing on the role of serotonin. In the initial phase, in the mid-1950s, LSD was hypothesized to exert its psychological actions by blocking serotonin's synaptic effect. These conclusions, however, were based exclusively on pharmacological studies of LSD's action in the periphery, and were soon criticized. Following this, in the early 1960s, the emphasis shifted to an effect upon serotonin in the central nervous system (CNS), but without regard to the precise site of action, i.e., presynaptic or postsynaptic. In the mid-1960s, studies employing fluorescence histochemistry delineated the localization of serotonin-containing neurons within the CNS, their projection pathways, and their axon terminal distribution. This information provided the foundation for theories in the 1970s which proposed that the effects of LSD and related hallucinogens were mediated specifically by an action upon the cell bodies of serotonergic neurons (hereafter referred to as the "presynaptic" effect). Finally, in the fourth phase, emphasis has switched to the action of hallucinogenic drugs directly upon the target neurons of serotonergic projections (hereafter referred to as the "postsynaptic" effect). The data supporting this latest concept, which have been gathered primarily within the last few years, will be the subject of this brief review. Because of space limitations, many of the issues discussed will be either minimally referenced or unreferenced. For more detailed information, the reader is referred to two recent reviews (Jacobs & Trulson 1981; Jacobs, in press).

---

[1] This study was supported by USPHS Grant MH-23433 from the National Institute of Mental Health.

[2] Program in Neuroscience, Department of Psychology, Princeton University, Princeton, NJ 08544.

The authors will first describe the presynaptic model. This will provide a more meaningful and appropriate context in which to discuss the postsynaptic model, as well as afford the opportunity to compare and contrast the two models.

Based on previous neurochemical data which indicated that LSD decreased serotonin turnover, Aghajanian and his co-workers reasoned that this might be mediated by a decrease in the unit activity of serotonergic neurons. They therefore set out to test this directly be examining the effects of systemic administration of LSD on unit activity of brain serotonergic neurons in the chloral hydrate anesthetized rat (Aghajanian et al. 1968). They lowered tungsten microelectrodes into the brain area with the densest aggregation of serotonergic neurons, the midbrain dorsal and median raphe nuclei, and observed the slow (1-2 spikes/sec) and regular discharge pattern that appears to characterize all serotonergic neurons in brain. When LSD was then administered intravenously, a dose of 25-50 μg/kg was sufficient to cause a complete suppression of activity. By contrast, none of the neurons outside of the raphe ceased firing in response to the drug. An important control experiment in this series demonstrated that, unlike LSD, brom-LSD exerted virtually no effect on serotonergic neurons in doses of 25-50 μg/kg. These same investigators went on to test the effects of a variety of systemically administered psychoactive drugs, including several hallucinogens (Aghajanian et al. 1970). They reported that DMT produced an effect very similar to that of LSD, but at significantly higher doses (approximately 700 μg/kg). Interestingly, mescaline and DOM depressed the activity of only a subgroup of midbrain raphe neurons, those in the ventral portion of the dorsal nucleus. Atropine, scopolamine, phencyclidine, and chlorpromazine were essentially without effect on serotonergic unit activity. In separate studies, Aghajanian's group also showed that psilocin was effective in depressing serotonergic unit activity, whereas amphetamine consistently increased the activity of these cells. Finally, an experiment from the authors' laboratory indicated that low doses (20 μg/kg, i.v.) of the hallucinogen 5MeODMT also exerted a potent depressant effect on the activity of serotonergic neurons (Mosko & Jacobs 1977).

The next issue was to determine whether LSD and related hallucinogens exerted their depressant effects directly on serotonergic neurons, or whether this action was mediated indirectly, perhaps by some type of feedback loop. The most straightforward approach to this question involved the direct application of LSD, psilocin, DMT, 5MeODMT, and mescaline onto neurons in the area of the dorsal raphe nucleus by means of microiontophoresis. In all cases, excluding those experiments with mescaline, the iontophoretic application of the hallucinogenic drugs produced a profound suppression of serotonergic unit activity at low ejection currents (Haigler & Aghajanian 1973; Aghajanian & Haigler 1975). This supported the hypothesis that the effect of hallucinogenic drugs is mediated by a direct action upon serotonergic neurons, possibly one mediated by serotonin receptors. Since the iontophoretic application of mescaline failed to depress serotonergic unit activity, even in the subset of those cells that were affected by systemic administration, it was concluded that unlike the other hallucinogens, mescaline's effect on serotonergic neurons is mediated indirectly.

A final, very important issue remained to be resolved. If the action of hallucinogenic drugs is mediated by a depressant action on serotonin-containing neurons, why then are not compounds such as l-5-hydroxytryptophan (5-HTP) and l-tryptophan, both of which depress raphe unit activity, hallucinogenic? The answer, at least in the context of this theoretical framework, is contained in two elegant experiments by Haigler and Aghajanian (1973, 1974). When serotonin is iontophoretically applied onto serotonergic neurons in the raphe nuclei and onto their postsynaptic target neurons in the ventral lateral geniculate or amygdala, it is approximately equipotent in depressing unit activity at these various sites. Contrary to this, when LSD or psilocin is tested in the same manner, it has a much more profound effect on the serotonergic cells than on their target neurons. In other words, hallucinogenic drugs have an action that appears to be *preferential* for serotonin-containing neurons. Thus, it is reasoned, when brain levels of serotonin are elevated by administration of its precursors 1-5-HTP or l-tryptophan (or any of a variety of other pharmacologic means), serotonergic unit activity is depressed, but so is the activity of target neurons receiving serotonergic inputs. On the other hand, when LSD is administered systemically, it acts to depress serotonergic unit activity, while having little direct effect on target neurons. Because much of serotonin's action on target neurons in the forebrain is inhibitory, it is hypothesized that the ultimate effect of LSD's preferentially depressant action on serotonergic neurons is to produce a disinhibition of target neurons, which is precisely the opposite of the depression produced by elevated synaptic levels of serotonin.

Since this disinhibition will be manifested most impressively in those areas with the densest aggregation of serotonin axon terminals, i.e., portions of the visual system and limbic system, an obvious neuronal model is available to account for two of the major aspects of hallucinogenic drug action: visual hallucinations and alterations of affect. This, then, is the presynaptic serotonergic model of hallucinogenic drug action. It is based on several assumptions: 1) All hallucinogenic drugs strongly depress the activity of at least some group of serotonergic neurons. 2) Serotonin's synaptic action in the forebrain is strictly inhibitory. 3) Hallucinogenic drugs exert little direct effect on postsynaptic serotonergic receptors. There is now reason to question the validity of all three of these assumptions, however, in this review, focus will be on only the first and the third.

All of the electrophysiological studies described above were conducted in anesthetized and/or immobilized animals, thus making it impossible to relate changes in unit activity produced by hallucinogenic drugs to changes in behavior. If our ultimate goal is to draw conclusions about functional relationships, such analyses are imperative. In an attempt to provide a more stringent test of the presynaptic model of hallucinogenic drug action, the authors decided to administer these drugs to awake freely moving cats and to study changes in the activity of brain serotonergic neurons concomitantly with changes in behavior. In order to analyze the behavioral effects of the hallucinogens, they employed an observational method of scoring changes in the spontaneous occurrence of specific response categories in the cat (Jacobs et al. 1977). In order to record the activity of single units in freely moving cats, they developed a technique that employs bundles of flexible large-tipped microwires (32 or 64 μm diam.) rather than the traditional small-tipped high-impedance metal or glass microelectrodes (Jacobs et al. in press). These bundles of microwires can be advanced through the brain by means of an attached mechanical microdrive. Using this technique, the authors had great success in isolating serotonergic units in various raphe nuclei of the cat brainstem (e.g., dorsalis, centralis superior, and pallidus). This technique also allows them to "hold" cells for long periods of time (from several hours up to several days) and in spite of vigorous movements on the part of the cat.

The authors first describe their experiments with 5-MeODMT, which has a molecularly more simple structure than LSD and produced more clearcut data. They were particularly interested in the temporal correlations between the onset, peak, and offset of the behavioral and unit data, and whether or not the behavioral and unit data would have a correlated dose dependency. In order to examine these issues, they administered 5-MeODMT in doses of 10, 25, 50, 100, or 250 μg/kg intramuscular (i.m.) and monitored the activity of serotonin-containing neurons in the dorsal raphe nucleus in conjunction with any gross behavioral effects (Trulson & Jacobs 1979a). Under baseline conditions, serotonergic neurons in the awake freely moving cat discharge with the same characteristic slow rhythmic activity seen in the anesthetized rat. Following injections of 5-MeODMT, serotonergic unit activity was rapidly depressed in a dose-dependent manner, and dose-dependent increases were observed in the rate of limb flicking and abortive grooming. Furthermore, the onset, peak, and offset of the behavioral effects were temporally correlated with the onset, peak, and offset of changes in unit activity. By directly correlating behavioral changes with changes in the activity of serotonin-containing neurons, the authors at the time, felt that this study provided perhaps the strongest direct evidence for the presynaptic serotonin hypothesis of hallucinogenic drug action.

When this approach was extended to the study of LSD, the results were generally similar to those seen with 5-MeODMT, but with two critical differences (Trulson & Jacobs 1979b). First, a 50 μg/kg dose of LSD produced a depression of serotonergic unit activity lasting, on the average, 3-4 hours, while the behavioral effects lasted for at least 6-8 hours. Second, when the 50 μg/kg dose was readministered 24 hours later, it produced little or no behavioral effect (tolerance), but the effect on serotonergic unit activity was as large as two dissociations of unit activity and behavior, the authors began to question the validity of the presynaptic serotonergic hypothesis.

This skepticism has been bolstered by their more recent experiments with DOM, mescaline, and psilocin (Trulson et al. 1981). With all three drugs, they observed the same temporal dissociations of serotonergic unit activity and behavior as observed with LSD. In addition, a low dose of psilocin (25 μg/kg, i.p.) produced no significant decrease in serotonergic unit activity in any of the cells tested, however, it did produce significant behavioral effects. Mescaline (5 mg/kg, i.p.) produced no overall significant change in unit activity (the discharge of three cells increased, three decreased, and two showed no change), but did produce large behavioral effects. Similarly, a low dose of DOM (50 μg/kg, i.p.) did not significantly affect any of the serotonergic units tested, but did have a significant behavioral effect. The highest dose of DOM (1 mg/kg), produced only increases in serotonergic unit activity, but nonetheless elicited significant behavioral changes. Furthermore, cells in the ventral portion of the dorsal raphe nucleus did not apoear to be preferentially sensitive to either mescaline or DOM. Finally, although not extensively examined, the authors observed similar results, with various hallucinogens, in experiments on serotonergic neurons in nucleus centralis superior (Rasmussen, Heym, and Jacobs, unpublished observations).

Also examined were the effects of LSD upon unit activity of neurons in nucleus raphe pallidus, the most caudal group of serotonergic neurons in the cat brainstem. Somewhat surprisingly, the majority of neurons examined were almost completely unresponsive to doses of LSD (50 μg/kg, i.p.) and 5-MeODMT (50 μg/kg, i.m.) that produced potent behavioral effects (Heym, Steinfels, and Jacobs, submitted for publication).

The authors most recent study in this series provided perhaps the most damaging evidence to the presynaptic serotonergic hypothesis of hallucinogenic drug action, and began to focus their attention on the postsynaptic actions of these drugs. When cats were administered mianserin (0.1-1.0 mg/kg, i.p.), a serotonin postsynaptic antagonist, 30 minutes prior to LSD (50 μg/kg) or DOM (250 μg/kg), it blocked their behavioral effects in a dose-dependent manner. This did not appear to be due to nonspecific effects, since the drug produced no decrease in spontaneous activity and the animals did not appear to be sedated or cataleptic. Furthermore, mianserin exerted no blocking action on the behavioral effects of the dopamine agonist apomorphine. When animals were pretreated with mianserin (1 mg/kg, i.p.) and then administered LSD (50 μg/kg, i.p.) 30 minutes later, an almost complete blockade of the behavioral effects of LSD was observed, but no alteration of the 40-60 percent depression of serotonergic unit activity that LSD typically produces in neurons in nucleus raphe dorsalis and centralis superior (Heym, Rasmussen, and Jacobs, unpublished observations).

There are a number of other reasons for emphasizing the behavioral importance of the direct serotonergic postsynaptic effects of hallucinogenic drugs. However, space limitations will allow only a brief description of each of them.

1. Administration of a number of different hallucinogens produces behavioral effects indicative of a direct serotonergic agonist action at postsynaptic receptor sites. This is the elicitation of the so-called "serotonin syndrome" (Jacobs 1976). Evidence that this is a direct action is provided by studies which show that the effect is not blocked by prior serotonin depletion. Repeated administration of LSD diminishes its behavioral potency (tolerance) (Trulson et al. 1976). This is unaccompanied by a change in sensitivity of serotonergic neurons to LSD, but is accompanied by a decrease in the number of available serotonergic postsynaptic receptor binding sites (Trulson & Jacobs 1979c).

2. Studies in a variety of different species, including humans, demonstrated that prior depletion of serotonin enhances the behavioral effects of hallucinogenic drugs. In many of these cases there is direct evidence for the presence of serotonergic postsynaptic supersensitivity at the time the hallucinogens are administered.

3. In a variety of different paradigms, including drug discrimination, operant responding, and spontaneous behavior, the behavioral effects, in rat, of a number of hallucinogens can be effectively blocked by several different serotonin antagonist drugs.

4. Chronic administration of a monoamine oxidase inhibitor (MAOI) for 1 or 2 weeks can totally block the behavioral effects of LSD and other hallucinogens in rat, cat, and humans. This blocking action may persist for as long as 2 weeks

following withdrawal from the MAOI. Neurochemical evidence strongly indicates that this decreased response to hallucinogenic drugs is mediated by a decrease in the availability of postsynaptic binding sites for serotonin.

5. Binding of [^{3}H]-LSD, whether examined autoradiographically or using receptor specific binding assays, is unchanged by destruction of serotonergic neurons. Since much of this binding can be displaced with serotonin, it indicates that it is associated with serotonin receptors but, apparently, not those localized on various aspects of the presynaptic neuron.

In summary, it is well-known that hallucinogens, such as LSD, psilocin, mescaline, DMT and DOM, produce similar effects in humans and also display cross-tolerance of action. The most parsimonious explanation for these similarities is that these drugs share, at least to some extent, a common biological action. Evidence from a variety of disciplines, some of which was reviewed here, indicates that this common action is exerted upon the brain serotonin system. (Although various hallucinogens may interact with neurotransmitter systems other than serotonin, they do not do so universally.) It may be useful at this point to review what is known regarding the synaptic interactions between the hallucinogens and serotonin. Hallucinogens produce: 1) depression of the activity of serotonergic neurons (the so-called presynaptic action); 2) a modest inhibitory action at serotonin postsynaptic receptor sites in the forebrain, especially subcortically; 3) a strong antagonist action to serotonin's excitatory effects on its postsynaptic target sites in a variety of brain areas, especially in cerebral cortex and brainstem; and 4) a potentiation (or facilitation) of the facilitatory effect exerted by serotonin on excitatory inputs to its target sites in the brainstem and spinal cord. Thus, the interactions of the hallucinogens with the brain serotonin system are complex, with mixed agonist, antagonist, and modulatory effects. As argued above, however, the critical effect is probably exerted directly upon cells postsynaptic to brain serotonin-containing neurons.

References

Aghajanian, G.K., Foote, W.E., and Sheard, M.H. Lysergic acid diethylamide: Sensitive neuronal units in the midbrain raphe. *Science*, 161:706-708, 1968.

Aghajanian, G.K., Foote, W.E., and Sheard, M.H. Action of psychotogenic drugs on midbrain raphe neurons. *J. Pharmacol. Exp. Ther.*, 171:178-187, 1970.

Aghajanian, G.K., and Haigler, H.J. Hallucinogenic indoleamines: Preferential action upon presynaptic serotonin receptors. *Psychopharmacol. Comm.*, 1:619-629, 1975.

Haigler, H.J., and Aghajanian, G.K. Mescaline and LSD: Direct and indirect effects on serotonin-containing neurons in brain. *Eur. J. Pharmacol.*, 21:53-60, 1973.

Haigler, H.J., and Aghajanian, G.K. Lysergic acid diethylamide and serotonin: A comparison of effects on serotonergic neurons and neurons receiving a serotonergic input. *J. Pharmacol. Exp. Ther.*, 188:688-699, 1974.

Heym, J., Steinfels, G.F., and Jacobs, B.L. Medullary serotonergic unit activity in freely moving cats: Insensitivity to hallucinogenic drugs. (Submitted for publication)

Jacobs, B.L. An animal behavioral model for studying central serotonergic synapses. *Life Sci.*, 19:777-786, 1976.

Jacobs, B.L. Mechanism of action of hallucinogenic drugs: Focus upon postsynaptic serotonergic receptors. In: Grahame-Smith, D.G., Hippius, H., and Winokur, G. (eds.), *Psychopharmacology*. Amsterdam: Excerpta Medica. (In press)

Jacobs, B.L., Heym, J., and Steinfels, G.F. Physiological and behavioral analysis of raphe unit activity. In: Iversen, L.L., Iversen, S.D., and Snyder, S.H. (eds.), *Handbook of Psychopharmacology*. New York: Plenum Press. (In press)

Jacobs, B.L., and Trulson, M.E. The role of serotonin in the action of hallucinogenic drugs. In: Jacobs, B.L., and Gelperin, A. (eds.), *Serotonin Neurotransmission and Behavior*. Cambridge: MIT Press, 1981, pp. 366-400.

Jacobs, B.L., Trulson, M.E., and Stern, W.C. Behavioral effects of LSD in the cat: Proposal of an animal behavior model for studying the actions of hallucinogenic drugs. *Brain Res.*, 132:301-314, 1977.

Mosko, S.S., and Jacobs, B.L. Electrophysiological evidence against negative neuronal feedback from the forebrain controlling midbrain raphe unit activity. *Brain Res.*, 119:291-303, 1977.

Trulson, M.E., Heym, J., and Jacobs, B.L. Dissociations between the effects of hallucinogenic drugs on behavior and raphe unit activity in freely moving cats. *Brain Res.*, 215:275-293, 1981.

Trulson, M.E., and Jacobs, B.L. Effects of 5-methoxy-N, N-dimethyltryptamine on behavior and raphe unit activity in freely moving cats. *Eur. J. Pharmacol.*, 54:43-50, 1979a.

Trulson, M.E., and Jacobs, B.L. Dissociations between the effects of LSD on behavior and raphe unit activity in freely moving cats. *Science*, 205:515-518, 1979b.

Trulson, M.E., and Jacobs, B.L. Alterations of serotonin and LSD receptor binding following repeated administration of LSD. *Life Sci.*, 24:2053-2062, 1979c.

Trulson, M.E., Ross, C.A., and Jacobs, B.L. Behavioral evidence for the stimulation of CNS serotonin receptors by high doses of LSD. *Psychopharmacol. Comm.*, 2:149-164, 1976.

Interaction of Monoamine Blocking Agents with Behavioral Effects of N,N-Dimethyltryptamine

David M. Stoff,[1,3] **Dilip V. Jeste, M.D.,**[1]
Egidio A. Moja, M.D.,[2] **Ken A. Stauderman,**[1]
and Richard J. Wyatt, M.D.[1]

Among the methylated hallucinogenic indoleamines, N,N-dimethyltryptamine (DMT) has been the most extensively studied concerning its possible role in schizophrenia (Gillin et al. 1976, 1978). Since the 5-hydroxytryptamine (5-HT) deficiency hypothesis for LSD was first proposed in the early 1950s, an impressive body of neurochemical and electrophysiological evidence has accumulated suggesting that DMT (and other indole hallucinogens) acts via interference of central 5-HT neurotransmission (Jacobs & Trulson 1981). In addition to possessing a serotonergic component, DMT may exert some of its effects by acting on other interrelated neurotransmitter systems. While there are a large number of studies demonstrating an interaction between drugs affecting the major monoamines (serotonin, dopamine, norepinephrine) in brain and some of the behavioral effects of other hallucinogens (Wyatt et al. 1976), similar data for DMT are sparse and conflicting. The human data are consistent with a 5-HT deficiency hypothesis since the monoamine oxidase inhibitor (MAOI), iproniazid, attenuated the psychological effects of DMT (Sai-Halasz 1963) while the serotonin receptor antagonists (2-bromo-LSD, methysergide) potentiated its effects (Sai-Halasz 1962). However, different results have been reported in animals where MAOIs potentiate some autonomic and behavioral effects caused by DMT (Moore et al. 1975; Vasko et al. 1974) while DMT-induced behavioral effects are antagonized, potentiated, or unaffected by different 5-HT receptor blockers (Corne & Pickering 1967; Jenner et al. 1980; Kovacic et al. 1978; Smythies et al. 1972; Winter 1972). Although neuroleptics block some behavioral effects of DMT (Jenner et al. 1980; Quock et al. 1979; Shah & Hedder 1978), similar blockade occurs among structurally unrelated hallucinogens and even these effects can be attributed to a behaviorally depressant action of the neuroleptic itself.

The authors previously reported DMT-induced disruption of rat shuttlebox avoidance (Stoff et al. 1977), an effect that occurs under conditions where the 5-HT behavioral syndrome was not observed. Here, they present a detailed series of dose response studies showing that various monoamine blocking agents (dopaminergic: chlorpromazine, clozapine, haloperidol, pimozide, thioridazine, noradrenergic: phenoxybenzamine, propranolol; serotonergic: cinanserin, cyproheptadine, methiothepin, methysergide) were unable to influence the DMT effect, at doses which by themselves did not alter avoidance behavior; as expected, pargyline potentiated DMT (*see* Table). Furthermore, DMT-induced disruption was uninfluenced by chronic neuroleptic treatment and pretreatments with 1) 1-methyl-1, 2, 5, 6-tetrahydropyridine-3-(N-, N-diethylcarboxamide) hypothesized to act at the site of action for DMT (Smythies et al. 1972); 2) BC-105, which blocks some behavioral effects of the close chemical relative, 5-methoxy-DMT (Winter 1978); or 3) alpha-methyl-para-tyrosine (AMPT). Some of the antagonists employed have more than one pharmacological action and little, if anything, is known about the ability of these compounds to interact with the site of action of DMT.

The authors' results may be consistent with the action of DMT through systems besides the major monoamines. Other data suggest the involvement of tryptamine receptors in the action of LSD and similar compounds (Martin et al. 1978) and tryptamine, the proposed biosynthetic precursor of DMT, causes similar effects to DMT in the same animal model (Vogel & Cohen 1977). More recently, an involvement of the opioids has been suggested since DMT-induced bar press disruption was antagonized by morphine and methadone and potentiated by naloxone (Ruffing & Domino 1981; Ruffing et al. 1979). The role of these and other putative neurotransmitter and peptide systems in the action of DMT deserves further attention.

---

[1] Adult Psychiatry Branch, National Institute of Mental Health, St. Elizabeths Hospital, Washington, DC 20032.

[2] Institute of Neurology and Psychiatry, University of Cagliari, Cagliari, Italy.

[3] Current Address: Department of Psychiatry, University of Chicago, Chicago, IL 60637.

Table

Effects of Monoamine Blocking Agents on DMT-Disruption

Pretreatment	Dose (mg/kg)	Conditioned Avoidance Responses (mean ± SEM)		
		Pretreat Time (mins)	Saline	DMT 4 mg/kg
Saline	–	30	89.3 ± .5	65.5 ± 2
AMPT	100	3 hrs	88.3 ± 1.2	58.4 ± 6.9
BC-105	12	60	90 ± 3	67 ± 10
Chlorpromazine	2.5	30	85 ± 2.1	58 ± 6.2
Cinanserin	35	60	91 ± 7	65.6 ± 12.4
Clozapine	2.5	30	81.6 ± 4.5	69.7 ± 4.4
Clozapine, 15 times	2.5	30	85.2 ± 1.4	61 ± 3.8
Cyproheptadine	20	15	86.2 ± 5.1	61 ± 5.6
Haloperidol	.05	30	87.8 ± 4.4	69.4 ± 9.8
Haloperidol, 14 times	.10	30	88.9 ± .7	65 ± 7.1
Methiothepin	.07	30	82.5 ± 5.1	61 ± 4.1
Methysergide	40	30	87.8 ± 4.5	65 ± 9
Pargyline	75	24 hrs	87.6 ± 1.8	46.5 ± 4.1*
Phenoxybenzamine	1.25	60	78 ± 4.9	55.8 ± 12.3
Pimozide	.20	60	83.6 ± 2.6	67.8 ± 7.1
Pimozide, 14 times	.20	60	87.4 ± 2.1	67 ± 6.2
Propanolol	20	15	94.2 ± 1.7	65 ± 2.6
Thioridazine	3.75	30	83.3 ± 4.1	64 ± 4.4
Thioridazine, 14 times	7.5	30	86.2 ± 2.1	63 ± 2.1
THPC	20	30	88.4 ± 7.4	67.4 ± 13.4

Values are expressed as the number of avoidance responses over a 100-trial session; drug pretreatments were tested after criteria of a high and stable avoidance rate was achieved (*see* Stoff et al. 1977).

*$p < .05$; matched t for DMT vs. saline, independent t for DMT vs. drug pretreatment.

References

Corne, S.J., and Pickering, R.W. A possible correlation between drug induced hallucinations in man and a behavioral response in mice. *Psychopharmacology (Berlin)*, 11:65-68, 1967.

Gillin, J.C., Kaplan, J., Stillman, R., and Wyatt, R.J. The psychedelic model of schizophrenia: The case of N,N-dimethyltryptamine. *Am. J. Psychiatry*, 133:203-208, 1976.

Gillin, J.C., Stoff, D.M., and Wyatt, R.J. Transmethylation hypothesis: A review of progress. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress*. New York: Raven Press, 1978, pp. 1097-1112.

Jacobs, B.L., and Trulson, M.E. The role of serotonin in the action of hallucinogenic drugs. In: Jacobs, B.L., and Gelperin, A. (eds.), *Serotonin: Neurotransmissions and Behavior*. New York: Pergamon Press, 1981, pp. 366-400.

Jenner, P., Marsden, C.D., and Thanki, C.M. Behavioral changes induced by N,N-dimethyltryptamine in rodents. *Br. J. Pharmacol.*, 69:69-80, 1980.

Kovacic, B., Lu, L.J.W., Ruffing, D., and Domino, E.F. Interactions of partial LSD analogs with behavioral disrupting effects of LSD and DMT in the rat. *Eur. J. Pharmacol.*, 47:37-44, 1978.

Martin, W.R., Vaupel, D.B., Sloan, J.W., Bell, J.A., Nozaki, M., and Bright, L.D. The mode of action of LSD-like hallucinogens and their identification. In: Stillman, R.C., and Willette, R.E. (eds.), *The Psychopharmacology of Hallucinogens*. New York: Pergamon Press, 1978, pp. 118-125.

Moore, R.H., Demetriou, S.K., and Domino, E.F. Effects of iproniazid, chlorpromazine, and methiothepin on DMT induced changes in body temperature, pupillary dilatation, blood pressure, and EEG in the rabbit. *Arch. Int. Pharmacol. Ther.*, 213:64-72, 1975.

Ruffing, D.M., and Domino, E.F. Effects of selected opioid agonists and antagonists on DMT- and LSD-25-induced disruption of food-rewarded bar pressing behavior in the rat. *Psychopharmacology (Berlin)*, 75:226-230, 1981.

Ruffing, D., Kovacic, B., Demetriou, S., and Domino, E.F. Naloxone enhancement of DMT and LSD-25 induced suppression of food-rewarded bar pressing behavior in the rat. *Psychopharmacology (Berlin)*, 62:207-210, 1979.

Quock, R.M., Lum, M.H., and Small, S.F. Interaction of N,N-dimethyltryptamine with central monoaminergic blocking drugs. *Proc. West. Pharmacol. Soc.*, 22:217-218, 1979.

Sai-Halasz, A. The effect of antiserotonin on the experimental psychosis induced by dimethyltryptamine. *Experientia*, 18:137-138, 1962.

Sai-Halasz, A. The effect of MAO inhibition on the experimental psychosis induced by dimethyltryptamine. *Psychopharmacology (Berlin),* 4:385-388, 1963.
Shah, N.S., and Hedder, M.P. Behavioral effects and metabolic fate of N,N-dimethyltryptamine in mice pretreated with β-diethylaminoethyl-diphenylpropyl acetate (SKF 525-A), iproniazid, and chlorpromazine. *Pharm. Biochem. Behav.,* 8:351-356, 1978.
Smythies, J.R., Beaton, J.M., Bennington, F., and Morin, R.D. The design of some new compounds to block psychotomimetic drugs. *Eur. J. Pharmacol.,* 17:270-272, 1972.
Stoff, D.M., Moja, E.A., Gillin, J.C., and Wyatt, R.J. Dose response and time course effects of N,N-dimethyltryptamine on disruption of rat shuttlebox avoidance. *Biol. Psychiatry,* 12:339-346, 1977.
Vasko, M.R., Lutz, M.P., and Domino, E.F. Structure-activity relations of some indolealkylamines in comparison to phenethylamines on motor activity and acquisition of avoidance behavior. *Psychopharmacology (Berlin),* 36:49-58, 1974.
Vogel, W.H., and Cohen, I. Effects of tryptamine on the conditioned avoidance response in rats. *Brain Res.,* 122:162-164, 1977.
Winter, J.C. Comparison of chlordiazepoxide, methysergide, and cinanserin as modifiers and antagonists of N,N-dimethyltryptamine. *Arch. Int. Pharmacodyn. Ther.,* 197:147-159, 1972.
Winter, J.C. Stimulus properties of phenethylamine hallucinogens and lysergic acid diethylamide: The role of 5-hydroxytryptamine. *J. Pharmacol. Exp. Ther.,* 204:416-423, 1978.
Wyatt, R.J., Cannon, E.H., Stoff, D.M., and Gillin, J.C. Interactions of hallucinogens at the clinical level. *Ann. NY Acad. Sci.,* 281:486-586, 1976.

Evidence for Opioids as Partial Antagonists for Indole Hallucinogens

Edward F. Domino, M.D.,[1, 2] **and Diane M. Ruffing,**[2]

Various observations have supported the hypothesis that endogenous opioid peptides are involved in psychoses either therapeutically or pathogenically (Rimón et al. 1980; Pickar et al. 1981). Prior to the advent of neuroleptics, opioids such as morphine were used historically to treat mental disease. Hence, the role of opioids in psychoses is obscure and complex. It was decided to use an animal model of drug-induced psychotic behavior to investigate this interaction further (Ruffing et al. 1979; Ruffing & Domino 1981). Several opioid agonists, antagonists, and synthetic enkephalin analogues were studied on N,N-dimethyltryptamine (DMT) and lysergic acid diethylamide (LSD-25) induced disruption of food-rewarded FR_4 bar-pressing behavior in the rat. The striking interactions observed are reported herein.

Method

Adult male Holtzman rats were maintained at 70 percent of their expected free-feeding weight. Stable food-rewarded fixed ratio 4 (FR_4) bar pressing behavior was established, followed by daily 60-minute bar pressing sessions for a minimum of days prior to injections. Animals were then randomly assigned to groups ($N = 5$-12), scheduling each rat to serve as its own control to compare hallucinogen-induced effects with and without assigned pretreatment drugs. Control groups were pretreated with 0.9 percent NaCl intraperitoneally (i.p.) prior to DMT (3.2-10.0 mg/kg) and LSD (0.1 mg/kg) injections. A minimum 7-day drug-free interval was observed between scheduled injections. Predetermined behaviorally noneffective pretreatment drug doses given 10-20 minutes prior to DMT or LSD were as follows: morphine sulfate and methadone hydrochloride (0.32-3.2 mg/kg), (+)-MR 2267 (5.6-10.0 mg/kg), (−)-MR 2266 (3.2 mg/kg), (+)-naloxone hydrochloride (3.2 mg/kg), (−)-naloxone hydrochloride (1.0-3.2 mg/kg), naltrexone (1.16-3.7 mg/kg), (+)- and (−)-WIN 44,441-2/3 enantiomers (1.47-3.52 mg/kg), Lilly 127623 (0.0032-0.32 mg/kg), and FK 33-824(0.0001-0.01 mg/kg). All drug dosages refer to free base and were administered i.p. Two-tailed Student's *t*-test paired comparison determinations, calculated according to Snedecor (1956), were used to analyze pretreatment and/or hallucinogen drug effect interactions (i.e., antagonism, potentiation, or no effect). Due to the limited quantity of (+)-naloxone HCl and (−)-MR 2266, incomplete dose-effect relations are reported.

---

[1] Department of Pharmacology, University of Michigan, Ann Arbor, MI 48109.

[2] Lafayette Clinic, Detroit, MI 48207.

Results

DMT (3.2-10.0 mg/kg) and LSD (0.1 mg/kg) induced a reproducible disruption of food-rewarded bar pressing. Characteristic DMT and LSD-induced gross behavioral effects (evident within 2-5 minutes following i.p. injections) consisted of: lying quietly with the eyes open in an excessively flattened position for prolonged intervals, periodic Straub tail, muscular twitching and/or body movements, circling in a flattened position or reverse crawling, splayed and/or extension of the hind limbs, periodic stereotypic repetitious body movements, sustained periods of arching, and disinterest in food and/or bar pressing. The DMT and LSD-induced gross behavioral effects described above or with pretreatment drugs were consistent in all groups tested excepting morphine, methadone, and (−)-MR 2266 pretreated groups. In the morphine pretreated animals fewer and less intense gross behavioral effects were observed with periodic interest in food and/or bar pressing. Paradoxically, intensified gross behavioral effects were observed in the methadone and (−)-MR 2266 pretreated groups (i.e., increased and excessive flattening with frequent sustained repetitious head/body movements and markedly increased Straub tail). At the cessation of drug effects the rats would appear normal and abruptly start and continue bar pressing at pre-injection response rates.

The opioid agonist pretreatment groups (Figure 1) showed selective biphasic effects, i.e., morphine (0.32-1.0 mg/kg) and methadone (0.32 mg/kg) antagonized the effects of DMT and LSD-induced bar pressing disruption, whereas larger doses of morphine (3.2 mg/kg) and methadone

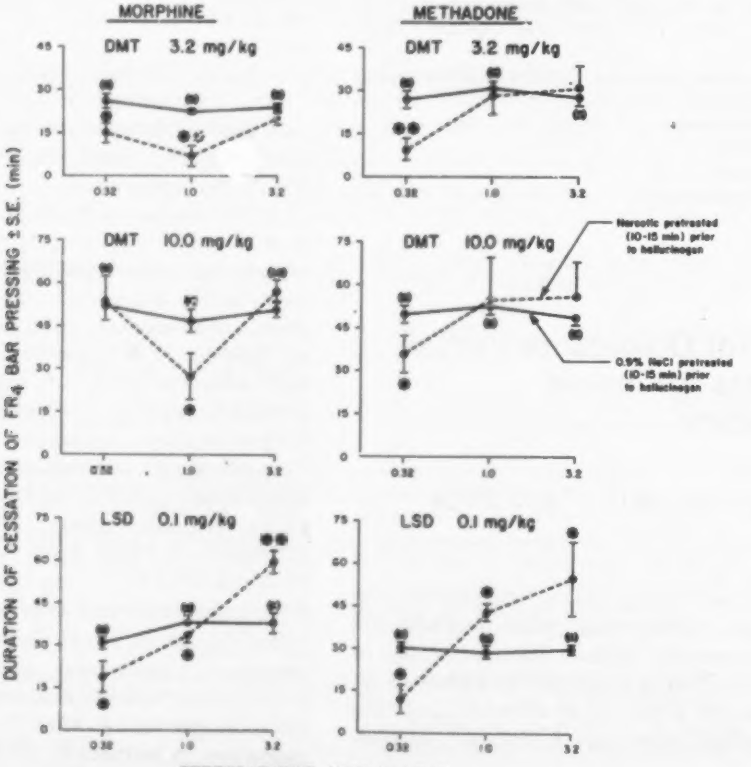


FIGURE 1. Effects of morphine and methadone pretreatment on DMT and LSD-induced disruption of FR_4 bar pressing behavior in the rat.

(1.0-3.2 mg/kg) selectively potentiated only LSD-induced effects with no differences noted in the DMT groups. The data indicate morphine as the more effective antagonist for DMT (3.2 mg/kg) and LSD-induced activity.

Conversely, the opioid antagonists, naloxone and naltrexone in pretreatment doses of 1.0-3.2 and 1.16-3.7 mg/kg, respectively, potentiated the behavioral DMT and LSD-induced effects as shown in Figure 2. Potentiation of DMT-induced effects was attributed to a stereospecific opioid antagonist effect of (−)-naloxone in that the (+)-naloxone enantiomer failed to interact or potentiate DMT (Ruffing & Domino 1981).

Pretreatment with stereo-isomers of two selected synthetic opioid antagonists, (+)-WIN 44,441-2, (−)-WIN 44,441-3, (+)-MR 2267, and (−)-MR 2266, unexpectedly demonstrated no interaction with DMT (3.2 mg/kg) induced disruption of FR_4 behavior, whereas both (+)- and (−)-WIN 44,441 enantiomers selectively potentiated the behavioral induced LSD effects, while only the (−)-MR 2266 stereo-isomer selectively antagonized behaviorally induced LSD effects (Figure 3).

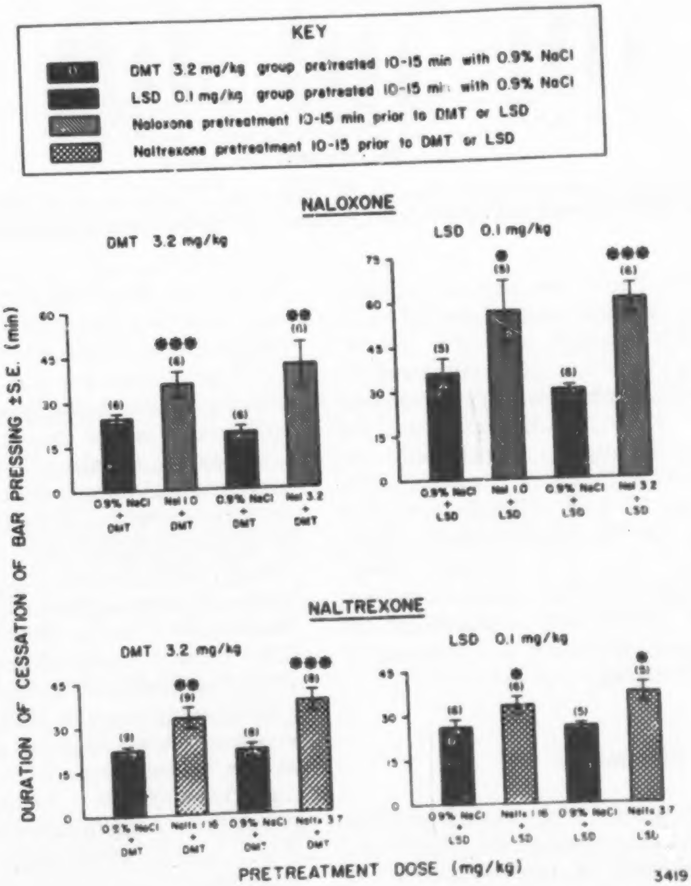


FIGURE 2. Potentiation of DMT and LSD-induced disruption of FR_4 bar pressing behavior in rats pretreated with naloxone and naltrexone.

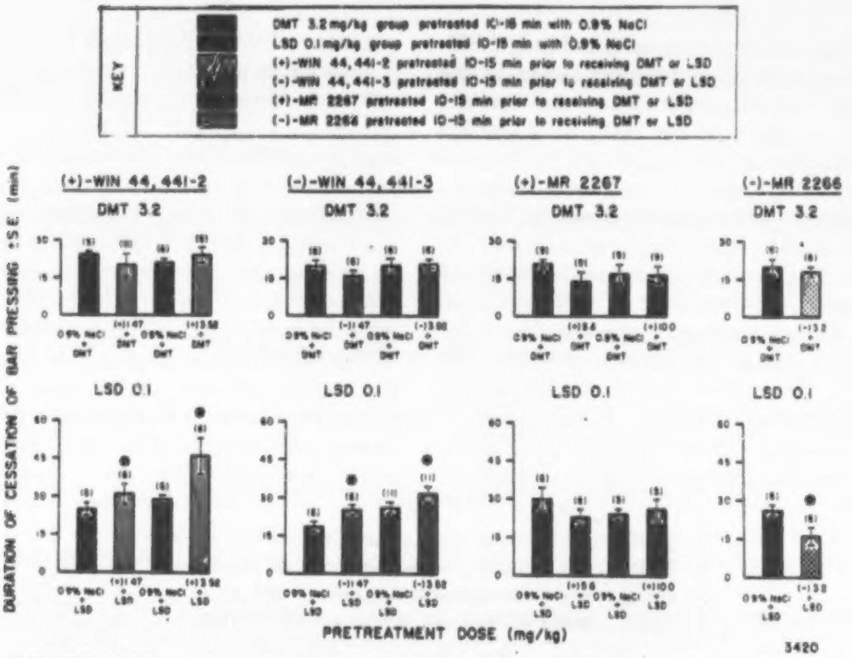


FIGURE 3. Effects of pretreatment with WIN 44,441-2, WIN 44,441-3, MR 2266, and MR 2267 on DMT and LSD-induced disruption of FR$_4$ bar pressing behavior in the rat.

As shown in the Table, the peptide synthetic enkephalinanalog pretreatment doses of Lilly 127623 (0.01-0.32 mg/kg) and FK 33-824 (0.001-0.01 mg/kg) significantly antagonized the effects of DMT (3.2 mg/kg), while pretreatment doses of Lilly 127623 (0.10-0.32 mg/kg) and FK 33-824 (0.00032-0.01 mg/kg) significantly antagonized the effects of DMT (3.2 mg/kg), while pretreatment doses of Lilly 127623 (0.10-0.32 mg/kg) and FK 33-824 (0.00032-0.01 mg/kg significantly antagonized LSD-induced effects. Additionally, Lilly 127623 (0.032 mg/kg) pretreatment also significantly antagonized the behaviorally induced disruptive bar pressing effects of DMT 10.0 mg/kg.

Discussion

The results of the present study extend previous observations that naloxone potentiated DMT and LSD-induced disruption of food-rewarded bar pressing in the rat (Ruffing et al. 1979). It is generally known that the biologically active narcotic antagonist is the (−)-naloxone isomer. Thus, it is of special interest that (+)-naloxone was inactive in potentiating the effects of DMT, confirming stereospecificity.

There is evidence that DMT and LSD, while sharing similar hallucinogenic effects, also show differences in the extent of dopaminergic and serotonergic agonist effects. For example, LSD has been shown to produce potent dopaminergic activity not produced by DMT (Nichols 1981). It is also abundantly clear that there are multiple neurotransmitter and opioid receptors, so that many of these agents differ in their molecular mechanism of action (Snyder & Goodman 1980). The present study indicates that the various opioid agonists and antagonists have very complex interactions with DMT and LSD. Although no simple theory explains all of the data obtained in this investigation, the present study indicates that there are very important interactions between these hallucinogens and opioids in the rat. The dramatic antagonistic effects of the opioid peptides, Lilly 127623 and FK 33-824, are especially prominent and deserve additional investigation with various behavioral paradigms in different species of animals including man.

Table

Mean Duration of DMT and LSD-Induced Disruption of Food-Rewarded FR_4 Bar Pressing in Control 0.9% NaCl Pretreated and Corresponding Lilly 127623 or FK 33-824 Pretreated Rats

	Mean duration of FR_4 bar pressing disruption (± S.E.)							
	DMT 3.2 mg/kg (i.p.)				LSD 0.1 mg/kg (i.p.)			
Pretreatment Drug/Dose mg/kg (i.p.)	(N)	Control 0.9% NaCl Pretreated	Drug Pretreated	p^a	(N)	Control 0.9% NaCl Pretreated	Drug Pretreated	p^a
Lilly 127623 (0.0032)	(6)	26 ± 2	27 ± 3	N.S.	—	—	—	—
Lilly 127623 (0.01)	(10)	27 ± 2	12 ± 3	***	—	—	—	—
Lilly 127623 (0.032)	(10)	28 ± 2	10 ± 4	***	(6)	31 ± 2	27 ± 3	N.S.
Lilly 127623 (0.10)	(12)	26 ± 1	14 ± 3	*	(8)	29 ± 1	10 ± 3	***
Lilly 127623(0.32)	(10)	27 ± 3	14 ± 4	*	(8)	28 ± 3	18 ± 2	*
FK 33-824 (0.0001)	-	-	-	-	(6)	30 ± 1	32 ± 3	N.S.
FK 33-824 (0.00032)	(6)	28 ± 2	25 ± 1	N.S.	(9)	29 ± 1	11 ± 4	***
FK 33-824 (0.001)	(8)	26 ± 2	7 ± 3	***	(8)	31 ± 1	13 ± 3	***
FK 33-824 (0.0032)	(6)	25 ± 3	14 ± 3	*	(8)	27 ± 3	10 ± 4	*
FK 33-824 (0.01)	(6)	30 ± 4	24 ± 5	*	(6)	29 ± 2	19 ± 2	**

	DMT 10.0 mg/kg (i.p.)			
Pretreatment Drug/Dose mg/kg (i.p.)	(N)	Control 0.9% NaCl Pretreated	Drug Pretreated	p^a
Lilly 127623 (0.032)	(6)	51 ± 3	21 ± 7	**

All pretreatment injections were given 15-20 min prior to DMT or LSD.
p_a values represent paired comparison t-tests.
$^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$; N.S. - not significant

References

Nichols, D.E. Structure-activity relationships of phenethylamine hallucinogens. *J. Pharm. Sci.*, 70:839-849, 1981.

Pickar, D., Davis, G.C., Schulz, S.C., Extein, I., Wagner, R., Naber, D., Gold, M., van Kammen, D.P., Goodwin, F.K., Wyatt, R.J., Li, C.H., and Bunney, W.E., Jr. Behavioral and biological effects of acute beta-endorphin injection in schizophrenic and depressed patients. *Am. J. Psychiatry*, 138:160-166, 1981.

Rimon, R., Terenius, L., and Kampman, R. Cerebrospinal fluid endorphins in schizophrenia. *Acta Psychiatr. Scand.*, 61:395-403, 1980.

Ruffing, D.M., and Domino, E.F. Effects of selected opioid agonists and antagonists on DMT- and LSD-25 induced disruption of food-rewarded bar pressing behavior in the rat. *Psychopharmacology (Berlin)*, 75:226-230, 1981.

Ruffing, D.M., Kovacic, B., Demetriou, S., and Domino, E.F. Naloxone enhancement of DMT- and LSD-induced suppression of food-rewarded bar pressing behavior in the rat. *Psychopharmacology (Berlin)*, 62:207-210, 1979.

Snedecor, G.W. *Statistical Methods.* Ames: Iowa State College Press, 1956.

Snyder, S.H., and Goodman, R.R. Multiple neurotransmitter receptors. *J. Neurochem.*, 35:5-15, 1980.

In Vitro Models to Examine Regulation of Transmitter Content and Adenylatecyclase Coupled Receptors in Neurons[1]

David C. U'Prichard, Ph.D.,[2,3] Karen M. Braas, B.S.,[2] and Deborah J. Kahn, B.S.[2]

Major psychoactive drug classes such as antidepressants and neuroleptics are now believed to exert their therapeutic effects by inducing long-term changes in receptor function at brain monoamine synapses. Chronic antidepressant treatment of rats, for example, causes a reduction in brain β_1-adrenergic receptor number and a down-regulation of both the proximal biochemical response, stimulation of adenylate cyclase activity (Wolfe et al. 1978; Moyer et al. 1981), and electrophysiological responses of neurons associated with β-receptor activation (Schultz et al. 1981). However, with other brain monoamine receptors there are apparent discrepancies between the effects of antidepressant treatment on receptor number obtained from binding studies, and receptor-mediated responses. Thus antidepressant treatment down-regulates the number of brain serotonin-2 (S2) receptors measured with ^{3}H-spiroperidol (Peroutka & Snyder 1980a, 1980b), but appears to cause serotonin receptor supersensitivity in electrophysiological experiments (de Montigny & Aghajanian 1978).

Similarly, although antidepressant treatment causes a functional subsensitivity of brain and peripheral α_2-adrenergic receptors (Crews & Smith 1980; McMillen et al. 1980), studies examining changes in binding of the agonist ligands ^{3}H-clonidine (CLO) and ^{3}H-*p*-aminoclonidine (PAC) to brain α_2-receptors have produced conflicting results, with antidepressant treatment reducing the B_{max} of ^{3}H-CLO in rat brain regions other than cortex (Smith et al. 1981) and clinically in human platelets (Garcia-Sevilla et al. 1981), while other laboratories, including the present investigators, observed that in rats, abbreviated (3 days) treatment with desmethylimipramine or iprindole increased the B_{max} of ^{3}H-PAC or ^{3}H-CLO (Reisine et al. 1980; Johnson et al. 1980). The investigators have also found that chronic immobilization stress down- regulates β-receptors in different rat brain regions, but causes an increase in the B_{max} of ^{3}H-CLO in cortex, and a decrease in the B_{max} of ^{3}H-CLO in other brain areas (U'Prichard & Kvetnansky 1980).

The investigators attempted to reconcile these differences between drug-induced binding and functional changes by investigating the mechanisms of monoamine receptor down-regulation as a result of chronic agonist exposure in cloned neural cells in culture. In particular, they were interested in comparing the mechanisms of down-regulation of receptors that stimulate adenylate cyclase (positively coupled), and of receptors that inhibit adenylate cyclase (negatively coupled). Among the former class are β-adrenergic, dopamine D1, and serotonin S1 receptors, while the latter class includes α_2-adrenergic and dopamine D2 receptors. S2 receptors show GTP-sensitivity (Hamon et al. 1980), and may turn out also to be negatively coupled to adenylate cyclase. Receptors of either class occur in two or more affinity states, mainly differentiated with respect to agonists, referred to as H (high) and L (low). Guanine nucleotides shift equilibrium between H and L states in favor of L, and so promote coupling of either type of receptor with adenylate cyclase (Hoffman & Lefkowitz 1980). An important corollary to this model is that whereas the B_{max} of an antagonist radioligand is likely to be a true indicator of total receptor density, the apparent B_{max} of an agonist ligand, measured over restricted ligand concentrations, will be more an index of the number of H states of the receptor rather than of total receptor density, and changes in the B_{max} of agonist ligands may indicate a shift in the equilibrium between H and L states, and thus altered receptor-effector coupling, rather than a change in receptor number.

---

[1] This study was supported in part by USPHS Grants NS-15595 and MH-36183. D.J.K. is the recipient of an ADAMHA predoctoral fellowship.

[2] Department of Pharmacology, Northwestern University Medical School, Chicago, IL 60611.

[3] Department of Neurobiology and Physiology, Northwestern University College of Arts and Sciences, Evanston, IL 60201.

Address Correspondence to: Dr. David C. U'Prichard, Department of Pharmacology, Northwestern University Medical School, 303 E. Chicago Ave. Chicago, IL 60611.

A number of laboratories have examined the molecular characteristics of β-receptor down-regulation in cultured neural cells. Su et al. (1980) have analyzed the consequences of exposure of 1321N1 human astrocytoma cells to the β-agonist isoproterenol. Through combined measurements of binding and cyclase response, they determined that 1321N1 β-receptors are down-regulated in two phases, the first being an uncoupling of receptors from adenylate cyclase, with a shift from H to L forms of the receptors, but no change in total receptor population, followed by a second long-term phase of loss of receptor number.

The investigators have examined regulation of the negatively coupled α_2-receptor on cultured neuroblastoma x glioma NG108-15 hybrid cells. These cells are cholinergic in nature, synthesize and release acetylcholine, and contain negatively coupled α_2-adrenergic, opiate and muscarinic cholinergic receptors. The investigators found immunocytochemical staining at the LM and EM level with anti-met^5-enkephalin and anti-leu^5-enkephalin antibodies in undifferentiated cells grown in serum-containing and serum-free defined medium. At the EM level, staining was localized to synaptic vesicles. No staining with β-endorphin or β-LPH antibodies was observed. These cells therefore synthesize enkephalin peptides as well as acetylcholine. In undifferentiated cultures, only 25-30 percent of the cells stained for enkephalins, and staining was localized to rounded or neurite-like cells either singly or in small clusters. When the cells in either medium were induced to differentiate with 1.0 mM dibutyryl cyclic AMP (dBcAMP) in the medium for up to 5 days, there was a progressive increase in the percent of the volume fraction of cells staining, up to 60-70 percent (Figure 1). Staining in differentiated cells was intense throughout the elongated processes which developed and, at the EM level, cells had an increased number of vesicles staining for enkephalins. Thus differentiation of these (and other) neural cells in culture caused greatly increased synthesis of opioid peptides (Braas et al. 1981).

Alpha$_2$-receptors on undifferentiated NG108-15 cells in either medium were labeled with the full agonist ^{3}H-epinephrine (EPI), the partial agonist ^{3}H-PAC, and the antagonists ^{3}H-yohimbine (YOH) and ^{3}H-rauwolscine (RAUW). The NG108-15 α_2-receptor was shown to occur in two states with ^{3}H-EPI and ^{3}H-PAC selectively labeling H, and ^{3}H-YOH and ^{3}H-RAUW labeling both H and L. The total density was 30,000-40,000 receptors per cell. Guanine nucleotides and divalent cations modulated the equilibrium between H and L states as observed for other cyclase-linked receptors (Kahn et al. 1982). To examine regulation, cells were exposed to (−)-epinephrine at 37°C for 0.1-16.0 hours, and binding of various ligands, and the response of inhibition of basal adenylate cyclase was measured in thoroughly washed membranes. The time course of binding and response changes is shown in Figure 2. Like β-receptors, regulation of NG108-15 α_2-receptors by 10 μM (−)-epinephrine appeared to be biphasic. At short exposure times (less than 60 min), there was a shift from L to H states of the receptor, as indicated by an increase in the B_{max} of ^{3}H-EPI and ^{3}H-PAC, with no change in total receptor number (B_{max} of ^{3}H-RAUW), while at the same time there was no change in the maximum receptor-mediated response, but there was a 2-fold reduction in the potency of (−)-epinephrine in inhibiting adenylate cyclase. Therefore this first

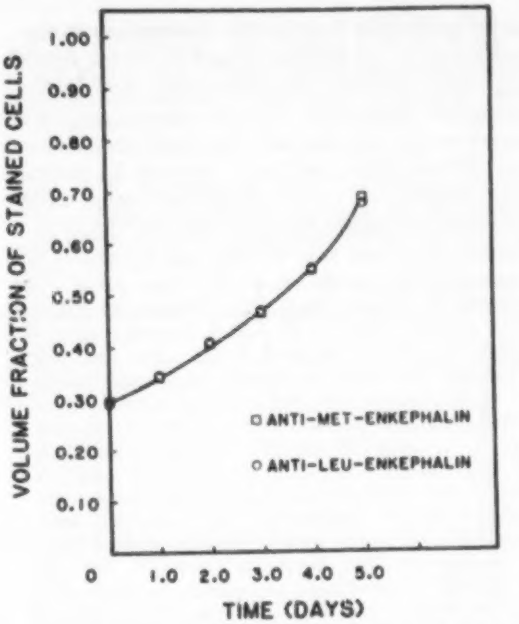


FIGURE 1. Increase in volume fraction of NG 108-15 cells in culture staining for met-enkephalin and leu-enkephalin, as a function of time of incubation of cells with 1.0 mM dBcAMP.

phase of regulation represents uncoupling of the receptor with a concomitant shift to H (desensitized?) states. At longer exposure times there was a progressive reduction in receptor number measured with any ligand, accompanied by no change in maximum response (Figure 2), but a reduced potency of (−)-epinephrine, suggesting the presence of a spare receptor reserve. Other experiments indicated that in this second phase of down-regulation, there was a selective loss of H states of the receptor (Kahn & U'Prichard 1981).

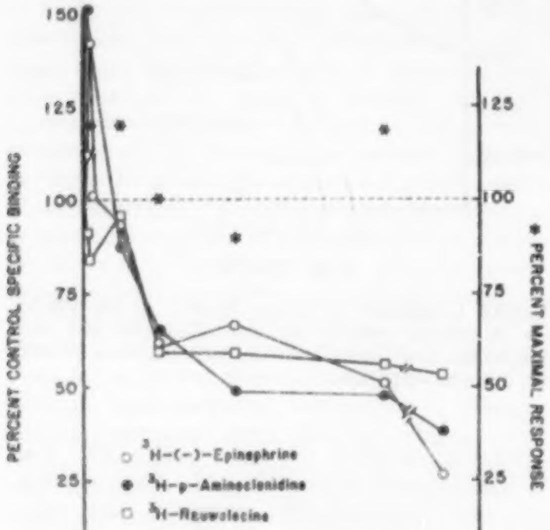


FIGURE 2. Changes in α_2-receptor binding (B_{max}) and adenylate cyclase response (inhibition by epinephrine) in washed membranes as a function of time of exposure of NG108-15 at 37° to 10μM (−)-epinephrine.

In other experiments, rats under mild restraint were continuously infused for 72 hours via the jugular vein with clonidine (0.001-1.0 mg/kg/hr). Infusion of clonidine had a bimodal effect on rat cortex ^{3}H-PAC sites, with lowest concentrations of clonidine increasing ^{3}H-PAC binding 50 percent above control, while higher doses decreased ^{3}H-PAC binding 60 percent below control values. However, rat cortex ^{3}H-RAUW binding (Perry & U'Prichard 1981) was not affected at any clonidine concentration (U'Prichard et al. 1981). This dose-dependent regulation of H states of the α_2-receptor with no change in total receptor population following a fixed time of agonist exposure may parallel the time-dependent bimodal regulation of agonist binding with a fixed concentration of agonist seen in NG108-15 cells.

The above results indicate that there is a phase of α_2-receptor down-regulation where one can observe an *increase* in agonist binding. It is clear that the relationship between changes in monoamine receptor binding and function due to increased agonist exposure, e.g., as a result of antidepressant treatment, can be quite complex, and apparently contradictory data can be obtained which are resolvable once the true significance of binding changes is understood. Regulation of neuronal serotonin receptors and responses can be analyzed in a parallel manner through the use of serotonin receptor-containing neuroblastoma hybrid NG108-15 and NCB-20 cells in culture.

Acknowledgment: We thank Veronica Whatley for manuscript preparation.

References

Braas, K.M., U'Prichard, D.C., and Childs, G.V. Immunocytochemical localization of opioid peptides in normal and differentiated neuroblastoma × glioma hybrid cells NG 108-15. *Neurosci. Soc. Abstr.* 7:94, 1981.

Crews, F.T., and Smith, C.B. Presynaptic α-receptor subsensitivity after long-term antidepressant treatment. *Science,* 202:322-324, 1978.

Garcia-Sevilla, J.A., Zis, A.P., Hollingsworth, P.J., Greden, J.F., and Smith, C.B. Platelet α_2-adrenergic receptors in major depressive disorder. *Arch. Gen. Psychiatry,* 38:1327-1333, 1981.

Hamon, M., Nelson, D.L., Herbet, A., and Glowinski, J. Multiple receptors for serotonin in the rat brain. In: Pepeu, G., Kuhar, M.J., and Enna, S.J. (eds.), *Receptors for Neurotransmitters and Peptide Hormones.* New York: Raven Press, 1980, pp. 223-233.

Hoffman, B.B., and Lefkowitz, R.J. Radioligand binding studies of adrenergic receptors: New insights into molecular and physiological regulation. *Ann. Rev. Pharmacol. Toxicol.,* 20:581-608, 1980.

Johnson, R.W., Reisine, T.D., Spotnitz, S., Wiech, N., Ursillo, R., and Yamamura, H.I. Effects of yohimbine and desipramine on α_2- and β-adrenoreceptor sensitivity. *Eur. J. Pharmacol.,* 67:123-127, 1980.

Kahn, D.J., Mitrius, J.C., and U'Prichard, D.C. α_2-Adrenergic receptors in neuroblastoma × glioma hybrid cells: Characterization with agonist and antagonist radioligands and relationship to adenylate cyclase. *Mol. Pharmacol.,* 21:17-26, 1982.

Kahn, D.J., and U'Prichard, D.C. Regulation of α_2-adrenergic receptor sites in neuroblastoma × glioma hybrid cells. *Neurosci. Soc. Abstr.,* 7:425, 1981.

Moyer, J.A., Greenberg, L.H., Frazer, A., and Weiss, B. Subsensitivity of the β-adrenergic receptor-linked adenylate cyclase system of rat pineal gland following repeated treatment with desmethylimipramine and nialamide. *Mol. Pharmacol.*, 19:187-193, 1981.

McMillen, B.A., Warnack, W., German, D.C., and Shore, P.A. Effects of chronic desipramine treatment on rat brain noradrenergic responses to α-adrenergic drugs. *Eur. J. Pharmacol.*, 61:239-246, 1980.

de Montigny, C., and Aghajanian, G.K. Tricyclic antidepressants: Long-term treatment increases responsivity of rat forebrain neurons to serotonin. *Science*, 202:1303-1306, 1978.

Peroutka, S.J., and Snyder, S.H. Long-term antidepressant treatment decreases spiroperidol-labeled serotonin receptor binding. *Science*, 210:88-90, 1980a.

Peroutka, S.J., and Snyder, S.H. Regulation of 5HT-2 receptors labeled with ^{3}H-spiroperidol by chronic treatment with the antidepressant amitriptyline. *J. Pharmacol. Exp Ther.*, 215:582-587, 1980b.

Perry, B.D., and U'Prichard, D.C. ^{3}H-Rauwolscine (α-yohimbine): A specific antagonist redioligand for brain α_2-adrenergic receptors. *Eur. J. Pharmacol.*, 76:461-464, 1981.

Reisine, T.D., U'Prichard, D.C., Wiech, N.L., Ursillo, R.C., and Yamamura, H.I. Effects of combined administration of amphetamine and iprindole on brain adrenergic receptors. *Brain Res.*, 188:587-592, 1980.

Schultz, J.E., Siggins, G.R., Schocker, F.W., Turck, M., and Bloom, F.E. Effects of prolonged treatment with lithium and tricyclic antidepressants on discharge frequency, norepinephrine responses and β-receptor binding in rat cerebellum: Electrophysiological and biochemical comparison. *J. Pharmacol. Exp. Ther.*, 216:28-38, 1981.

Smith, C.B., Garcia-Sevilla, J.A., and Hollingsworth, P.J. Alpha-2 adrenoreceptors in rat brain are decreased after long-term tricyclic antidepressant drug treatment. *Brain Res.*, 210:413-418, 1981.

Su, Y.F., Harden, T.K., and Perkins, J.P. Catecholamine-specific desensitization of adenylate cyclase. Evidence for a multistep process. *J. Biol. Chem.*, 255:7410-7419, 1980.

U'Prichard, D.C., and Kvetnansky, R. Central and peripheral adrenergic receptors in acute and repeated immobilization stress. In: Usdin, E., Kvetnansky, R., and Kopin, I.J. (eds.), *Catecholamines and Stress: Recent Advances*. Amsterdam: Elsevier, 1980, pp. 299-308.

U'Prichard, D.C., Wang, C.H., and Freed, C.R. Brain monoamine receptor changes associated with catecholamine depletion and hypotension during continuous α-methyldopa infusion. *Neurosci. Soc. Abstr.*, 7:427, 1981.

Wolfe, B.B., Harden, T.K., Sporn, J.R., and Molinoff, P.B. Presynaptic modulation of β-adrenergic receptors in rat cerebral cortex after treatment with antidepressants. *J. Pharmacol. Exp. Ther.*, 207:446-457, 1978.

Mental Illness in Pregnancy and the Puerperium

Chair: **Merton Sandler, M.D.**
University of London
Queen Charlotte's Maternity Hospital
London, England

Model Utility in Postpartum Psychosis

James A. Hamilton, Ph.D., M.D.[1]

Over the past half-century many physicians have suspected that severe psychiatric illness which follows childbearing, or postpartum psychosis, is critically related to hormonal changes in the puerperium (Karnosh & Hope 1937; Bürgi 1953). The author noted that very little progress has been made toward translating the suspicions of hormonal involvement into therapeutic applications. Postpartum patients continue to be treated as if they have run-of-the-mill psychiatric diseases, often with unsatisfactory results.

Among the reasons cited for current failure to explore and exploit a likely hormonal component is the fact that the presenting psychiatric syndromes of postpartum patients vary widely and may change abruptly or slowly to other syndromes. Mixed syndromes are of frequent occurrence. Along with the instability of clinical syndromes is a complex and rapidly-changing hormonal situation. The complexity and changeability of the psychiatric and hormonal situations have worked against definitive analysis. Furthermore, the severity of illness, with grave suicidal hazards, has discouraged the pursuit of studies with traditional experimental controls.

The author suggested that the understanding and treatment of patients might profit by the use of models, an approach which has been useful in other complex scientific problems. Specifically, he suggested that known hormonal events be plotted in temporal sequence on a logarithmic scale. Psychiatric phenomena would be superimposed on this scale. In the interest of simplicity, the first model would be limited to a distribution of the first occurrence of symptoms in patients with two constellations of symptoms, those exhibiting agitation ranging to mania, and those whose illness begins with depression. When mixed cases are eliminated, there is reasonable agreement that the first symptoms of the agitated group usually develop from the 4th to the 12th day postpartum, while the first symptoms of the depressed patients usually begin from the 3rd to the 5th week (Karnosh & Hope 1937; Paffenbarger et al. 1961; Pauliekhoff 1964).

Figure 1 indicates thyroid changes in the puerperium. The only comprehensive data on this were reported in 1943 (Danowski). The standard of measurement was protein-bound iodine (PBI), so there is no separation of thyroid fractions. With a pre-pregnancy mean of 5.40, the final mean, 280 days after childbearing, is 4.40. The standard deviation of the final measure is 0.90, so many values are far below the pre-pregnancy range. The author recalculated Danowski's data to eliminate nursing mothers and cases of amenorrhoea and found a value of 4.46 at 280 days. With estrogen cycles back to normal it is difficult to ascribe this low level to anything else than a

---

[1] Suite 1515, 490 Post Street, San Francisco, CA 94102.

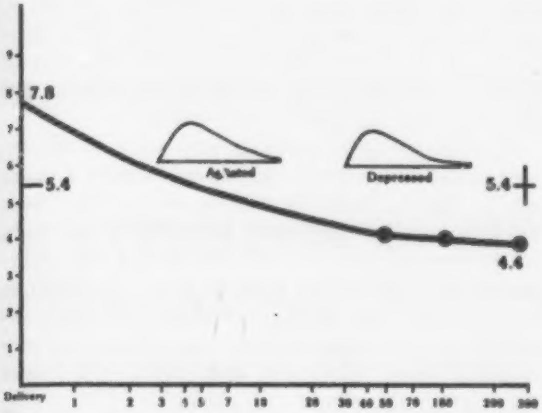


FIGURE 1. Late depression and mean PBI levels.

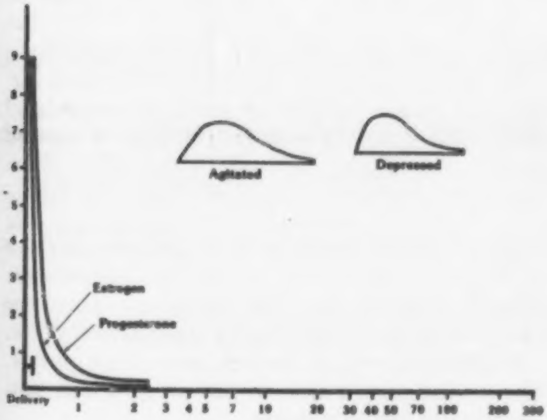


FIGURE 2. Estrogen and progesterone.

substantial, long-lasting drop in the output of thyroxine.

The author noted that postpartum symptoms which begin with depressive symptoms tend to occur as the PBI drop reaches the beginning of its low plateau. Two clinicians with large numbers of cases have reported independently that many cases of depression in the late puerperium respond favorably to thyroid administration, but this form of treatment is not widely accepted (Hamilton 1962; Baker 1967).

Figure 2 indicates the postpartum drop in fetoplacental hormones. The author noted that estrogen and progesterone are at very low levels within 24 hours after delivery, while symptoms of psychiatric illness almost never appear before the 3rd or 4th day. He pointed out that this fact makes it unlikely that deprivation of fetoplacental

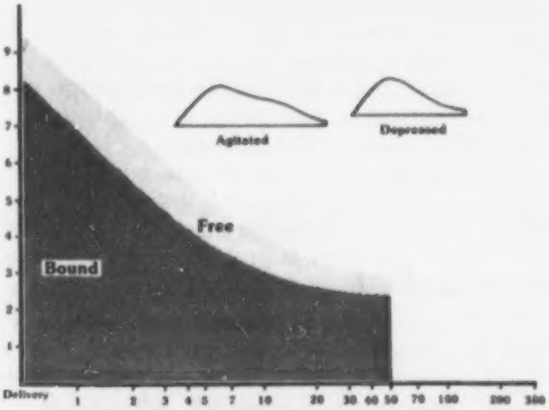


FIGURE 3. Adrenal corticoids: The trend.

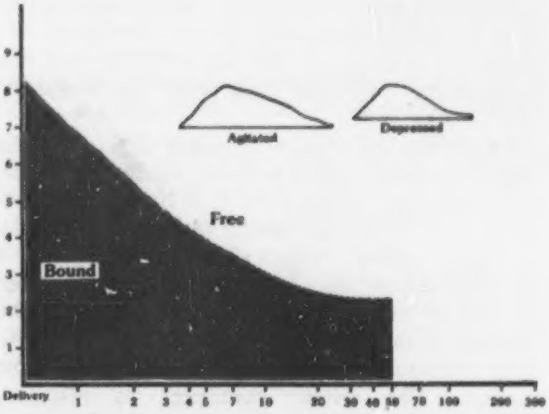


FIGURE 4. Variability of free cortisol: A possible cause of early symptoms.

hormones acts *directly* to produce psychiatric symptoms. Indirect causal effects are not ruled out, and indeed there is some indication that if the postpartum fall in estrogen is cushioned by parenteral estrogen at delivery and for a few days thereafter, high-risk patients may be protected from recurrence of postpartum illness (Hamilton 1977).

Figure 3 is a crude portrayal of the postpartum changes in adrenal corticoids (Tulchinsky 1980). During the latter part of pregnancy, total serum corticoids rise to a level which is three times that of the nonpregnant state. Most of the corticoids are bound to a specific protein, transcortin. About 90 percent of the principal corticoid, cortisol, is bound while 10 percent is free. As corticoids fall over a period of 2 to 3 weeks postpartum, the tendency is for free, physiologically active cortisol to decrease at about the same rate.

However, the author pointed out evidence from the work of Sachar and others indicates that the input of new free cortisol is pulsatile, so that the decrease in corticoids is probably more correctly represented in Figure 4 (Sachar 1973).

The maintenance of optimal levels of free cortisol is mainly achieved through a feedback sensing mechanism located in the hypothalamus. This mechanism generates a peptide releasing factor which is carried by the primary capillary plexus to the anterior pituitary, which in turn releases adrenocorticotropic hormone (ACTH) and thereby stimulates the production of cortisol (Jubiz 1979).

After childbirth the pituitary moves rapidly from hyperemia to ischemia, and its cells change from a phase of hyperactivity to a resting phase. This is reflected in the observation that the postpartum pituitary response is "sluggish" (Tulchinsky 1980).

Inspection of Figure 4 leads directly to a hypothesis with regard to early, agitated postpartum symptoms. During the first 10 days postpartum, total corticoids remain fairly high, but the principal active component, free cortisol, is variable. It may reach a low point, inciting a reaction by its sensor in the hypothalamus, but the response of the "sluggish" pituitary may be insufficient to stimulate the required amount of new free cortisol. The sensor continues to respond, perhaps more and more vigorously. Increased hypothalamic activity may spread to other hypothalamic functions, with sleep disturbance and heightened sympathetic activity, which is perceived as severe anxiety. This kind of disturbance, in the absence of a reasonable cause, could lead to the thinking disturbances which are observed in early postpartum cases.

The foregoing hypothesis is supported by experimental evidence which was reported 8 years ago by Steiner and his associates (1973). These workers treated alternate admissions of early postpartum psychosis with propranolol and chlorpromazine. Only five patients were included in each group, but admission data indicated excellent group comparability. The results with propranolol were strikingly and uniformly better than the results with chlorpromazine. This study, which may well be a landmark in the treatment of postpartum psychosis, has been virtually disregarded. The use of propranolol, a drug with many receptor sites in the hypothalamus, may be a specific medication for responses which can evolve rapidly into early postpartum psychosis.

To explore the model-generated hypothesis further, the author used small doses of propranolol with small doses of sedation to treat a case of known (iatrogenic) corticoid withdrawal which had been unresponsive to other treatment. Symptoms of episodic palpitation, severe anxiety and visceral distress, dyspnea, sleep disturbances and panic which had persisted for 3 months were relieved immediately. The symptoms were very similar to those found in early postpartum cases. The difference was in the response to symptoms. The patient was aware of the event which had precipitated her symptoms.

The case of known corticoid withdrawal is not submitted as a necessary equivalent to early postpartum cases. It is, rather, an instance in which a model-generated hypothesis can stimulate cautious clinical experimentation along lines relating to the area of the hypothesis.

In summary, models can be useful in the visualization of complex psychophysiological relationships, such as may exist in postpartum psychosis. Models, such as that presented, could be useful in relating experimental findings and clinical observations which, without a model, are likely to remain isolated, disconnected, unexplored and neglected. An outstanding and unacceptable fragmentation of this kind is found in the area of psychiatric illness which follows childbearing.

References

Baker, A.A. *Psychiatric Disorders in Obstetrics*. Oxford:Blackwell, 1967.

Bürgi, V.S. Puerperalpsychose oder Diencephalosis puerperalis? (Puerperal psychosis or puerperal disease of the diencephalon?) *Schweiz. Med. Wochenschr.*, 84:1222-1225, 1954.

Danowski, T.S., Huff, S.J., Mrvos, B.S., et al. Is pregnancy followed by relative hypothyroidism? *Am. J. Obstet. Gynecol.*, 65:77-80, 1953. Also Danowski, T.S. *Clinical Endocrinology*. Vol. II. *Thyroid*. Baltimore, Md.:Williams and Wilkins, 1962.

Hamilton, J.A. *Postpartum Psychiatric Problems*. St. Louis, Mo.:C.V. Mosby, 1962.

Hamilton, J.A. Puerperal Psychoses, Chapt. 24N. In: Sciarra, J.J. (ed.), *Gynecology and Obstetrics*. Hagerstown, Md.:Harper & Row, 1977.

Jubiz, W. *Endocrinology: A Logical Approach for Clinicians*. NY: McGraw Hill, 1979.

Karnosh, L.J., and Hope, J.M. Puerperal psychoses and their sequelae. *Am. J. Psychiatry*, 94:537-550, 1937.

Paffenbarger, R.S., Jr., Steinmetz, C.H., Pooler, B.G., and Hyde, R.T. The picture puzzle of postpartum psychoses. *J. Chron. Dis.*, 13:161-173, 1961.

Pauleikhoff, B. *Seelische Störungen in der Schwangerschaft und nach der Geburt*. (Psychiatric illness during pregnancy and after childbirth.) Stuttgart:Enke, 1964.

Sachar, E.J., Hellman, L., Roffwarg, M.D., et al. Disrupted 24-hour patterns of cortisol secretion in psychotic depression. *Arch. Gen. Psychiatry*, 28:19-24, 1973.

Steiner, M., Latz, A., Blum, A., et al. Propranolol versus chlorpromazine in the treatment of psychoses associated with childbearing. *Psychiatr. Neurol. Neurochirg. (Amst.)*, 76:421-426, 1973.

Tulchinsky, D.: The postpartum period. Ch. 9. In: Tulchinsky, D., and Ryan, K.J. (eds.), *Maternal-Fetal Endocrinology*. Philadelphia: W.B. Saunders, 1980.

Hormonal Modulation of Central Dopamine Receptor Sensitivity in the Postpartum Period

Umberto Scapagnini, M.D.,[1] Filippo Drago, M.D.,[1] Ferdinando Nicoletti, M.S.,[1] Francesco Patti, M.S.,[1] Mario Matera, M.D.,[1] and Pier L. Canonico, M.D.[1]

It has long been known that neurological or psychiatric disturbances may occur in women in the course of physiological disendocrine states. Depression and/or anxiety, for instance, are frequent in the premenstrual syndrome (Reid & Yen 1981), while there is evidence that postmenopausal women have the highest incidence of tardive dyskinesia (Crane 1968). The postpartum period is associated with sharp hormonal modification, including changes in prolactin (PRL), 17-β-estradiol, or progesterone levels (Rolland et al. 1976).

In the present study, the authors focused attention on the central effects of PRL, estrogens (E), and progesterone (PG) in an attempt to establish whether changes in hormonal levels may be involved in the occurrence of neuropsychiatric disorders, including psychosis, in the postpartum period (Hatotani et al. 1980). As a first step, the authors investigated the effects of PRL, E, or PG on dopaminergic transmission which is apparently implicated in the pathophysiology of psychiatric or extrapyramidal syndromes. Toward this end, the effects of PRL on dopamine (DA)-dependent behaviors such as grooming or motor behavior were investigated in male rats. Animals displayed excessive grooming in conditions of chronic endogenous hyperprolactinemia induced by anterior pituitary transplantation under the kidney capsule (Table 1). This increase in grooming behavior is considered as a consequence of PRL-induced stimulation of nigro-striatal DAergic transmission since it is elicited by i.c.v. or intranigral PRL injection (Table 1). The grooming is apparently prevented by intrastriatal injection of haloperidol or 6-hydroxy-DA injection (Table 1).

---

[1] University of Catania, Catania, Italy.

Table 1

Influence of PRL on Grooming Behavior

Treatment	Grooming Score
Pituitary homograft	89.0 ± 5.0*
Smooth muscle graft	15.0 ± 2.0*
i.c.v. PRL + intrastriatal saline	72.8 ± 6.1**
i.c.v. PRL + intrastriatal haloperidol	24.2 ± 2.0**
i.c.v. PRL + intrastriatal 6-OHDA	44.9 ± 4.2†
i.c.v. saline + intrastriatal saline	26.2 ± 4.1
intranigral saline	21.2 ± 2.2
intranigral PRL	84.7 ± 5.0‡

Values are mean ± S.E.
*$p = 0.01$ (Student's *t*-test) in comparison with smooth muscle graft,
**$p = 0.01$ and
†$p = 0.05$ (Dunnett's test) in comparison with i.c.v. + intrastriatal saline-injected animals;
‡$p = 0.01$ (Student's *t*-test) in comparison with intranigral saline-injected animals.

As evidence for the hypothesis of a PRL interference with central DAergic function, graft-induced hyperprolactinemia significantly potentiates apomorphine or amphetamine-induced stereotypies (Table 2) and PRL increases striatal DA turnover *in vitro* (Perkins & Westfall 1978). However, the lack of *in vivo* biochemical evidence led the authors to investigate whether PRL may interfere with DA-dependent messages by influencing other neural system functionally linked to DAergic transmission. In this connection, it is remarkable that i.c.v. PRL injection results in a decrease in striatal acetylholine turnover (Wood et al. 1980). In view of the well-documented functional linkage between nigro-striatal DAergic and striato nigral GABAergic transmission (Bartholini et al. 1977), the authors have investigated the effects of hyperprolactinemia on the activity of the GABA-synthesizing enzyme glutamate decarboxylase (GAD, EC 4.1.1.15) in substantia nigra (SN). This parameter mainly reflects the synthesis of GABA at the levels of nigral nerve endings originating from corpus striatum (Fonnum et al. 1974). A significant increase of plasma PRL levels (Table 3) is observed under conditions of hyperprolactinemia resulting from anterior pituitary homograft or acute or chronic injection of sulpiride, a hyperprolactinemic neuroleptic that, at the dose used (2 mg/kg, i.p.), poorly crosses the blood-brain barrier (Benakis & Rey 1976). Involvement of PRL in the effects of sulpiride is also suggested by the evidence that no change in nigral GAD activity is observed in sulpiride-injected hypophysectomized animals (Table 3). Thus, it is tempting to speculate that PRL interferes with the extrapyramidal motor system by influencing, at least in part, strio-nigral GABAergic transmission.

Table 2

Effect of Endogenous Hyperprolactinemia on Apomorphine or Amphetamine-Induced Stereotypes

Treatment	Time (sec)	
	Sham Op.	Graft
Saline, i.p.	18.2 ± 1.6	16.2 ± 1.5
Amphetamine (1mg/kg, i.p.)	30.3 ± 3.6	78.4 ± 4.6*
Saline, i.p.	20.4 ± 1.8	18.3 ± 2.0
Apomorphine:		
100 μg/kg, s.c.	41.7 ± 2.2	67.3 ± 4.8**
250 μg/kg, s.c.	83.7 ± 5.9	199.6 ± 8.4**

Values are mean ± S.E.
*$p = 0.01$ (Student's *t*-test) in comparison with sham-operated amphetamine-injected animals;
**$p = 0.01$ in comparison with sham-operated apomorphine-injected animals.

Table 3

Effects of PRL on Nigral GAD Activity

Treatment	Nigral GAD Activity (umol$^{14}CO_2$/100mg prot./60 min)	PRL (ng/ml)
Smooth muscle graft	41.57 ± 2.20	22.3 ± 1.9
Anterior pituitary graft	55.28 ± 0.21*	64.6 ± 4.1*
Saline, i.p.	41.78 ± 4.10	19.9 ± 2.4
Acute sulpiride (2 mg/kg, i.p.)	59.06 ± 7.44**	73.4 ± 6.2**
Chronic sulpiride (2.5-5 mg/kg, i.p.)	59.97 ± 9.75**	65.6 ± 4.7**
Saline, i.p. + hypophysectomy	39.13 ± 6.52	3.2 ± 0.9
Acute sulpiride + hypophysectomy	42.58 ± 4.93	2.8 ± 1.1
Sesam oil	42.36 ± 5.41	21.2 ± 2.5
Estradiol benzoate (5 μg/rat)	32.69 ± 3.95†	53.8 ± 5.1†

Values are mean ± S.E.
*$p = 0.01$ (Student's *t*-test) in comparison with sham-operated;
**$p = 0.01$ (multiple variance analysis test) in comparison with saline-injected animals;
†$p = 0.01$ (Student's *t*-test) in comparison with sesame oil-injected animals.

Several studies were performed concerning the influence of E on nigro-striatal DAergic transmission. Specifically, in view of clinical and animal studies, E appear to decrease DAergic tonus. In this line, E have been shown to display a striking effect on L-DOPA or neuroleptic-induced dyskinesia (Bèdard et al. 1979). Moreover, E appeared to potentiate spiperone-induced catalepsy (Chiodo et al. 1979), decrease apomorphine-induced stereotypies (Euvrard et al. 1980), impair DA response on striatal cholinergic interneurons (Euvrard et al. 1979) and increase the number of DA receptors (Hruska et al. 1980). Since hypophysectomy completely prevents these effects (Euvrard et al, 1979; Hruska et al. 1980) it has been proposed that the anti-DAergic activity of estrogens might be mediated by PRL, the secretion of which is strongly stimulated by E (Labrie et al. 1978). However, as above reported, PRL presumably potentiates the DA-related behavioral parameters. We have also demonstrated (Table 3) that E treatment results in a decrease of nigral GAD activity in spite of the high PRL levels. Thus, it is conceivable that PRL does not mediate E central effects but rather displays an opposite effect in comparison with E, at least with respect to the striato-nigral GABAergic system.

In regard to PG, no data concerning a possible interference with the extrapyramidal motor system are available. However, in view of the evidence that pregnancy or oral contraceptive therapy are sometimes associated with chorea (Fernando 1966), it has been suggested that PG can increase DAergic transmission (Bèdard et al. 1979). In the present study we have investigated the effects of PG in patients affected by Parkinson's disease. A preliminary clinical evaluation carried out using semiquantitative scales and electromyography would indicate that PG, in association with L-DOPA + decarboxylase inhibitor (DI) improves the therapeutic efficacy of L-DOPA + DI significantly more than a placebo. This evidence would be consistent with the DAergic hypothesis of PG central effects, even though the mechanism of action of the sexual hormone remains unclear.

References

Bartholini, G., Stadler, H., Gadea-Ciria, M., and Lloyd, K.G. Interactions of dopaminergic and cholinergic neurons in the extrapyramidal and limbic system. In: Costa, E., and Gessal, G.L. (eds.), *Advances in Biochemical Psychopharmacology*. Vol. 16. New York:Raven Press, 1977, pp. 391-402.

Beaven, M.A., Wilcox, G., and Terpstra, G.K. A microprocedure for the measurement of $^{14}CO_2$ release from ^{14}C-carboxylabelled aminoacids. *Anal. Biochem.*, 84:638-641, 1978.

Bèdard, P.J., Langelier, P., Dankova, J., Villeneuve, Di Paolo, Barder, Labrie, Boissier, and Euvrard. Estrogens, progesterone, and extrapyramidal system. In: Poirier, L.J., and Bèdard, P.J. (ed.), *Advances in Neurology*. Vol. 24. New York:Raven Press, 1979, pp. 411-422.

Benakis, A., and Rey, C. Etude autoradiographique du sulpiride ^{14}C chez la souris et le rat. Localization specification au niveau de l'hypophyse du rat après administration unique et administrations repéteés. *J. Pharmacol. (Paris)*, 3:367-374, 1976.

Chiodo, L.A., Caggiula, A.R., and Saller, C.F. Estrogen increases both spiperone-induced catalepsy and brain levels of ^{3}H-spiperone in the rat. *Brain Res.*, 212:360-366, 1979.

Crane, G.E. Tardive dyskinesia in patients treated with major neuroleptics. A review of the literature. *Am. J. Psychiatry, (Suppl.)*, 124:40-48, 1968.

Euvrard, C., Labrie, F., and Boissier, J.R. Effects of estrogens on changes in the activity of striatal cholinergic neurons induced by DA drugs. *Brain Res.*, 169:215-220, 1979.

Euvrard, C., Oberlander, C., and Boissier, J.R. Estrogens and extrapyramidal system. in: Usdin, E., Sourkes, Y.L., and Youdin, M.B.H. (eds.), *Enzymes and Neurotransmitters in Mental Disease*. New York: John Wiley & Sons, 1980, pp. 303-315.

Fernando, S.J.M. An attack of chorea complicating oral contraceptive therapy. *Practitioner*, 197:210-211, 1966.

Fonnum, F., Grofova, J., Rinvik, E., Storm-Mathisen, J., and Walberg, F. Origin and distribution of glutamate decarboxylase in the substantia nigra of the cat. *Brain Res.*, 71:77-87, 1974.

Hatotani, N., Nomura, J., Yamaguchi, T., Inoue, and Kitaiama. Psychoneuroendocrine studies on recurrent psychoses. In: Brambilla F., Racagni, G., and deWied, D. (eds.), *Progress in Psychoneuroendocrinology*. Amsterdam:Elsevier/North Holland 1980, pp. 253-262.

Hruska, R.E., Ludmer, L.M., and Sibergeld, E.K. Characterization of the striatal dopamine receptor supersensitivity produced by estrogen treatment of male rats. *Neuropharmacology*, 19:923-927, 1980.

König, J.F.R., and Klippel, R.A. *The Rat Brain*. Baltimore: Williams & Wilkins, 1963.

Labrie, F., Beaulieau, M., Caron, M., and Raymond, V., The adenoipophyseal dopamine receptors, specificity and modulation of its activity by estradiol. In: Robin, C., and Harter, M. (ed.) *Proceedings of the International Symposium on Prolactin*. Amsterdam: Elsevier/North Holland, 1978, pp. 121-136.

Nisticò, G., Di Giorgio, R.M., De Luca, G., and Macaione, S. Effects of ethanolamine-O-sulphate and γ-acetylenic-GABA on GABA content, after i.v.c. microinjection. *J. Neurochem.*, 33:343-350, 1979.

Perkins, N.A., and Westfall, T.C. The effects of prolactin on dopamine released from rat striatum and medial basal hypothalamus. *Neurosci. Lett.*, 3:59-63, 1978.

Reid, L.R., and Yen, S.S.C. Premenstrual syndrome, *Am. J. Obst. Gynec.*, 1:84-105, 1981.

Rolland, R., Hammond, J.M., Schellekens, L.A., Lequin., and deLong. Prolactin and ovarian function. In: James, V.H.T., Serio, M., and Guisti, G. (eds.) *The Endocrine Function of the Human Ovary*. London, New York, San Francisco:Academic Press, 1976, pp. 305-321.

Welsch, C.V., Negro-Vilar, A., and Meites, J. Effect of pituitary homograft on host pituitary prolactin and hypothalamic PIF levels. *Neuroendocrinology*, 3:238-245, 1968.

Wood, P.L., Cheney, V.L., and Costa, E. A prolactine action on acetylcholine metabolism in striatum, hippocampus and thalamus. *J. Neurochem.*, 34:1053-1057, 1980.

Membrane Lipids in Neuropsychiatric Disorders

Co-Chair: David L. Garver, M.D.
Department of Psychiatry
University of Cincinnati
School of Medicine
Cincinnati, Ohio

and

John Rotrosen, M.D.
Psychiatry Service
VA Medical Center
New York, N.Y.

Membrane Abnormalities in Schizophrenia[1]

Robert Hitzemann, Ph.D.,[2] and
David Garver, M.D.[2]

Introduction

Recent studies from this laboratory have described a lithium-responsive schizophrenia (Hirschowitz et al. 1980). This disorder is characterized by an acute and remitting illness and thus such patients meet the criteria both for "good prognosis schizophrenia" (McCabe et al. 1971) and Diagnostic and Statistical Manual-III (DSM-III) schizophreniform disorder. In addition, these patients, in contrast to non-lithium responders, show an excessive growth hormone response to apomorphine (Hirschowitz et al. 1982) and an elevated erythrocyte lithium ratio (Garver et al. 1982). The increase in lithium ratio appears to be related to a decrease in Na^+-Li^+ counterflow activity and in some patients to an increase in passive Li^+ leak.

It was hypothesized that the abnormalities in Li^+ transport may be a reflection of a more general abnormality in membrane composition. Indeed, preliminary studies (Hitzemann & Garver 1981) revealed that there was a significant decrease in phosphatidylcholine (PC) levels in the erythrocyte ghost membranes of high lithium ration – good prognosis patients. The magnitude of the decrease in PC is similar to that reported by Stevens (1972) for a general schizophrenic population and subsequently confirmed by Henn (1981).

These authors found an increase in phosphatidylserine (PS) to compensate for the decrease in PC. These data differ from the results in schizophreniform patients where ethalolamine plasmalogen (EP) or sphingomyelin (SP) levels were found to increase in the PC deficient membranes (Hitzemann & Garver 1982). Thus, there is some evidence that there may be differences between schizophrenic and schizophreniform patients as to the membrane lipid abnormalities. In order to examine this issue in greater detail, the authors studied the erythrocyte ghost lipid com-

---

[1] This study was supported in part by PHS Grant MH-32666 from the National Institute of Mental Health and a BSRG grant from the University of Cincinnati.

[2] Department of Psychiatry, University of Cincinnati School of Medicine, Cincinnati, OH 45267.

position of 23 DSM-III schizophrenics, 9 DSM-III schizophreniform patients, and 15 age- and sex-matched controls. The possibility was also examined that the membrane abnormalities in the lithium-responsive schizophreniform patients may impart some unique mechanisms of action to lithium. The first site examined was the phospholipid methylation system (Hirata & Axelrod 1980), since it seemed conceivable that lithium could stimulate methylation and reverse the decrement in membrane PC at critical sites for the regulation of membrane activity.

Method

The patient population used in this study has been described previously (Hirschowitz et al. 1980). All patients undergo a 2-week drug washout prior to sampling. Four of the schizophreniform patients had no prior history of drug use. Three of the control patients had common migraine and were under treatment, aspirin and/or propranalol, for this disorder. Ghost membranes were prepared from well-washed red cells as described by Dodge et al. (1965). The membranes were then analyzed for the content of the major phospholipid classes as described by Horrocks (1968). Phospholipid methylation was measured in *fresh* ghost membranes at pH = 8.0 essentially as described by Crews et al. (1980).

The methylated products were isolated by thin-layer chromotography (Crews et al. 1980). The amount of radioactivity found in phosphatidylethanolamine (PE) was taken to be the blank value and was subtracted from the counts in phosphatidylmonomethylethanolamine (PME), phosphatidyldimethylethanolamine (PDC), and PC. Statistical significance was determined by the Student's *t*-test for unpaired data.

Results and Discussion

The data in Table 1 show that there was a significant decrease from control levels in erythrocyte ghost PC for both the schizophrenic and schizophreniform groups. For most patients, this deficiency in PC was compensated by an increase in SP. Thus, the total amount of lipid-choline (PC + SP) was conserved. These data differ from previous results for schizophreniform patients (Hitzemann & Garver 1982) in which the decrement in PC was primarily compensated by an increase in EP. In this study, the increase in EP was observed in 2 of the 23 schizophrenic and 4 of the 9 schizophreniform patients, suggesting the greater incidence of the EP change in schizophreniform patients but not as great an incidence as reported in the original cohort.

The distribution of the PC data was such that 31 percent PC could be used to discriminate between the control and patient populations. Nineteen of the 23 schizophrenic patients, 9 of the 9 schizophreniform patients, but only 2 of the 15 control patients had PC values less than 31 percent. One of the two control subjects who showed the abnormality was a migraineur. The other control with a low PC level was a medical student with no apparent illness. Overall, these results

Table 1

Distribution of Erythrocyte Ghost Phospholipids in Controls, Schizophrenics, and Schizophreniform-Disorder Patients

Phospholipid	Control $N = 15$	Percent of Total Schizophrenia $N = 23$	Schizophreniform $N = 9$
Phosphatidylcholine	33.7 ± 1.2	29.3 ± 1.1*	28.7 ± 0.5*
Phosphatidylethanolamine	18.8 ± 1.5	17.1 ± 0.9	18.4 ± 1.2
Phosphatidylserine	15.4 ± 1.2	15.1 ± 1.0	15.9 ± 0.7
Phosphatidylinositol	3.1 ± 0.5	2.3 ± 0.2	2.3 ± 0.2
Ethanolamine Plasmalogen	10.3 ± 0.9	12.0 ± [illegible]	11.9 ± 1.1
Sphingomyelin	19.7 ± 0.9	24.1 ± 1.5*	23.3 ± 1.8†

* - Significantly different from control, $p < 0.05$ (two-tailed)
† - Significantly different from control, $p < 0.05$ (one-tailed)

confirm the marked enrichment of the PC deficiency in schizophrenic populations found by others (Stevens 1972; Henn 1981). However, these results do not confirm the increase in PS to compensate for the loss of PC. The reason for this difference is not clear. The data suggest the need for interlaboratory verification of results and standardization of analytical techniques. The observation that a small percentage of controls (13%) gave a "false-positive" result indicates the need to evaluate an extensive and varied control population before it will be possible to use the membrane lipid abnormalities as a "blood-test" for schizophrenia.

Although the membrane abnormalities did not discriminate between schizophrenic and schizophreniform populations, the effect of lithium on erythrocyte ghost phospholipid methylation did discriminate between these groups. The kinetics of phospholipid methylation in erythrocyte ghosts in shown in Table 2. These data confirm the results of others (Hirata & Axelrod 1980) that methylation is probably catalyzed by two methyltransferases, inasmuch as the Km for [^{3}H] PME formation (0.92 uM) is distinctly different from that for [^{3}H] PDE (2.74 uM) and [^{3}H] PC (3.15 uM) formation. A concentration of 3 uM [^{3}H] S-adensoylmethionine (SAM) or approximately the apparent Km concentration for methyl-transferase-II was used in subsequent studies.

The data in Table 3 show the effect of lithium (0.5 and 1.0 mM) on phospholipid methylation in erythrocytes ghosts prepared from controls, schizophreniform-disorder patients, and schizophrenics. The lithium effects were highly individual. For example, in controls #1 and #3, lithium had relatively little effect on methylation while on control #2, lithium inhibited methylation, particularly the formation of [^{3}H] PME. In contrast, lithium markedly stimulated [^{3}H] PME formation in the schizophreniform patients, although the magnitude of the increase was quite variable, e.g., from 158 percent in Patient #2, to 646 percent in Patient #1. Lithium either inhibited or had no significant effect on phospholipid methylation in three schizophrenic patients. Although the sample is quite small, these data suggest that further study of the phospholipid methylation system as a potential site of lithium action is warranted.

Table 2

Kinetics of Phospholipid Methylation In Human Erythrocyte Ghost Membranes*

Parameter**	[^{3}H]PME	[^{3}H]PDE	[^{3}H]PC
Km†	0.92	2.74	3.15
Vmax†	2.81	6.38	14.67

*Various concentrations of [^{3}H]SAM (.1 to 10 μM) were used to determine the kinetic plots. The methylated products were isolated by thin layer chromotography (Crews et al. 1980).

**The kinetic parameters, Km and Vmax, were determined as described by Wilkinson (1961).

†Km - μM; Vmax - p mol/mg protein/30 min.

Acknowledgments: The authors wish to thank Elizabeth Day for her editorial and typing assistance and Cynthia Mark for her technical assistance.

Table 3

Effect of Lithium on Phospholipid Methylation in Controls, Schizophrenics and Schizophreniform-Disorder Patients*

Group	[Lithium] mM	Percent of Control (no added lithium) [^{3}H]PME	[^{3}H]PDE	[^{3}H]PC
Control #1	0.5	96	97	90
	1.0	93	97	93
Control #2	0.5	49	90	90
	1.0	32	74	60
Control #3	0.5	82	84	76
	1.0	103	103	101
Schizophreniform #1	0.5	300	23	105
	1.0	646	84	155
Schizophreniform #2	0.5	125	149	202
	1.0	158	214	214
Schizophreniform #3	0.5	225	98	139
	1.0	323	152	219
Schizophrenic #1	1.0	60	91	85
Schizophrenic #2	1.0	82	104	68
Schizophrenic #3	1.0	67	75	76

*Methylation was measured as described in the legend to Table 2 except that 3 μM [^{3}H]SAM was used in all experiments and various concentrations of lithium were added in vitro. All incubations were done at 37 °C, pH = 8.0 and in the presence of 2 mM $MgCl_2$. Data are expressed as percent of the value obtained in the absence of lithium.

References

Crews, F.T., Hirata, F., and Axelrod, J. Identification and properties of methyltransferases that synthesize phosphatidylcholine in rat brain synaptosomes. *J. Neurochem.*, 34:1491-1498, 1980.

Dodge, J.T., Mitchell, C.D., and Hanahan, D.J. Enzyme and hemoglobin retention in human erythrocyte stroma. *Biochem. iophys. Acta*, 104:348-358, 1965.

Garver, D.L., Hitzemann, R.J., and Hirschowitz, J. Li ratio, Li response, and the schizophrenias. In: Hanin, I., and Usdin, E. (eds.) *Biological Markers in Psychiatry and Neurology*. New York: Pergamon Press, 1982, pp. 169-176.

Henn, F. Phospholipid alterations in schizophrenia. Paper read at the Annual Meeting of the American College of Neuropsychopharmacology, Coronado, California, 1981.

Hirata, F., and Axelrod, J. Phospholipid methylation and biological signal transmission. *Science*, 209:1082-1090, 1980.

Hirschowitz, J., Casper, R., Garver, D., and Chang, S. Lithium response in good prognosis schizophrenia. *Am. J. Psychiatry*, 137:916-920, 1980.

Hirschowitz, J., Zemlan, F., and Garver, D. Growth hormone response *in vitro* and lithium ratio predict success of lithium therapy in the schizophrenias. In: Hanin, I., and Usdin, E. (eds.) *Biological Markers in Psychiatry and Neurology*. New York: Pergamon Press, 1982, pp. 307-316.

Hitzemann, R.J., and Garver, D.L. Membrane abnormalities in lithium responsive illnesses. In: Hanin, I., and Usdin, E. (eds.) *Biological Markers in Psychiatry and Neurology*. New York: Pergamon Press. 1982, pp. 177-182.

Horrocks, L.A. The alk-1-enyl group content of mammalian myelin phosphoglycerides by quantitative two-dimensional thin-layer chromotography. *J. Lipid Res.*, 9:469-472, 1968.

McCabe, M.S., Fowler, R.C., Cadoret, R.J., and Winokur, H. Familial differences in schizophrenia with good and poor prognosis. *Psychol. Med.*, 1:326-332, 1971.

Stevens, J.D. The distribution of the phospholipid fractions in the red cell membrane of schizophrenics. *Schizophren. Bull.*, 6:60-61, 1972.

Phospholipids and Phospholipid Methylation in Platelets and Brain

Donna Mandio Cordasco,[1] David Wazer,[1] David J. Segarnick,[1] Andrew Lautin, M.D.,[1] Arnold Lippa, Ph.D.,[2] and John Rotrosen, M.D.[1]

Recent studies of membrane phospholipid composition and metabolism indicate that phospholipids are integrally involved in regulating membrane biochemistry and biological signal transmission. In all biological organisms, bilayer membranes separate the intracellular cytosol from the extracellular environment and provide a supportive matrix within which numerous "membrane-bound" enzymes and proteins reside. Phospholipids are the major structural components of membranes, and synthetic phospholipids will spontaneously form membrane-like bilayers in aqueous media. In biological membranes (unlike artificial bilayers) the phospholipids are nonrandomly distributed between the two membrane leaflets. For example, in erythrocytes, phosphatidylcholine (PC) is primarily localized on the extracellular membrane surface, while phosphatidylserine (PS) is nearly all localized on the inner cytoplasmic membrane surface [these asymmetries are tissue-specific, e.g., in platelets PC is evenly distributed between the two membrane surfaces (Zwaal et al. 1977)]. Recent research indicates that phospholipid asymmetry effects cellular function by altering surface charge and membrane fluidity.

Certain aspects of membrane asymmetry are reflected in the enzymatic biosynthesis of (PC) through successive N-methylations of phosphatidylethanolamine (PE). Two enzymes catalyze this reaction sequence. The first enzyme which is located on the inner, cytoplasmic surface of the membrane synthesizes phosphatidyl-N-monomethylethanolamine (PME) by adding one methyl group to PE. The second enzyme is located near the outer membrane surface and

---

[1] Psychiatry Service, Veterans Administration Medical Center, New York, NY 10010 and Department of Psychiatry, New York University Medical Center, New York, NY 10016.

[2] Lederle Laboratories, Division of American Cyanamid Co., Pearl River, NY 10965.

adds two additional methyl groups to PME to form phosphatidyl-N,N-dimethylethanolamine (PDE) and PC. S-adenosyl-L-methionine (SAM) is the methyl donor for both enzymes. In erythrocytes, the products of phospholipid methylation are asymmetrically distributed; PME is localized on the intracellular membrane surface while PDE and PC are on the extracellular surface (Hirata & Axelrod 1978). This product distribution is established through a flip-flop mechanism whereby PME is translocated through the lipid matrix and methylated to PDE and PC on the extracellular side of the bilayer. Associated with phospholipid methylation are localized changes in membrane fluidity, and receptor exposure (Strittmatter et al. 1979a), Ca^{++} ATPase activity (Strittmatter et al. 1979b), receptor-cyclase coupling (Hirata et al. 1979) and other membrane-mediated events.

Phosphatidylserine, a negatively charged phospholipid, is almost exclusively localized on the inner membrane leaflet in red blood cells (Zwaal et al. 1977); recent reports (Henn 1981) suggest that PS may play an important role in the etiopathology of schizophrenia. PS is unique amongst the phospholipids insofar as it has a number of "pharmacologic" effects when administered (in low doses) *in vivo* or (at low concentrations) *in vitro*. Amongst these are the following central nervous system (CNS) effects: PS causes a rapid increase in acetylcholine release in rat cortex (Mantovani et al. 1976), it increases levels of homovanillic acid in rat brain, and enhances norepinephrine turnover in rat hypothalamus (Toffano et al. 1978). A study by Stevens (1972) which has recently been replicated by Henn (1981), indicates that schizophrenics' red blood cells contain approximately 40 percent more PS and 10-15 percent less PE and PC than red blood cells from controls.

Preliminary work from our laboratory investigating phospholipid methylation and membrane phospholipid composition is described.

Platelet Phospholipid Methylation

Since platelets have many properties in common with monoaminergic neurons and are often used in psychiatric research as peripheral models of CNS biochemistry, the authors undertook to study the role of phospholipid methylation in the regulation of platelet function.

Phospholipid methylation was assayed by incubation of intact platelets with ^3H-methionine as previously described (Cordasco et al. 1981). Three major lipid extractable products—PME PDE, and PC were synthesized. Formation of these products was pH, time- and temperature-dependent, and saturable with respect to precursor concentration. As in other tissue types, platelet phospholipid methylation is sensitive to certain agents which elicit tissue-specific responses. Physiological concentrations of epinephrine, adenine, and thrombin inhibited formation of ^3H-methylated phospholipids. In some aspects, however, phospholipid methylation in platelets differs from that in other tissues.

Although phospholipid methylation is a minor pathway for PC biosynthesis, in leukocytes methylation derived PC comprises a discrete, highly active pool which is the primary source of free arachidonic acid released in response to chemoattractants (Hirata et al. 1979). In the interest of determining whether platelets also contain differentially active PC pools, platelet PC was labeled by incubation with ^3H-methionine, ^3H-choline, or ^{14}C-arachidonic acid and then stimulated arachidonic acid release with thrombin. PC synthesized from each of the three precursors was equally reduced by thrombin treatment indicating that in platelets, PC formed through methylation does not comprise a functionally distinct pool.

Table 1

Product Remaining After Phospholipase C Digestion (% of Control)

	3H-PME	3H-PDE	3H-PC
No Phospholipase C	100	100	100
Phospholipase C Incubated with Intact Platelets	80	74	66
Phospholipase C Incubated with Lysed Platelets	17	16	14

Phospholipase C digestion of 3H-PME, 3H-PDE, and 3H-PC in intact or osmotically lysed pre-labeled platelets. Values are expressed as % of control samples which were run with each assay and did not contain added phospholipase C.

A further distinction between phospholipid methylation in platelets and in other tissues lies in the distribution of tritiated PME, PDE, and PC between the cytoplasmic and extracellular membrane surfaces. Intact and hypotonically lysed platelets were enzymatically digested with phospholipase C to determine the localization of ^{3}H-methylated phospholipids (Table 1). The products of platelet phospholipid methylation were found to be equally distributed on the intracellular and extracellular membrane surfaces. The symmetrical distribution of methylation derived PC in platelets is compatible with a report by Zwaal et al. (1977), indicating that total platelet membrane PC is also symmetrically distributed (in contrast to asymmetrically distributed erythrocyte membrane PC).

Given the differences in the pharmacological and biochemical characteristics of phospholipid methylation in platelets and other tissues (including synaptosomes), the authors question whether studying platelet phospholipid methylation in psychiatric patients will be of value as a model of CNS function.

Synaptosomal Phospholipid Methylation

In erythrocytes (Hirata et al. 1979) and cultured astrocytoma cells (Strittmatter et al. 1979c), agonist stimulation of β-receptors increases phospholipid methylation. These findings and their potential implications in neuroscience have encouraged the authors to examine norepinephrine (NE) stimulation of synaptosomal phospholipid methylation.

The ability of NE to enhance phospholipid methylation was assessed in a crude synaptosomal preparation by the method of Crews et al. (1980). NE stimulation consistently increased chloroform extractable radioactivity by 100% - 200% initially suggesting that NE stimulated phospholipid methylation. In order to verify product identities, the authors chromatographed the extracts in three thin layer chromatography (TLC) systems and serially scraped the TLC plates. The serial scrapes revealed several large NE-stimulated peaks of radioactivity which could not clearly be attributed to 3H-PME, 3H-PDE, or 3H-PC but which chromatographed with these methylated phospholipids in some TLC systems.

Table 2

	Chromatography System		
Product	(1)	(2)	(3)
PME	+	+	–
PDE	–	+	–
PC	–	+	+

NE stimulation of phospholipid methylation as observed in three chromatography systems. + indicates NE stimulated increase in radioactivity co-chromatographing with authentic standards of PME, PDE, or PC.
Chromatography system key:
(1) = chloroform:propanol:propionic acid:water 4:6:2:1
(2) = chloroform:methanol:4N ammonium hydroxide 70:35:4
(3) = chloroform:acetone:methanol:acetic acid:water 10:4:2:2:1

When the results from the three chromatography systems are compared (Table 2), it is apparent that the NE induced stimulation does not consistently correspond to PME, PDE, or PC indicating that NE does not stimulate phospholipid methylation under the conditions studied. In an attempt to identify the NE-stimulated product or products, several methylated substances which were reasonable candidates were chromatographed in the three previously described chromatography systems (Table 3). A test-substance must co-chromatograph with a NE stimulated peak in each of the three systems for a positive correlation to be made. To date, no substance has met these criteria and the chloroform extractable, NE stimulated products have not been identified.

Phospholipid Methylation in Aging

Comparative studies of phospholipid methylation were undertaken in synaptosomes from young adult and aged rats. The process of phospholipid methylation alters membrane fluidity and also generates PC which can be metabolized to free choline (Blusztajn & Wurtman 1981). Since both membrane fluidity and cholinergic neurotransmission are altered during the aging process, the authors theorized that phospholipid methylations may either underlie these processes, or be modified in a compensatory way in older animals.

Phospholipid methylation was assayed in cerebral cortical synaptosomes from 5- and 24-month-old rats. Accumulation of 3H-PME was significantly increased in the tissue preparation from the older rats, while 3H-PC was unaltered (Table 4). This data is in agreement with results of a similar study (Crews et al. 1981).

Erythrocyte Phospholipids in Schizophrenia

In clinical studies (similar to those presented in this session by Fritz Henn), we have investigated alterations in erythrocyte membrane lipid composition as a marker for schizophrenia. Henn has reported that schizophrenics' erythrocytes differ markedly from those of controls in the distribution of the major membrane phospholipids. Phosphatidylserine levels are elevated (40% > controls) while PE and PC levels are decreased (15% < controls). The authors' laboratory has initiated a pilot study attempting to replicate these findings. Preliminary data (Table 5) indicate that red blood cell membranes from schizophrenics do not differ significantly from those of controls in lipid composition. Discussions with Henn suggested that differences in methodology may account for the discrepancies between the authors' data and his. The authors have conducted a series of experiments employing Henn's extraction methods, but are still unable to identify any substantive differences between schizophrenics and controls.

Table 3

	Chromatography System		
	(1)	(2)	(3)
SAM	+	+	−
Methionine	−		
Epinine	−		
3-Methoxytyramine	+	+	−
Norepinephrine	−		
Epinephrine	−		
DL-alpha-linolenic acid	−		
Arachidonic acid	+	+	−
Linoleic acid methyl ester	+	−	−
Arachidonic acid methyl ester	+	−	−
Linolenic acid methyl ester	+	−	−
DL-normetanephrine	−	−	+
DL-metanephrine	−	−	+
DL-4-hydroxy-3-methoxy-mandelic acid	+	−	−
3-Methoxy-4-hydroxy-phenyl-glycol	+	+	−

Association of NE stimulated peaks with co-chromatographed substances is indicated as +. Chromatography systems are those described in Table 2.

Table 4

	Age (months)	
	5	24
SAM (0.7 μM)		
PME	25.0 ± 1.4	30.1 ± 1.2*
PC	19.9 ± 1.3	21.5 ± 1.2
SAM (200 μM)		
PME	89.0 ± 4.8	97.2 ± 6.5*
PC	197.2 ± 9.2	211.2 ± 11.9

Phospholipid methylation in rat cerebral cortical synaptosomes. Values are in femtomoles of 3H-CH3 groups incorporated into each phospholipid per mg. protein. (*$p < .02$)

Table 5

	Controls ($N = 14$)	Schizophrenics ($N =$)
PE	32.8 ± 1.5	31.8 ± 1.0
PC	34.1 ± 3.0	33.1 ± 2.6
SPM	23.8 ± 3.0	24.6 ± 2.1
PS	9.3 ± 2.2	10.5 ± 2.1

Phospholipids as % of total phospholipid in washed, lysed red blood cell membranes. PE = phosphatidylethanolamine, PC = phosphatidylethanolamine, SPM = spingomyelin, PS = phosphatidylserine

References

Blusztajn, J.K., and Wurtman, R.J. Choline biosynthesis by a preparation enriched in synaptosomes from rat brain. *Nature*, 290:417-418, 1981.

Cordasco, D.M., Segarnick, D.J., and Rotrosen, J. Human platelet phospholipid methylation. *Life Sci.*, 29:2299-2309, 1981.

Crews, F.T., Calderini, G., Battistella, A., and Toffano, G. Age dependent changes in the methylation of rat brain phospholipids. *Brain Res.*, 229(1):256-259, 1981.

Crews, F.T., Hirata, F., and Axelrod, J. Identification and properties of methyltransferases that synthesize phosphatidylcholine in rat brain synaptosomes. *J. Neurochem.*, 34(6):1491-1498, 1980.

Henn, F. Phospholipid alterations in schizophrenia. Paper read at the Annual Meeting, American College of Neuropsychopharmacology, Coronado, California, 1981.

Hirata, F., and Axelrod, J. Enzymatic synthesis and rapid translocation of phosphatidylcholine by two methyltransferases in erythrocyte membranes. *Proc. Natl. Acad. Sci. USA*, 75(5):2348-2352, 1978.

Hirata, F., Corcoran, B.A., Venkatasubramanian, K., Schiffman, and Axelrod, J. Chemoattractants stimulate degradation of methylated phospholipids in rabbit leukocytes. *Proc. Natl. Acad. Sci. USA*, 76(6):2640-2643, 1979.

Hirata, F., Strittmatter, W.J., and Axelrod, J. β-Adrenergic receptor agonists increase phospholipid methylation, membrane fluidity, and β-adrenergic receptor adenylate-cyclase coupling. *Proc. Natl. Acad. Sci. USA*, 76(1):368-372, 1979.

Montovani, G., Pepeu, L., and Amaducci, L. Investigations into the relationship between phospholipids and brain acetylcholine. *Adv. Exp. Med. Biol.*, 72:285-292, 1976.

Stevens, J.D. The distribution of the phospholipid fractions in the red cell membrane of schizophrenics. *Schizophr. Bull.*, 6:60-61, 1972.

Strittmatter, W.J., Hirata, F., and Axelrod, J. Phospholipid methylation unmasks cryptic β-adrenergic receptors in rat reticulocytes. *Science*, 204:1205-1207, 1979a.

Strittmatter, W.J., Hirata, F., and Axelrod, J. Increased Ca++ ATPase activity associated with methylation of phospholipids in human erythrocytes. *Biochem. Biophys. Res. Commun.*, 88(1):147-153, 1979b.

Strittmatter, W.J., Hirata, F., Axelrod, J., et al. Benzodiazepine and β-adrenergic receptor ligands independently stimulate phospholipid methylation. *Nature*, 282:857-859, 1979c.

Toffano, G., Leon, A., Mazzari, G., et al. Modification of noradrenergic hypothalamic system in rat injected with phosphatidylserine liposomes. *Life Sci.*, 23:1093-1102, 1978.

Zwaal, R., Comfurius, P., and Van Deenen, L. Membrane asymmetry and blood coagulation. *Nature*, 268:358-360, 1977.

Occurrence and Significance of Beta-Carbolines and Tetrahydroisoquinolines

Co-Chairs: **Bo. P. Holmstedt, M.D.**
Department of Toxicology
Karolinska Institutet
Stockholm, Sweden

and

Earl Usdin, Ph.D.
Neurosciences Research Branch
National Institute of Mental Health
Rockville, Maryland

Cellular Actions and Localization of Beta-Carbolines and Tetrahydroisoquinolines

Floyd E. Bloom, M.D.[1] and Jack D. Barchas, M.D.[2]

One of the more intriguing scientific issues in neuropharmacology is the hypothesis that novel metabolites of the monoamine transmitters norepinephrine, dopamine, or serotonin may be formed in the body during ethanol intoxication. In the test tube, it is abundantly clear that the metabolic product of ethanol, acetaldehyde, can condense with the catecholamine transmitters to form a class of chemical called tetrahydroisoquinolines (TIQs), and with serotonin to form the class of compounds termed tetrahydro-beta-carbolines. When these compounds are administered to animals, they have been shown to be very active in altering behavior, transmitter actions, and neuronal activity. In fact, some scientists have proposed that such compounds could underlie the addictive properties of ethanol. This view is based upon experiments in which rats that have received several injections of certain TIQs into their brains will then greatly increase their voluntary consumption of alcohol for many months afterwards. Unfortunately, this intriguing issue is also one of great controversy, and the arguments rage on two fronts: Are these compounds actually ever formed in the brain of humans or experimental animals in relationship to the alcohol they consume and, secondly, do the effects of these compounds help us understand either the basis for intoxication or the mechanisms by which certain individuals become dependent on alcohol?

In an attempt to come to some closure on the most controversial aspects of the biological significance of these elusive substances and their possible broader medical implications, an international workshop was held at the Salk Institute Alcohol Research Center on December 12 and 13, 1981, supported by a supplemental grant from NIAAA. The Workshop, organized by Drs. F. Bloom (Salk Institute), J. Barchas (Stanford University), E. Usdin (National Institute of Mental Health) and M. Sandler (Queen Charlotte's Maternity Hospital), brought together scientists from throughout the United States and Europe for an extensive discussion of the alleged endogenous compounds, their relationship to tissue ethanol content, and the possible actions that—if formed—could be produced in experimental animals. The proceedings of this meeting will be published later this year; the present report summarizes some of the highlights and critical points of the meeting.

The premiere question which faced the workshop was whether these compounds can actually be measured in the body of experimental animals or human subjects and, if so, whether the amounts measured can in any way be influenced by prior ingestion of alcohol. Molecules in tissue fluids or in extracts of homogenized tissues can be measured in many ways, and the methods vary considerably in their accuracy and sensitivity. Among the most sensitive and specific of the available methods are determinations by mass spectrometry. When these methods are applied to the measurements of beta-carbolines, it has so far proven to be extremely difficult to detect them under conditions in which the chemical being measured can be rigorously documented to have arisen in the animal rather than in the test tube during extraction and preparation of the sample for measurements. Thus, while there are several published reports that beta-carbolines can be extracted from human urine, spinal fluid, or from platelets after ethanol exposure, it is difficult to rely strongly on such reports without convincing evidence that the already detected sources of contaminating aldehydes, and other sources of artifactual carboline formation, have wholly been eliminated. Furthermore, many at the workshop shared the view that even if beta-carbolines could be authenticated as endogenous constituents of urine or platelets, this is insufficient to document their endogenous occurrence in central or peripheral nervous tissue.

---

[1] The Arthur Vining Davis Center for Behavioral Neurobiology, The Salk Institute, La Jolla, CA 92037.

[2] The Nancy Pritzker Laboratory for Behavioral Neurochemistry, Stanford University Medical School, Stanford, CA 94305.

The most "negative" series of detection attempts were reported by Dr. T. Bosin, presently of Indiana University, who perfected his methodology in the Laboratory of Dr. Bo Holmstedt of the Karolinska Institute. In the course of these studies, Bosin and Holmstedt recognized that beta-carboline-like structures were arising during the preparation of the samples to be measured, and that to a large extent these artifactual formations far outweighed the beta-carboline that might have been present in the original tissue or biological fluid source. Important sources of these artifactually formed carbolines included covert formaldehyde and acetaldehyde contamination of even extremely pure reagents such as dichloromethane and chloroform, and the nitrogen gas used to dry the specimens. In some cases Bosin inferred that significant aldehyde contamination could even have existed in the distilled water supply. Although the absolute amounts of such contaminating aldehydes may be relatively small, the amounts of presumptive carbolines are already vanishingly small and, in the hands of Bosin, disappear completely when steps are taken to trap out the contaminants. A particularly perplexing contaminant was their discovery that the 5-HT source to be used as an internal standard was itself contaminated with carbolines.

Similar problems of internal chemical contamination contributing to the exogenous formation of beta-carbolines during sample preparation also led Dr. Kym Faull of Stanford University to conclude that he was unable to document the endogenous formation of any beta-carboline in rat brain except for tetrahydro-beta-carboline (THBC), and the maximum amount detectable here was less than 0.5 nanogram/brain. This group terms indoleamine-aldehyde condensation products tryptolines using a serotonin numbering system. Using a form of mass spectrometry (negative chemical ionization with capillary columns) that would have permitted detection at 100 picograms per sample or below, Faull could not find evidence for the carboline products of tryptamine with acetaldehyde, serotonin with formaldehyde or acetaldehyde, or 5-methoxytryptamine with formaldehyde. The Stanford group is very concerned about artifactual formation; however, THBC, if verified, could have important implications, as it would strongly suggest that tryptamine (from which THBC is formed by the addition of formaldehyde) could exist as a transmitter substance independently of 5-hydroxytryptamine, much in the same way that dopamine exists as a transmitter independently of norepinephrine. THBC was shown to be the most potent displacer of $[H^3]$-tryptamine in ligand binding studies reported to the workshop by Dr. K. Kellar (Georgetown University), and those data would support the possibility of a functionally independent tryptaminergic system.

On the other hand, Dr. Steve Barker (University of Alabama), also using GC/MS, detected extremely large amounts of carbolines (500-1000 nanogram/g) in the adrenal glands of singly housed rats, as well as in their brains (20-50 ng/g). Barker conjectured that his values were so high because the rats were under the stress of isolation; the amounts he measured were considerably lower, although well above his threshold for detection, in rats which were group housed. Dr. Olaf Beck, also of the Karolinska Institute, was able to confirm that beta-carbolines could be detected in the urine of rodents and humans, and that it could be elevated after a drinking episode. However, even in this case, Beck found it difficult to conclude that the carboline was formed *in vivo* from aldehyde byproducts of the alcohol metabolism. He favored instead the possibility that the carbolines may have arisen from dietary sources, including the alcoholic beverages themselves, since foods such as cheeses and fruits, especially grapes, are known to have high carboline content.

A somewhat stronger case was developed for the natural occurrence of aldehyde condensation products of the catecholamines. In this case, the resulting TIQs have been more reproducibly documented in tissue and body fluid extracts, and have been shown to be elevated further by recent alcohol ingestion. This body of evidence was comprehensively summarized by Dr. Mike Collins of Loyola University, Chicago, and by Dr. Gerald Cohen, of Mt. Sinai Hospital Medical School, New York. Dr. Birgitta Sjoqvist of the Karolinska Institute pursued the question of whether the particular TIQ which she was able to measure in the urine and cerebrospinal fluid (CSF) of non-alcoholic humans and in higher amounts in urine and CSF of acutely intoxicated humans, originated in the central nervous system; she measured TIQs in postmortem brain specimens from alcoholic and control subjects. Her results indicated that TIQs were detectable in amounts of 20-50 ng/g in dopamine-rich regions such as caudate and putamen, as well as in regions with much less dopamine, such as cerebral cortex and hippocampus. In general, the levels were 5 to 10-fold lower in control (non-alcoholic subjects) and in alcoholics who had died while sober for at least 2 weeks, although underlying neuropathologic consequences of the long-term alcoholism, which reduced endogenous dopamine and increased the content of its metabolite, homovanillic acid, may have contributed to the differences.

On the other hand, attempts by Drs. T. Shier and L. Koda (Salk Institute) to show the formation of DA-related TIQs in the brains of normal or ethanol intoxicated rats by following products formed from intraventricularly injected [H^3]-dopamine, failed to detect any known TIQ, with a method capable of detecting femtomolar amounts. Taken at face value, however, the data from human and some animal studies (summarized by Collins, and by M. Hirst, University of Western Ontario) would certainly be compatible with the view that TIQs may arise normally during catabolism of dopamine or norepinephrine, even without ethanol, and that larger amounts can be formed in the presence of alcohol, perhaps through the classical non-enzymatic condensation reaction of Pictet-Spengler. Dr. Virginia Davis (Veteran's Administration Hospital, Houston, Texas) presented the observations which had led her to hypothesize that tetrahydropapaveroline (THP) might also arise in a similar fashion by condensation of dopamine and dopa-acetaldehyde during dopamine metabolism in the presence of ethanol, but no new data documenting the occurrence of THP in brain or body fluids were presented.

Theoretical calculations by Dr. Henry Weiner (Purdue University) based upon known amounts of catecholamines and known rates of metabolism, and theoretical yields for the condensation reaction conditions which would exist *in vivo*, suggested that conclusive proof that beta-carbolines and TIQs did not exist may be difficult to obtain given that the maximum amounts which could be found could still be below the minute levels towards which the chemists had pushed the levels of detectability. A provocative idea, which appeared at least partially supported by existing data, was the possibility raised by Dr. A. Brossi (National Institutes of Health, Bethesda, Maryland) that TIQs arose not from acetaldehyde dopamine condensations, but rather from pyruvate-dopamine condensations in which oxidative decarboxylation lead to quinoline formation. If this suggestion could be validated, it might answer the unsettled puzzle of how measurable TIQs could be found when acetaldehyde remains below detectable levels.

The Workshop then turned its attention towards possible biological effects which beta-carbolines and TIQs might mediate. The majority of such studies were based on characterizing the pharmacological actions of synthetic carbolines and TIQs, while overlooking—at least for the moment—the critical issue of endogenous formation and its relevance to ethanol intoxication. In fact, several series of interesting biological actions were reported, but it is critical to realize that all such actions required doses of carbolines or TIQs which are orders of magnitude greater than even the most optimistic endogenous measurements.

The workshop participants heard a broad range of observations reported which indicated that synthetic TIQs and carbolines could exert actions at almost every step of monoaminergic function, including interactions with monoamine transmitter ligand binding sites (K. Kellar, Georgetown University, Washington, D.C., and Y. Nimit, VA Hospital, Houston, Texas), possible endogenous inhibitors of monoamine oxidase (M. Sandler, Queen Charlotte's Maternity Hospital, London), and monoamine transmitter synthesis rates (R. Bruce Holman, University of Redding, U.K., and Dr. C. Coscia, St. Louis University) as well as benzodiazepine binding sites (K. Braestrup, A/S Ferrosan, Roskilde, Denmark, and S.M. Paul, NIMH, Bethesda, Maryland), and benzodiazepine actions on sleep stages (W. Mendelson, NIMH, Bethesda, Maryland).

Many of the pharmacological studies of beta-carbolines and TIQs could be viewed as tests of the general hypothesis that addictive or reinforcing properties of ethanol could be mediated by an ethanol-derived condensation product, and the related subhypothesis that such products produced their effects by interaction with one of the endogenous opiate peptide systems.

At the level of single neurons, a strong case for such relationships was established by G. Siggins (Salk Institute) who reported that synthetic salsolinol and 7-methoxy salsolinol (the TIQ formed from dopamine and acetaldehyde) applied by micro-iontophoretic methods, and ethanol, applied by micro-pressure pulse ejection tended to affect neuronal discharge in various brain regions with a qualitative pattern similar to the effects of opiate peptides in these same regions. In general, all compounds were inhibitory in all regions except hippocampus, where all produced excitatory actions. Furthermore, many of the opiate like excitatory responses of hippocampal neurons to ethanol or salsolinal could be antagonized by parenteral or locally applied opiate antagonists. However, the TIQ and ethanol effects were also antagonized by the cholinergic receptor antagonist scopolamine, suggesting that the sites at which TIQs are able to elicit effects are not restricted to endogenous opiate receptors. It is possible that the TIQs, opiates, and ethanol share common actions through an ion channel effect, such as the changes in transmembrane Ca movements described by D. Ross (University of Texas Medical School, San Antonio, Texas).

At the level of the behaving animal, an intriguing set of data which furthered the uncertain linkage between TIQ effects and endogenous opiates was presented by H. Altshuler (TRIMS, Houston, Texas). After laboriously training rats in a two-way drug discrimination task (in which animals reliably gave one response when injected with low intoxicating doses of ethanol and another response when injected with saline), Altshuler investigated the degree to which rats could generalize (or discriminate) their response to potentially related drugs. For example, neither ethanol nor THP (when injected into the cerebroventricles) could produce an effect interpreted by the rats as "like intraperitoneal ethanol"; likewise, acetaldehyde injected either into the cerebroventricles or intravenously was also interpreted as "not alcohol." However, the injection of 50 ng doses of salsolinol intracerebroventricularly was generalized as alcohol-like, and this effect could be antagonized by the opiate antagonist naltrexone. In a conceptually related experiment, Altshuler also reported that he had been able to train some baboons to self-administer oral ethanol and, in a well-balanced control series of animals, he had observed the ethanol self-administration was significantly diminished by naltrexone or another opiate antagonist, naloxone. However, the doses are higher than those required to antagonize injected opiates.

It was, of course, evident to all those at the workshop that a very controversial series of ethanol self-administration experiments had fanned the embers of the various carboline-TIQ hypotheses of ethanol dependence at a time when strong supportive data in the central nervous system had been lagging. Those experiments, reported in the early 1970s by R.D. Myers and his colleagues (*see* Myers 1980; Dietrich & Erwin 1980; Melchior & Collins 1982) indicated that intracerebroventricular injections of THP and certain other TIQs could cause permanent increases in voluntary alcohol ingestion in rats. Although there have been some replications of the basic observation, the original phenomenon has proven to be far from reproducible even when rat species, strain, injection technique and evaluation methods are followed stringently. Furthermore, J.D. Sinclair (Alko, Finland) reported at the workshop that when he and Myers attempted to replicate this experiment together in the Myers' laboratory, they were unable to replicate the THP effect reported previously, although some rats given infusions of beta-carbolines did show modest increases in ethanol ingested.

Dr. Z. Amit (Concordia University, Montreal) reported that he had been unable to replicate the enhancement of ethanol ingestion in rats with any carboline or TIQ, but that he had been able to demonstrate to his own satisfaction that rats would self-administer salsolinol intravenously. However, even rats which exhibited salsolinol self-administration would not accept ethancl as a substitute nor consume significant amounts of oral ethanol. Dr R. Dietrich (University of Colorado Alcohol Research Center, Denver, Colorado) reported that he and his colleagues had in part replicated the THP effect on increased ethanol consumption, but noted that the amounts of ethanol ingested were in general quite modest, generally less than 5 g/kg/day. Others noted that rats which seemed to give the greatest increase in consumption were those with lower initial intake before drug infusion; after the THP treatments the levels consumed by these rats then approached the levels consumed by uninjected controls.

Dr. C. Melchior (University of Illinois Medical Center, Chicago, Illinois) who had participated in the original Myers experiments turned her attention in the interim to the possible interactions between the development of ethanol tolerance and the importance of environmental cues, in order to confront more directly the possibility that such cues could help to distinguish physiological factors which regulate the development and expression of tolerance. In these experiments, mice were trained by receiving daily injections of various doses of ethanol in one laboratory setting with distinctive lighting and sensory cues, and then subsequently tested for the hypothermic effects of a test dose of ethanol either in the training environment or in a novel testing environment. A purely metabolic effect of prior ethanol injection was ruled out in a separate group of mice who were exposed to the same training environments but received their ethanol only in their home cages. Although some tolerance developed in all mice, hypothermia was much less pronounced (i.e., tolerance was greatest) in those mice tested in their training environments. In an extension of these studies, Melchior also observed that injection of 3-carboxyl salsolinol or THP could regulate this process, appparently preventing the development of tolerance by diminishing, through an unknown mechanism, the brain ethanol content in response to the test i.p. dose. She then linked this effect to the earlier reports on THP increasing ethanol consumption by suggesting that one effect of the THP could be to inactivate normal adaptive mechanisms which would normally act to suppress ethanol consumption, perhaps by interfering with the release or effects of some natural transmitter system.

This workshop helped to crystallize certain important open issues which must be experimentally settled before it can be stated that any carboline or TIQ mediates an action of ethanol. The primary open issue is the establishment of the formation of these compounds *in vivo* in nervous tissue in any system in which the formation can be shown to be linked to ethanol content of the tissue, rather than to an artifact of the measuring methods. The evidence available at the time of the workshop seemed to most observers to favor the interpretation that the existence of carbolines under verified uncontaminated conditions was doubtful. The evidence was somewhat more convincing that TIQs formed in brain without ethanol and were increased after long-term ethanol exposure.

The next major open issue was whether the effects ascribed to injections of hundreds of nanograms of these compounds could be considered relevant to the issue of whether if formed endogenously in picogram amounts their release and actions could in any way be shown to be analogous to the effects of the ethanol. Again, the data presented were intriguing and interesting, but far from comprehensive and reproducible. Several actions of TIQs, those on single neurons and those on animals exhibiting one or another effect of ethanol, seemed to be generally similar and antagonized by opiate antagonists. At the same time, a variety of transmitter ligand binding sites were also found to be capable of weak interactions with synthetic carbolines and TIQs.

A third open issue centers on the interpretation of the relatively low doses of ethanol ingestion which some investigators have been able to observe after central injections of TIQs or after other drug treatments. Some held that any treatment that will cause experimental subjects to increase their consumption of ethanol is interesting if the phenomenon to be studied is defined as the basis for ethanol consumption. Others took the view that the critical phenomenon to be studied is the intoxicating and reinforcing pharmacological actions of ethanol which require detectable blood and tissue alcohol levels. Under the latter view, experimental perturbations which increase ethanol consumption above baseline but not far enough above to give detectable blood alcohol levels may be dependent upon totally different mechanisms than those which maintain excessive alcohol consumption in humans.

These three major open issues then can be distilled to one final important question: Given the rather marked disparity between the observed endogenous levels of these substances and their pharmacologically effective concentrations, is it possible to conceive of circumstances in which the necessary pharmacological levels could be attained and measured in a discrete locale, like a synaptic cleft? Although this and other solid issues offer an attractive hypothetical motivation for further research, it seems likely that the will-of-the-wisp nature of these pharmacologically potent substances is likely to persist for some time. Solution to these open questions would, however, be of important benefit to the explanation of problems of alcohol and opiate abuse.

References

Barchas, J.D., Akil, H., Elliott, G.R., Holman, R.B., and Watson, S.J. Behavioral neurochemistry: Neuroregulators and behavioral states. *Science*, 25:964-969, 1978.

Bloom, F.E. Neuropeptides. *Sci. Am.*, 245:148-168, 1981.

Buckholtz, N.S. Neurobiology of tetrahydro-beta-carbolines. *Life Sci.*, 27:893-903, 1980.

Cohen, G. Alkaloid products in the metabolism of alcohol and biogenic amines. *Biochem. Pharmacol.*, 25:1123-1127, 1976.

Dietrich, R., and Erwin, V.E. Biogenic amine-aldehyde condensation products: Tetrahydroisoquinolines and tryptolines (beta-carbolines). *Ann. Rev. Pharmacol. Toxicol.*, 20:55-69, 1980.

Melchior, C., and Collins, M.A. The route and significance of endogenous synthesis of alkaloids in animals. *CRC Crit. Rev. Toxicol.* (In press)

Myers, R.D. Pharmacological effects of amine-aldehyde condensation products. In: Rigter, H.E., and Crabbe, J.C. (eds.), *Alcohol Tolerance and Dependence*. Amsterdam: Elsevier, 1980, pp. 337-361.

Endogenous Opioid Mechanism in Neuroendocrine Regulation in Normal and Psychopathological States

Co-Chairs: **David S. Janowsky, M.D.**
Department of Psychiatry
University of California School of Medicine
La Jolla, California

and

S. Craig Risch, M.D.
Department of Psychiatry
University of California School of Medicine
La Jolla, California

The Effect of a Methadone Challenge on the Prolactin and Growth Hormone Responses of Psychiatric Patients and Normal Controls

Lewis L. Judd, M.D.[1,2] S. Craig Risch, M.D.,[1,2] Donal C. Parker, M.D.,[3] David S. Janowsky, M.D.[1,2] David S. Segal, Ph.D.,[1] and Leighton Y. Huey, M.D.[1,2]

The endogenous opiate-like peptide systems appear to be implicated in a number of important behavioral and physiological functions. The authors, like others, have been interested in the potential role endorphins may play in the pathophysiology of major psychiatric disorders. Based on previous studies, the authors hypothesized that a potentially important interrelationship may exist between the endogenous opioid peptide systems, specific neuroendocrine regulatory factors, and affective disorders (Judd et al. 1981, in press).

Endorphins are involved in the regulation of two neurohormones which have been reported to be abnormal in some depressed patients; these are prolactin (Gold et al. 1978; Judd et al. 1981) and growth hormone (Koenig et al. 1980; Meites et al 1979; Shaar et al. 1977). There have been conflicting reports in the literature on prolactin levels in depression, but Asnis et al. (1980) and Linkowski et al. (1980) have reported lower basal prolactin levels in depressed patients. In addition, Linkowski et al. (1980) and Extein et al. (1980) both reported blunted prolactin responses to respective challenges of thyrotropin-releasing hormone (TRH) and morphine in depressive disorders.

It has also been reported that growth hormone responses to various provocative agents are blunted in depression. Specifically, growth hormone responses to L-DOPA, insulin-induced hypoglycemia, and to amphetamine—all potent stimulators of growth hormone release—are absent or diminished in depressed patients (Sachar et al. 1975; Langer et al. 1976).

Here we report the results of a methadone challenge on prolactin and growth hormone responses in a diagnostically mixed sample of psychiatric patients and normal controls.

Method

Forty-one medically healthy male psychiatric inpatients and normals participated in the study after completing informed consent procedures. The patients' research diagnoses were derived by

---

[1] Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla, CA 92093.

[2] Psychiatry Service, San Diego VA Medical Center, La Jolla, CA 92093.

[3] Department of Medicine, School of Medicine, University of California, San Diego, La Jolla, CA 92093 and Medical Service, San Diego VA Medical Center, La Jolla, CA 92093.

Address reprint requests to Dr. Lewis L. Judd, Department of Psychiatry (M-003), School of Medicine, University of California, San Diego, La Jolla, CA 92093.

the Schedule for Affective Disorders and Schizophrenia-Research Diagnostic Criteria (SADS-RDC) method, and were based upon independent agreement of two psychiatrists. There were four experimental groups as follows: Schizophrenics, $N = 8$, age range 23-45 years, mean age 31.1 years; Manics, $N = 6$, age range 22-46 years, mean age 34.2 years; Depressive Disorders, $N = 16$, age range 22-54 years, mean age 35.86 years; Normal Controls, $N = 11$, age range 22-32 years, mean age 24 years. Subjects were drug-free at time of testing, with the patients having been removed from all psychoactive agents 7 days prior to the experimental sessions. It should be noted that several subjects required single doses of phenothiazines for clinical management a day or two preceding the experiment. Sessions began at 9:00 a.m. with the placement of a heparinized intravenous catheter to which the subjects were allowed 30 minutes for accommodation. Following this, blood samples were drawn once at baseline and at 30 and 60 minutes following the administration of 10 mg intramuscular (i.m.) of methadone-HCl. All the samples were assayed in duplicate within the same assay and blindly by those performing the assay (Parker et al. 1973).

Results

The results of the prolactin assay are included in Table 1. As anticipated, methadone increased prolactin secretion for the entire subject sample from a mean baseline level of 11.7 ± 1.5 ng/ml to a peak of 27.5 ± 5.25 ng/ml at 60 minutes post methadone ($t = 2.78$, df = 40; $p < 0.01$). Methadone induced a mean prolactin rise of approximately two- to three-fold over baseline levels in all four groups of subjects. There were, however, significant differences between the groups in both the baseline levels and in the net prolactin response to methadone. The depressive disorder patients stood out by having a significantly lower mean basal prolactin level ($p < 0.05$) than was observed in the other three groups of subjects. Further, the depressed patients had significantly lower mean levels in both 30 ($p < 0.01$) and 60 ($p = 0.01$) minute samples as compared to the schizophrenic, manic, and normal groups who responded to methadone with a much more marked and robust increase in prolactin.

An examination of the raw data revealed that eight of sixteen (50%) of the depressed patients had absent or very attentuated prolactin responses to methadone, while the remaining eight manifested prolactin increases. When a blunted prolactin response was defined by a rise of less than 2 ng/ml in either 30 or 60 minute samples, then eight depressed patients and two normals had blunted responses.

The mean growth hormone levels for the four experimental groups are presented in Table 2. As can be seen, methadone significantly increased the mean growth hormone levels in all four groups of subjects over baseline levels. It rose from a mean of 3.02 ± 1.34 mIU/ml at baseline to a high of 20.55 ± 9.66 mIU/ml at 60 minutes ($F = 12.03$; df = 40; $p < 0.05$). Although no

Table 1

Mean Serum Prolactin Levels (Ng/Ml) at Baseline, 30, and 60 Minutes Post-methadone (10 Mg) in the Three Psychiatric Patient and the Normal Control Groups

	Baseline	30 minutes	60 minutes	Δ Baseline to 60 minutes
Schizophrenics ($N = 8$)	15.9 ± 3.6	33.1 ± 9.4	42.0 ± 10.9	26.1
Manics ($N = 6$)	13.0 ± 4.5	30.8 ± 12.9	34.4 ± 13.5	21.4
Depressed ($N = 16$)	7.5 ± 0.9	10.6 ± 1.9	15.4 ± 3.5	7.9
Controls ($N = 11$)	14.1 ± 3.2	25.5 ± 6.3	30.6 ± 7.7	16.5
Mean for Entire Subject Sample	11.7 ± 1.5	21.9 ± 5.0	27.5 ± 5.3	15.8

Kruskal-Wallis One-Way ANOVA

Group Difference at Baseline	$H = 10.09$; df 3; $p < 0.05$
Group Difference at 30 Minutes	$H = 12.7$; df 3; $p < 0.01$
Group Difference at 60 Minutes	$H = 10.6$; df 3; $p < 0.01$

statistically significant differences emerged in growth hormone response in regard to diagnosis, there was evidence that the manic and depressed patients responded to methadone with a less marked increase in growth hormone in the 30- and 60-minute serum samples than did the schizophrenic and normal control groups. An examination of the raw data revealed that ten of thirteen depressed patients and five of seven manic patients had blunted growth hormone responses to the methadone challenge. However, three of seven patients in the schizophrenic and four of eleven in the control group also had blunted growth hormone responses. Thus, the blunted growth hormone responses did not occur as exclusively among the depressive disorder patients as was seen with the blunted prolactin response.

Eleven of the thirteen depressed patients for whom both growth hormone and prolactin data were available manifested either a blunted prolactin or growth hormone response or both to the same methadone challenge.

Discussion

Before discussing the data, which were derived under these experimental conditions, there are some issues potentially affecting the data which should be mentioned. One manic and two schizophrenic patients required single p.r.n. (as needed) doses of phenothiazine during the time they were on "drug-free" status. This slightly increased the baseline prolactin levels in these three patients, which in turn had an effect on the mean basal levels for the experimental groups of which they were members. There are reports that attenuated prolactin responses have been observed in subjects who are relatively hyperprolactinemic, but this was not manifested in these three patients, since each had robust prolactin increases following the methadone administration.

Another issue deserving of comment is the fact that the age range in the control group was lower and therefore not comparable to the three patient groups. This is an acknowledged flaw in the design, but on the other hand this should not affect the results presented here. Specifically, there is no evidence that age per se, at least within the range studied here (i.e., 21-54 years), would have any effect on either basal levels or upon the response to challenge agents of prolactin or growth hormone.

The mean basal prolactin level in the depressed patients was significantly lower than it was for the manic, schizophrenic, and control groups. Because the p.r.n. phenothiazine administration slightly increased the mean basal prolactin levels in the manic and schizophrenic groups, it is not our intention to highlight this particular finding, other than to mention that it is consistent with the reports by Asnis et al. (1980) and Linkowski et al. (1980), both of whom reported lower basal levels in depression. The blunted prolactin response to methadone we observed in eight of sixteen depressed patients is consistent with the findings of Linkowski et al. (1980) and Extein et al. (1980) who observed the same response from the challenges of TRH and morphine, respectively.

Table 2

Effect of Methadone-HCl (10 Mg Im) on Growth Hormone (mIU/Ml) in Psychiatric Patients and Normal Controls

	Baseline	30 Minutes	60 Minutes
Schizophrenics (*N* = 7)	2.53 ± 0.51	17.60 ± 14.10	46.29 ± 25.43
Manics (*N* = 7)	3.18 ± 0.89	6.17 ± 3.86	9.43 ± 5.40
Depressed (*N* = 13)	4.60 ± 2.90	4.19 ± 1.49	11.36 ± 5.43
Normals (*N* = 11)	2.09 ± 0.53	21.11 ± 9.96	22.15 ± 7.48
Mean for Entire Subject Sample	3.02 ± 1.34	12.46 ± 4.29	20.55 ± 9.66

Kruskal-Wallis One-Way ANOVA

Group Difference at Baseline	N.S.
Group Difference at 30 Minutes	N.S.
Group Difference at 60 Minutes	N.S.

There is clear evidence that methadone significantly increased the mean growth hormone secretion in the entire subject sample. Whereas there are reports in the literature indicating that opiate/opioids stimulate growth hormone secretion in animals (Meites et al. 1979; Shaar et al. 1977; Koenig et al. 1980), this is the first report of which we are aware reporting an opiate-induced growth hormone rise in normal subjects and in psychiatric patients. There were no significant group differences in the mean growth hormone response following methadone. Blunted growth hormone responses were present in subpopulations in each of the three patient groups and in the normal controls as well. Of specific interest was the fact that the majority of the patients in both the manic (five of seven) and the depressed (ten of thirteen) groups had blunted growth hormone responses to methadone. While the blunted growth hormone response did not occur exclusively in the affective disorder patients, it was predominantly manifested in these patients.

It is intriguing that eleven of the thirteen depressed patients, on whom we have both prolactin and growth hormone data, manifested blunting of prolactin or growth hormone or both to the same opiate challenge.

It is possible that the blunted prolactin and/or growth hormone response may be an additional neuroendocrine dysfunction that is correlated with the presence of affective disorder (e.g., depressive disorders). It is also possible that this neuroendocrine dysfunction may prove to be a useful diagnostic marker for the identification of this group of psychiatric disorders.

These findings are consistent with our original hypothesis that a potentially important interrelationship exists between the opioid peptide systems, certain neuroendocrine regulatory factors, and the pathophysiology of affective disorders. The exploration and characterization of this relationship continues to be a promising direction for future research.

References

Asnis, G.M., Nathan, R.S., Halbreich, U., Halpern, F.S., and Sachar, E.J. Prolactin changes in major depressive disorders. *Am. J. Psychiatry,* 137(9):1117-1118, 1980.

Extein, I., Pottash, A.L.C., Gold, M.S., Sweeney, D.R., Martin, D.M., and Goodwin, F. Deficient prolactin response to morphine in depressed patients. *Am. J. Psychiatry,* 137:845-846, 1980.

Gold, M.S., Redmond, D.E., Jr., Donabedian, R.K., Goodwin, F.K., and Extein, I. Increase in serum prolactin by exogenous and endogenous opiates: Evidence for antidopamine and antipsychotic effects. *Am. J. Psychiatry,* 135:1415-1416, 1978.

Gruen, P.H., Sachar, E.J., Altman, N., and Sassin, J. Growth hormone responses to hypoglycemia in postmenopausal depressed women. *Arch. Gen. Psychiatry,* 32:31-33, 1975.

Judd, L.L., Janowsky, D.S., Segal, D.S., Parker, D.C., and Huey, L.Y. Behavioral effects of methadone in schizophrenic patients. *Am. J. Psychiatry,* 138(2): 243-245, 1981.

Judd, L.L., Janowsky, D.S., Zettner, A., Huey, L.Y., and Takahashi, K. Effects of naloxone HCl on cortisol levels in patients with affective disorder and normal controls. *Psychiatr. Res.,* 4:277-283, 1981.

Judd, L.L., Parker, D.C., Janowsky, D.S., Segal, D.S., Risch, S.C., and Huey, L.Y. The effect of methadone on the behavioral and neuroendocrine responses of manic patients. *Psychiatry Res.* (In press)

Koenig, M., Mayfield, M.A., Coppings, R.J., McCann, S., and Krulich, L. Role of central nervous system neurotransmitters in mediating the effects of morphine on growth hormone and prolactin secretion in the rat. *Brain Res.,* 197:453-468, 1980.

Langer, G., Heinze, G., Reim, B., and Matussek, N. Reduced growth hormone responses to amphetamine in "endogenous" depressive patients. *Arch. Gen. Psychiatry,* 33:1474-1475, 1976.

Linkowski, P., Brauman, H., and Mendelwicz, J. Prolactin secretion in women with unipolar and bipolar depression. *Psychiatry Res.,* 3:265-271, 1980.

Meites, J., Bruni, J.F., and Van Vugt, D.A. Effects of endogenous opiate peptides on release of anterior pituitary hormone. In: Collu, R., Barbeau, A., Ducharme, J.R., Rochefort, J.G. (eds.), *Central Nervous System Effects of Hypothalamic Hormones and Other Peptides.* New York: Raven Press, 1979, pp. 261-271.

Parker, D.C., Rossman, L.G., and Vanderlan, E.F. Sleep related nycotohumeral and briefly episodic variation in human plasma prolactin concentrations. *J. Clin. Endocrin. Metab.,* 36:1119-1124, 1973.

Sachar, E.J., Frantz, A.G., Altman, N., and Sassin, J. Growth hormone and prolactin in unipolar and bipolar depression patients: Responses to hypoglycemia and L-DOPA. *Am. J. Psychiatry,* 130(12):1362-1367, 1973.

Sachar, E.J., Frederickson, R.C.A., Dininger, M.B., and Jackson, L. Enkephalin analogues and naloxone modulate the release of growth hormone and prolactin—evidence for regulation by an endogenous opioid peptide in the brain. *Life Sci.,* 21:853-868, 1977.

Response of Plasma Cortisol and β-Endorphin Immunoreactivity to Surgical Stress

David Pickar, M.D.,[1] Martin R. Cohen, M.D.,[1] Michel Dubois, M.D.,[2] and William E. Bunney, Jr., M.D.[3]

Introduction

Considerable data now exist from animal experimentation that the endogenous opioid system plays an important role in the biological response to stress and in endogenous analgesic mechanisms (Amir et al. 1980; Rossier et al. 1980; Madden et al. 1977). Several lines of evidence support the notion that the endogenous opioid system is involved in pain perception in humans. Stimulation of the periaqueductal gray area in chronic pain patients has been shown to produce both analgesia and increased CSF levels of opioids (Hosobuchi 1977; Akil et al. 1978), while profound and long-lasting analgesia has resulted from the intrathecal administration of β-endorphin (Oyama et al. 1980). Naloxone-reversible stress-induced analgesia has recently been demonstrated to occur clinically (Willer et al. 1981). The relationship between stress and behaviors such as pain perception are, however, complex (Antelman & Cagguilla 1980) and biologic responses are known to vary with stress paradigm (Mason 1975) and with individuals (Naber et al. 1981).

The authors have used general surgery as a paradigm for studying stress effects on circulating levels of plasma β-endorphin immunoreactivity and cortisol in humans and for investigating relationships between pain perception and hormone levels.

Method

Nine adults (seven males, two females; ages 18-60) who underwent laparotomies as part of a National Cancer Institute protocol for the assessment of testicular or ovarian malignancy were studied. Patients were medication-free for at least 72 hours prior to surgery and were free of medical complications other than regional malignancy. Pre-medication was with pentobarbital (100 mg, i.m.) and anesthesia was induced with thiopental and muscle relaxant. No opiates were given until the 1st-3rd postoperative hour when the patient was awake, at which time morphine sulfate (1.5-3.5 mg/hr i.v.) was administered as needed (patient request) for relief of postoperative pain.

Plasma was collected from each patient prior to intubation and anesthetic induction, 10 minutes after skin incision, and at 30-minute intervals during surgery until skin closure. In six of the nine patients plasma was also collected immediately after intubation and during the period of postoperative morphine administration. Plasma assay for β-endorphin included antiserum prepared from rabbits against synthetic human β-endorphin and demonstrates by weight <50 percent cross-reactivity with β-lipotropin, <0.01 percent with α-endorphin and α-MSH, <0.004 percent with leu- and met-enkephalin and <5 percent with ACTH.

Results

Anesthesia induction did not significantly effect either plasma β-endorphin (ir) or plasma cortisol: pre-induction means ± SEM were 20.5 ± 2.9 pmole/liter and 23.7 ± 2.5 μg percent and post-induction means ± SEM were 26.9 pmole/liter and 26.1 ± 4.2 μg percent, respectively. In contrast, surgery was associated with significant increases in both variables (Figure 1). These elevated levels typically persisted throughout the surgical procedure and, in some patients, plasma β-endorphin (ir) increased still further upon awakening from anesthesia. Morphine administration was associated with significant decreases in both plasma cortisol and β-endorphin (ir) (Figure 2).

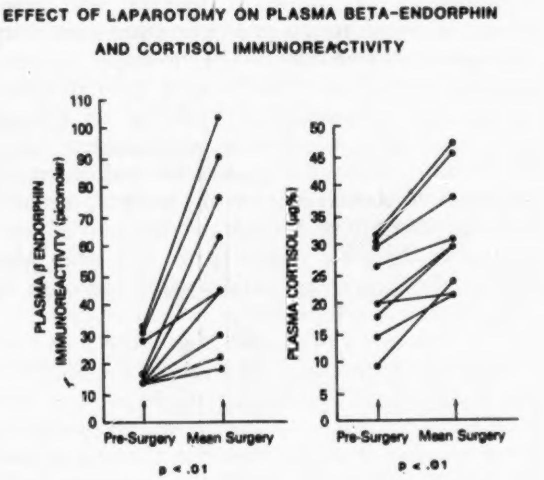
The authors used the total amount of morphine administered over the first 24 postoperative hours as an objective assessment of the degree of subjects, postoperative pain. Total morphine requirement was related to patient age ($r = -.69$, $p < .05$) and patient weight ($r = .55$, $p < .1$), findings consistent with known morphine pharmacokinetics. Neither age nor weight, however, were significantly related to mean surgery levels of β-endorphin (ir) (Table). Mean surgery levels of plasma β-endorphin (ir) were negatively correlated with total morphine requirement (Figure 3), while those of plasma cortisol showed a similar tendency ($r = -.65$, $p < .1$). Presurgery cortisol levels were significantly related to mean surgery cortisol levels ($r = .85$, $p < .01$).

---

[1] Neuroscience Branch, National Institute of Mental Health, Bethesda, MD 20205.

[2] Department of Anesthesia, National Institutes of Health, Bethesda, MD 20205.

[3] Department of Psychiatry and Human Behavior, California College of Medicine, University of California at Irvine, Irvine, CA 92717.



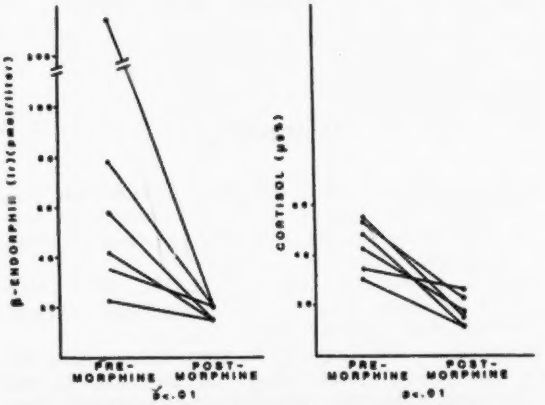


FIGURE 2. The effect of postoperative morphine on levels of plasma β-endophin (ir) and cortisol in six patients. Samples were collected after patients awoke from anesthesia but before postoperative analgesics and during morphine administration.

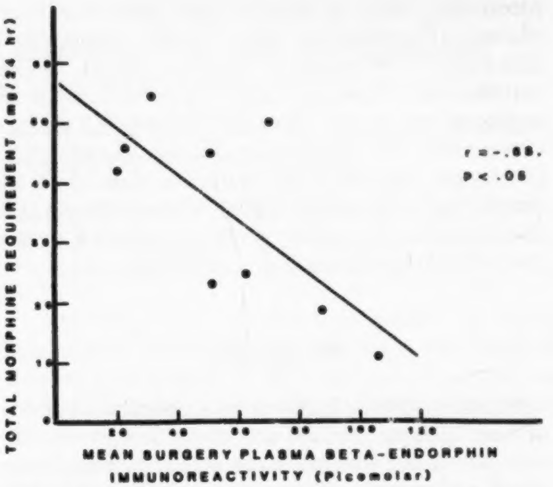


FIGURE 3. Correlation between mean surgery levels of plasma β-endorphin (ir) and total amount of morphine administered during the first 24 postoperative hours (1.5-3.5 mg/hr, i.v.)

Table

Patient Demography, Levels of Plasma β-Endorphin Immunoreactivity, and Post-Operative Morphine Requirements

Patient No.	Age	Weight (kgs)	Pre-surgery β-endorphin (ir) (picomolar)	Mean Surgery β-endorphin (ir) (picomolar)	Morphine Requirement* (mg/24 hr)
1	21	75.4	< 14.4	62.4	24
2	30	72.5	< 14.4	22.5	46
3	41	62.7	31.0	91.1	18
4	59	57.5	28.2	45.0	22
5	60	47.5	32.6	103.7	12
6	16	67.3	16.0	76.2	50
7	21	63.0	< 14.4	30.4	56
8	28	81.0	< 14.4	17.4	44
9	43	85.5	< 14.4	45.0	45

*mg per 1st 24 post-operative hours

Age vs Morphine Requirement: $r = -.69$, $p < .05$

Weight vs Morphine Requirement: $r = .55$, $p < .1$

Mean Surgery Plasma β-endorphin (ir) vs Morphine Requirement: $r = -.68$, $p < .05$

Because plasma β-endorphin (ir) levels prior to surgery were often lower than the sensitivity of our assay, no parametric testing of a correlation between these levels and postsurgical morphine requirement could be made. It was possible, however, to divide the patients into groups on the basis of data distribution (Table): six patients with low plasma β-endorphin (ir) levels (< 17 picomolar) prior to surgery and three with high plasma β-endorphin (ir) (≥28 picomolar). Similarly, morphine requirements were distributed biomodally: high requirements, 44-56 mg, and low requirements, 12-24 mg. All six patients with low presurgery plasma β-endorphin (ir) levels required high morphine doses and all three patients with high levels of plasma β-endorphin (ir) required low morphine doses ($p < .05$, Fisher Exact Test, two-tailed).

Discussion

Surgical stress proved to be a potent stimulator of both plasma cortisol and β-endorphin (ir). In contrast to the surgical stress itself, plasma levels of β-endorphin (ir) and cortisol were not significantly effected by anesthesia induction. Although this latter finding lends little support for an involvement of the endogenous opioid system in anesthesia effects, it does not exclude a role for brain opioids, whose contents have been shown to vary independently from pituitary β-endophrin (Rossier et al. 1977), or for other circulating opioids, in the mediation of anesthetic effects. The parallel cortisol and β-endorphin (ir) increases during surgical stress also support the close association between β-endorphin (ir) and the hypothalamic-pituitary-adrenal (HPA) axis (Mains et al. 1977; Guillemin et al. 1977; Vale et al. 1981). The marked decrease in both cortisol and β-endorphin (ir) associated with postoperative morphine administration suggests the possibility of a common feedback inhibition by opiates. It is also possible, however, that decreases in these neurohormones may relate to decreased conscious pain perception produced by morphine.

The wide individual differences in subjects, postoperative morphine requirements are consistent with clinical belief. This variance was in part explained by pharmacokinetic considerations such as relationships with age and body weight, and by non-pharmacokinetic variables such as plasma levels of β-endorphin (ir). Multiple regression analysis of patient age and mean surgery plasma β-endorphin (ir) increased the degree of variance predicted to 70 percent. Age and mean surgery plasma β-endorphin (ir) were individually able to predict 46 and 48 percent, respectively. Although this increase in variance predicted did not reach statistical significance, it does suggest the possibility that age and plasma β-endorphin (ir) may relate independently to postoperative morphine requirement.

The similar, although not quite as strong, negative correlation between stress-induced cortisol levels and postoperative morphine requirement may support a hypothesized link between human arousal and analgesia. Furthermore, the negative relationship between plasma β-endorphin (ir) prior to surgery and postoperative morphine usage suggests that variability in physical trauma may not be the major determinant of variance in postoperative pain. Rather, the patient's physiological response or arousal prior to surgery, which may be dependent upon the intensity of psychological stress and/or simply the innate responsiveness of the patient's arousal systems, seems to be a major determinant of postoperative analgesic requirement and may also predict the degree of physiological response to surgical stress.

Although levels of plasma β-endorphin (ir) are in actuality a composite of levels of β-endorphin and β-lipotropin, the results suggested that this complex may relate to important physiological processes. It is doubtful, however, that the plasma levels detected are, in and of themselves, sufficient to produce significant analgesia. More likely, these levels of circulating plasma β-endorphin (ir) reflect a central nervous system arousal which may involve the endogenous opioid system.

References

Akil, H., Richardson, D.E., Hughes, J., and Barchas, J.D. Enkephalin-like material elevated in ventricular cerebrospinal fluid of patients after focal stimulation. *Science,* 201:463-465, 1978.

Amir, S., Brown, Z.W., and Amit, A. The role of endorphins in stress: Evidence and speculation. *Neurosci. Biobehav. Rev.*, 4:77-78, 1980.

Antelman, S., and Caggiula, A. Stress-induced behavior: Chemotherapy without drugs. In: Davidson, J., and Davidson, R.M. (eds.), *Psychobiology of Consciousness.* New York: Plenum Press, 1980.

Guillemin, R., Vargo, T., Rossier, J., Minick, S., Ling, N., Rivier, C., Vale, W., and Bloom, F.E. β-Endorphin and adrenocorticotropin are secreted concomitantly by the pituitary gland. *Science,* 197:1368-1369, 1977.

Hosobuchi, Y., Adams, J.E., and Lipchitz, R. Pain relief by electrical stimulation of the central gray matter in humans and its reversal by naloxone. *Science,* 197:183-186, 1977.

Madden, J., Akil, H., Patrick, R., and Barchas, J. Stress-induced parallel changes in central opioid levels and pain responsiveness in the rat. *Nature,* 267:358-360, 1977.

Mains, R.E., Eipper, B.A., and Ling, N. Common precursor to corticotropins and endorphins. *Proc. Natl. Acad. Sci. USA,* 74:3014-3018, 1977.

Mason, J. Emotions as reflected in patterns of endocrine regulation. In: Levi, L. (ed.), *Emotions: Their Parameters and Measurements.* New York: Raven Press, 1975.

Naber, D., Bullinger, M., Zahn, T., Johnson, J.L., Huhtaniemi, P., Pickar, D., Cohen, M.R., and Bunney, W.E., Jr. Stress effects of β-endorphin in human plasma: Relationships to psychophysiological and psychological variables. *Psychopharmacol. Bull.,* 17:187-189, 1981.

Oyama, T., Jin, T., Yamaya, R., Ling, N., and Guillemin, R. Profound analgesic effects of β-endorphins in man. *Lancet,* ii:122-125, 1980.

Rossier, J., Bloom, F., and Guillemin, R. Endorphins and stress. In: Selye, H. (ed.), *Selye's Guide to Stress Research, Vol. 1.* New York: van Nostrand Reinhold Co., 1980.

Rossier, J. Vargo, T.M., Minick, S., Ling, N., and Guillemin, R. Independent variation of β-endorphin and enkephalin levels in rat brain regions. *Proc. Natl. Acad. Sci. USA,* 74:5162-5165, 1977.

Vale, W., Spiess, J., and Rivier, C. Characterization of a 41-residue bovine hypothalamic peptide that stimulates secretion of corticotropin and β-endorphin. *Science,* 1394-1397, 1981.

Willer, J., Dehen, H., and Cambier, H. Stress-induced analgesia in humans: Endogenous opioids and naloxone-reversible depression of pain reflexes. *Science,* 212:989-991, 1981.

Elevated Plasma β-Endorphin Concentrations in Depression and Cholinergically Supersensitive Release Mechanisms[1]

S. Craig Risch, M.D.,[2] David S. Janowsky, M.D.,[2] Lewis L. Judd, M.D.,[2] and Leighton Y. Huey, M.D.[2]

Morning plasma concentrations of beta-endorphin immunoreactivity were significantly higher in a group of depressed patients meeting the Research Diagnostic Criteria for Major Depressive Disorder or Schizoaffective Disorder, depressed, than in age- and sex-matched groups of normal controls and psychiatric patients without affective disorders. Furthermore, physostigmine stimulated release of beta-endorphin immunoreactivity was also significantly greater in the depressed patients. These results provide the first evidence for elevated plasma concentration of beta-endorphin in depression and also represent further evidence for cholinergic supersensitivity in depression. These results suggest that elevated plasma concentrations of beta-endorphin and cholinergically stimulated hypothalamic-pituitary beta-endorphin release, might potentially represent biological state or trait markers for depression.

Introduction

Adrenal cortisol hypersecretion, as well as flattened cortisol circadian periodicity, and failure to suppress plasma cortisol concentrations with the overnight low-dose dexamethasone suppression test, occur in a significant number of endogenously depressed patients, and have now been well established as substantive neuroendocrine markers highly specific for primary affective disorders (Stokes et al. 1975; Brown 1979; Carroll et al. 1976a, 1976b, 1981; Sachar 1976; Sachar et al. 1980a; Schlesser et al. 1980). Many investigators also believe that this neuroendocrine abnormality reflects limbic-hypothalamic-

---

[1] This study was supported in part by the Medical Research Service of the San Diego Veterans Administration Medical Center (MRIS #4576) and the USPHS Grant MH-30914.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego and San Diego Veterans Administration Medical Center, San Diego, CA 92161.

hypophyseal hyperactivity. In this regard, Fang et al. (1981), comparing pre- and post-dexamethasone plasma adrenocorticotropic hormone (ACTH) concentrations in cortisol-hypersecreting dexamethasone-resistant depressed patients and in normal controls, failed to detect any differences between the two groups in plasma ACTH concentrations, either before or after the standard 1.0 mg dexamethasone suppression test. However, Reus et al. (1980) have recently reported that although dexamethasone-resistant depressed patients did not differ statistically from dexamethasone-sensitive depressed patients in predexamethasone plasma ACTH concentrations, the dexamethasone-resistant depressed patients did have significantly higher post-dexamethasone plasma ACTH concentrations than did the dexamethasone-sensitive patients. Most recently, Kalin et al. (1982) have reported that dexamethasone-resistant patients have significantly higher pre- and post-dexamethasone plasma ACTH concentrations than do dexamethasone-sensitive patients. Obviously more studies are needed, but, to date, two of three investigations suggest that cortisol hypersecretion and dexamethasone resistance in depressed patients may be accompanied by elevated ACTH plasma concentrations.

Abnormalities in central noradrenergic (Sachar et al. 1980b), serotonergic (Carroll et al. 1979), and cholinergic (Carroll et al. 1979) neurotransmitter functions have all been mechanistically implicated in the pathophysiology of the presumed limbic-hypothalamic-pituitary-adrenal (CRF-ACTH-cortisol) hypersecretion in depression. With respect to central cholinergic mechanisms, substantial evidence from *in vitro* (Bradbury et al. 1975; Edwardson & Bennett 1974) and *in vivo* animal (Endroczi et al. 1963; Suzuki et al. 1964; Otsuka 1966; Naumenko 1968; Krieger & Krieger 1970; Balfour et al. 1975; Suzuki et al. 1975) and human (Cozanitis 1974; Hill & Wynder 1974; Davis & Davis 1980; Janowsky et al. 1980) investigations suggest that cholinergic agonists may activate the hypothalamic-hypophyseal-adrenal axis to increase cortisol secretion. In addition, Carroll et al. (1979) have demonstrated that dexamethasone resistance can be induced in normal subjects by infusions of physostigmine, an acetylcholinesterase inhibitor with both nicotinic and muscarinic properties. That cholinergic mechanisms might be significantly implicated was suggested by the fact that pretreatment of the subjects with atropine abolished this response. Also administration of ipecac, a potent stimulator of nausea and vomiting, failed to induce dexamethasone resistance, suggesting that this effect may not simply reflect "nonspecific stress."

If central cholinergic mechanisms are involved in the pathophysiology of cortisol hypersecretion in depression, and if the observed elevated plasma cortisol concentrations reflect on increased hypophyseal secretion of ACTH, then it might be hypothesized that plasma beta-endorphin concentrations might also be elevated. In fact, we have recently demonstrated that ACTH and beta-endorphin are co-released in humans under conditions of central cholinergic stimulation (Risch et al., in press). These results parallel the original observations of Guillemin et al. (1977) and others (Pellefier et al., 1977; Rossier et al. 1977) in animal stress paradigms.

An abnormality in acetylcholine neurotransmitter function has also been implicated in depression. Janowsky et al. (1972) have hypothesized that acetylcholine may play an important role in the pathophysiology of affective disorders, and more recently have demonstrated that affective disorder patients are both behaviorally and neuroendocrinologically supersensitive to the effects of physostigmine when compared with nonaffective disorder patients (Janowsky et al. 1980; Risch et al. 1981). Also, Sitaram et al. (1980) have suggested that affective disorder patients may be supersensitive to central cholinergic induction of rapid-eye-movement (REM) sleep, possibly reflecting a generalized cholinergic receptor supersensitivity in depression. Thus a cholinergically regulated hypothalamic-hypophyseal ACTH-beta-endorphin axis might also be cholinergically supersensitive in affective disorder patients.

Method

These studies were conducted under the Food and Drug Administration's approved Investigational New Drug application and with local human subjects committee approval. All subjects gave written informed consent. All subjects were male and there was no significant difference in age composition among experimental and control groups. To be included, subjects had to be off medication for at least 2 weeks prior to participating in the studies. All subjects received a Research Diagnostic Criteria (RDC) diagnosis based on a Schedule of Affective Disorder and Schizophrenia interview by an experienced diagnostician and collateral information obtained from previous hospitalizations, medical records, and interviews with family members.

Plasma samples for basal morning plasma beta-endorphin immunoreactivty concentrations in the subject groups were obtained as follows. On two separate days, varying between 3 and 7 days apart, an 18-gauge heparin lock catheter was inserted at 8 a.m. in a forearm vein for subsequent plasma sampling. After an accommodation period of 30 minutes, three plasma samples were drawn at 15-minute intervals for subsequent beta-endorphin determinations. The beta-endorphin values from these six samples were averaged to give a mean morning plasma beta-endorphin concentration for each subject.

Differences in cholinergically stimulated hypothalamic-pitutary plasma beta-endorphin concentrations among individuals were determined as follows. After an 8 a.m. insertion of an indwelling heparin-lock venous catheter and subsequent plasma samplings as described above, each subject received methscopolamine 1.0 mg intramuscularly 20 minutes prior to physostigmine or placebo infusions to induce partial peripheral cholinergic blockage. Each individual received infusions of physotigmine salicylate (22 μg/kg) and placebo (sterile saline), 100 cc infused over 10 minutes, in a randomized, double-blind, counter balanced paradigm. Physostigmine and placebo infusions were separated by 3 to 7 days. Plasma samples were obtained from the indwelling venous heparin lock catheters at 10, 20, 30, 45, and 60 minutes subsequent to the physostigmine and placebo infusions. The average of the three baseline pre-infusion plasma beta-endorphin concentrations was subtracted from peak post-infusion plasma beta-endorphin concentrations, to determine each individual's physostigmine and placebo associated increase in plasma beta-endorphin immunoreactivity concentrations.

Four subject groups were compared with respect to: 1) basal morning plasma beta-endorphin concentrations and 2) cholinergically stimulated hypothalamic-hypophyseal plasma beta-endorphin increases. The composition of the groups was SADS/RDC: normals, $N=12$; major depressive disorder (unipolar 6, bipolar 6), $N=12$; nonaffective disorder psychiatric patients, $N=6$; and schizoaffective disorder, depressed, $N=4$.

Significance of changes in plasma beta-endorphin immunoreactivity was determined by repeated measures analysis of variance. Significance of differences among groups in basal plasma beta-endorphin immunoreactivity concentrations and in cholinergically stimulated plasma beta-endorphin immunoreactivity concentrations were determined by one-way analysis of variance and subsequent Scheffé's S Method analysis to compare specific groups.

Plasma beta-endorphin concentrations were measured by radioimmunoassay as previously reported (Risch et al. 1980). The antibody for beta-endorphin has a 50 percent cross-reactivity with beta-lipotropin but less than 0.1 percent with alpha-endorphin and alpha-melanocyte-stimulating hormone, and less than 0.004 percent with leucine and methionine enkephalin. Within assay variability for beta-endorphin is approximately 5 percent and between assay variability is approximately 9 percent. Sensitivity varies from 25-50 pg/ml.

Results

Morning basal plasma beta-endorphin immunoreactivity concentrations were significantly elevated in patients with major depressive illness (123 ± 9.5 pg/ml) and schizoaffective disorder, depressed (131 ± 11.3 pg/ml) as compared with normal subjects (65 ± 6.6 pg/ml) and patients without major affective illnesses (61 ± 4.6 pg/ml): $F(3,30) = 16.2$; $p<0.0001$ (*see* Figure 1). There was no statistically significant difference in basal plasma beta-endorphin immunoreactivity concentrations between patients with major depressive illness and schizoaffective illness, depressed.

In each group, physostigmine infusions resulted in significant increases in plasma beta-endorphin immunoreactivity concentrations as compared to placebo infusion, in agreement with similar results previously reported (Risch et al. 1980). Physostigmine associated increases in plasma beta-endorphin immunoreactivity concentrations were significantly higher in patients with major depressive illness (143 ± 19.4 pg/ml) and schizoaffective disorder (287 ± 51 pg/ml) as compared with normal subjects (73 ± 21 pg/ml) or psychiatric patients without affective illnesses (57 ± 25 pg/ml): F (3,30) = 10.5; $p < 0.0001$ (*see* Figure 2). Physostigmine associated increases in plasma beta-endorphin immunoreactivity concentrations were significantly higher in the schizoaffective group than in the major depressive disorder group, $p < 0.01$, (Scheffé's "S" A Posteriori Method).

Discussion

These findings represent the first report suggesting that plasma concentrations of beta-endorphin, like ACTH and cortisol, may be elevated in depressed subjects, possibly reflective of limbic-hypothalamic-hypophyseal hyperactivity. These results parallel the observation of Terenius et al. (1977) of elevated cerebrospinal fluid "Fraction I" endorphins in severely depressed patients, although presumably cerebrospinal fluid endorphins derived from arcuate nucleus projections to the third ventricle, while the plasma endorphins observed in this study originate from the anterior pituitary. The significance of elevated plasma beta-endorphin concentrations in depressed subjects is unclear. The elevated beta-endorphin concentrations could conceivably be of mechanistic significance in the etiology of the depressed state, or might result as a consequence of the depressed state. Further experimental studies will be necessary to discern the role of elevated plasma endorphin concentrations in depression.

These differences in basal plasma beta-endorphin concentrations among the different nosological groups confound the interpretation of the observed differences in physostigmine asssociated plasma beta-endorphin increases in these same groups. However, the observed enhanced responsivity of the depressed patients, as measured by absolute change scores, is at least consistent with the

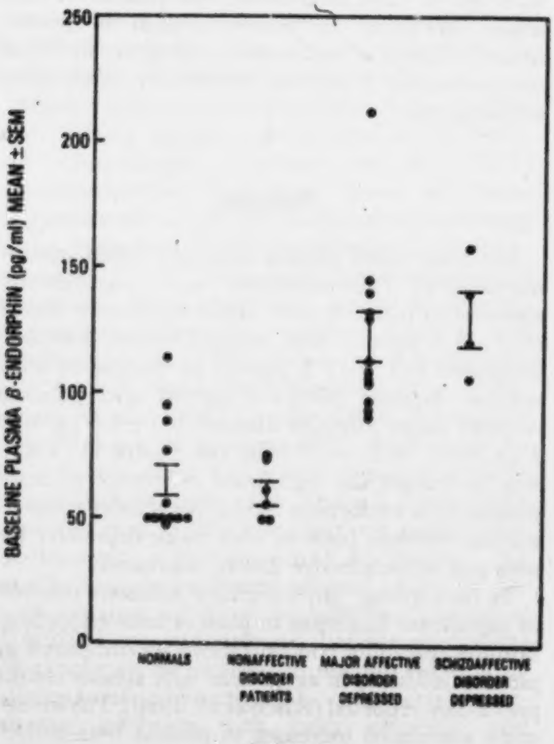


FIGURE 1

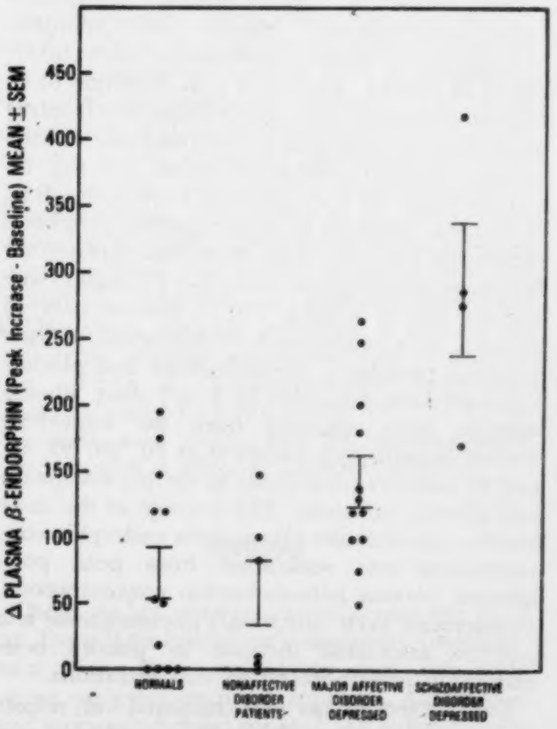


FIGURE 2

possibility of a hypersensitivity of the hypothalamic-hypophyseal beta-endorphin axis to central cholinergic stimulation in depressed patients. These findings add further support for the possibility of cholinergic supersensitivity in affective disorders (Janowsky et al. 1973, 1980; Risch et al. 1981) and parallel the findings of Sitaram and coworkers (1980) of apparent supersensitivity of affective disorder patients to central cholinergic induction of REM sleep. These findings are consistent with the possibility, as suggested by Carroll and colleagues (1979), that central cholinergic hyperactivity could be of mechanistic significance in the elevated plasma concentrations of ACTH and cortisol (and beta-endorphin in this study) observed in depressed patients.

Finally, if the elevated plasma beta-endorphin concentrations and the enhanced release of beta-endorphin in response to physostigmine are specific for depressed patients, beta-endorphin could represent a potential biological state or trait marker for depression.

References

Balfour, D.J., Khyllar, A.K., Longden, A. Effects of nicotine on plasma corticosterone and brain amines in stressed and unstressed rats. *Pharmacol., Biochem. Behav.*, 3:179-184, 1975.

Bradbury, M.W., Burden, J., Hillhouse, E.W., and Jones, M.T. Stimulation electrically and by acetylcholine at the rat hypothalamus *in vitro*. *J. Physiol. Lond.*, 239:269-283, 1974.

Brown, W.A., Johnston, R., and Mayfield, D. The 24-hour dexamethasone suppression test in a clinical setting: Relationship to diagnosis, symptoms, and response to treatment. *Am. J. Psychiatry*, 136:543-547, 1979.

Carroll, B.J., Curtis, G.C., and Mendels, J. Neuroendocrine regulation in depression: I. Limbic system-adrenocortical dysfunction. *Arch. Gen. Psychiatry*, 33:1039-1044, 1976a.

Carroll, B.J., Curtis, G.C., and Mendels, J. Neuroendocrine regulation in depression: II. Discrimination of depressed from non-depressed patients. *Arch. Gen. Psychiatry*, 33:1051-1058, 1976b.

Carroll, B.J., Greden, J.F., Haskett, R., et al. Neurotransmitter studies of neuroendocrine pathology in depression. *Acta Psychiatr. Scand. (Suppl.)*, 280(61):183-199, 1979.

Carroll, B.J., Feinberg, M., Greden, J.F., et al. A specific laboratory test for the diagnosis of melancholia: Standardization, validation, and clinical utility. *Arch. Gen. Psychiatry*, 38:15-22, 1981.

Cozanitis, D.A. Galanthamine hydrobromide versus neostigmine. *Anaesthesia*, 29:163-168, 1974.

Davis, B.M. and Davis, K.L. Cholinergic mechanisms and anterior pituitary hormone secretion. *Biol. Psychiatry*, 15:303-310, 1980.

Edwardson, J.A., and Bennett, G.W. Modulation of corticotropin-releasing factor release from hypothalamic synaptosomes. *Nature*, 251:425-427, 1974.

Endroczi, E., Schreiberg, G., and Lissak, V. The role of central nervous activating and inhibiting structures in the control of pituitary-adrenocortical function. Effects of intracerebral cholinergic and adrenergic stimulation. *Acta Physiol. Lung.*, 24:211-221, 1963.

Fang, V.S., Tricou, B.J., Robertson, A., and Meltzer, H.Y. Plasma ACTH and cortisol levels in depressed patients: Relation to dexamethasone suppression test. *Life Sci.*, 29(9):931-938, 1981.

Guillemin, R., Vargo, T., Rossier, J. Beta-endorphin and adrenocorticotropin are secreted concomitantly by the pituitary gland. *Science*, 197:1367-1369, 1977.

Hill, P., and Wynder, E.L. Smoking and cardiovascular disease. *Am. Heart J.*, 87:491-496, 1974.

Janowsky, D.S., El-Yousef, M.K., Davis, J.M., and Sekerke, H.I. A cholinergic-adrenergic hypothesis of mania and depression. *Lancet*, ii:632-635, 1973.

Janowsky, D.S., Risch, S.C., Parker, D., Huey, L., and Judd, L. Increased vulnerability to cholinergic stimulation in affective disorder patients. *Psychopharmacol. Bull.*, 16(4):29-31, 1980.

Kalin, N.H., Weiler, S.J., McKinney, W.T., Kraemer, G.W., and Shelton, S.E. Where is the "lesion" in patients who fail to suppress plasma cortisol concentrations with dexamethasone? *Psychopharmacol. Bull.*, 18(3):219-221, 1982.

Krieger, H.P. and Krieger, D.T. Chemical stimulation of the brain: Effect on adrenal corticoid release. *Am. J. Physiol.*, 218:1632-1641, 1970.

Mains, R.E., Eipper, B.A., and Ling, N. Common precursor to corticotrophins and endorphins. *Proc. Natl. Acad. Sci. USA*, 74:3014-3018, 1979.

Naumenko, E.V. Hypothalamic chemoreactive structures and the regulation of pituitary-adrenal function. Effects of local injections of norepinephrine carbachol, and serotonin into brain of guinea pigs with intact brains after mesencephalic transection. *Brain Res.*, 11:1-10, 1968.

Otsuka, K. Effects of atropine, eserine, and tetramethylammonium on the adrenal 17-hydroxycorticosteroid secretion in anaesthetized dogs. *Tohoku J. Exp. Med.*, 88:165-170, 1966.

Pelletier, G., Leclerc, R., Labrie, F., Immunohistochemical localization of beta-lipotropic hormone in the pituitary gland. *Endocrinology*, 100:770-776, 1977.

Reus, V.I., Joseph, M.S., and Dallman, M.F. ACTH levels after the dexamethasone suppression test in depression. *New Engl. J. Med.*, 306(4):238-239, 1982.

Risch, S.C., Cohen, R.M., Janowsky, D.S., et al. Mood and behavioral effects of physostigmine on humans are accompanied by elevations in plasma beta-endorphin and cortisol. *Science*, 209:1545-1546, 1980.

Risch, S.C., Kalin, N.H., Janowsky, D.S. Cholinergic challenges in affective illness: Behavioral and neuroendocrine correlates. *J. Clin. Psychopharmacol.*, 1(4):180-185, 1981.

Risch, S.C., Kalin, N.H., Janowsky, D.S., et al. Co-release of ACTH and beta-endorphin immunoreactivity in human subjects in response to central cholinergic stimulation. *Science.* (In press)

Rossier, J., French, E.D., Rivier, C., Ling, N., Guillemin, R., Bloom, F.B. Foot shock induced stress increases β-endorphin levels in blood but not brain. *Nature (Lond.)*, 270:618-620, 1977.

Sachar, E.J. Neuroendocrine dysfunction in depressive illness. *Ann. Rev. Med.*, 27:389-396, 1976.

Sachar, E.J., Asnis, G., Halbreich, U., et al. Recent studies in the neuroendocrinology of major depressive disorders. In: Sachar, E.J. (ed.), *Psychiatric Clinics of North America: Advances in Psychoneuroendocrinology*, 1980a; pp. 313-326.

Sachar, E.J., Asnis, G., Nathan, R.S., et al. Dextroamphetamine and cortisol in depression. *Arch. Gen. Psychiatry*, 37:755-757, 1980b.

Schlesser, M.A., Winokur, G., and Sherman, B.M. Hypothalamic-pituitary-adrenal axis activity in depressive illness: Its relationship to classification. *Arch. Gen. Psychiatry*, 37:737-743, 1980.

Sitaram, N., Nurnberger, J.I., Jr., Gershon, E.S., and Gillin, J.C. Faster cholinergic REM sleep induction in euthymic patients with primary affective illness. *Science*, 208:200-201, 1980.

Stokes, P.E., Pick, G.R., Stoll, P.M., and Nunn, W.D. Pituitary-adrenal function in depressed patients: Resistance to dexamethasone suppression. *J. Psychiatr. Res.*, 12:271-281, 1975.

Suzuki, T., Hirai, K., Yoshio, H., et al. Effect of eserine and atropine on adrenocortical hormone secretion in unanesthetized dogs. *J. Endocrinology*, 31:81-82, 1964.

Suzuki, T., Abe, K., and Hirose, T. Adrenal cortical secretion in response to pilocarpine in dogs with hypothalamic lesions. *Neuroendocrinology*, 17:75-82, 1975.

Terenius, L., Wahlstrom, A., and Agren, H. Naloxone (Narcan) treatment in depression: Clinical observation and effects on CSF endorphins and monoamine metabolites. *Psychopharmacology (Berlin)*, 54:31-33, 1977.

Endorphins May Be Involved in the Behavioral Response to Dextro-Amphetamine[1]

Uriel Halbreich, M.D.,[2] Susanna Goldstein, M.D.,[2] Ee-Sing Lo, Ph.D.,[3] and Jean Endicott, Ph.D.[4]

Halbreich et al. (1981a), reported that normal postmenopausal women had a dysphoric response to intravenously administered 0.15 mg/kg dextroamphetamine—a dose that usually causes elation and increased activity in normal young men. This finding has been confirmed by the investigators in a second group of subjects, and may provide a model for the study of the mechanism of the mood and behavioral responses to amphetamine.

Both normal postmenopausal women and normal young men have an increase in plasma levels of cortisol in response to the drug (Halbreich et al. 1981b). Postmenopausal women have a blunted growth hormone response (Halbreich et al. 1980) and they do not show an increase of plasma levels of prolactin (PRL) in response to amphetamine, while PRL levels of young men are increased in response to the same stimulus (Halbreich et al. 1981c). The hormonal responses were also confirmed in the second group of subjects.

Even though some correlations were reported between the baseline levels or the magnitude of change in levels of these hormones, and the behavioral response to amphetamine (Halbreich et al. 1981d; Nurnberger et al. 1981), the authors believe that these do not shed much light on the mechanism of the behavioral response to the drug. Some other mechanisms, compatible with previous findings, should be tested.

It has been proposed (Byck 1976; Belluzzi & Stein 1979) that an excess of endorphins may be involved in euphoria, mania, and amphetamine-induced psychostimulation. There were some suggestions, including that of Gerner et al.

---

[1] This study was supported in part by Clinical Research Center Grant #55, Biomedical Research Service Grant #0454801, Montefiore Hospital and Medical Center, USPHS Grant MH-30906, and New York State Department of Mental Hygiene.

[2] Department of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461.

[3] Center for Neurosciences, Ward's Island, NY 10035.

[4] New York State Psychiatric Institute, New York, NY 10032.

Table

Interaction of Naloxone with Amphetamine Animal Studies

Study	Subjects	Measurement	Antagonism	Dose of Naloxone mg/kg	Dose of d-amphetamine mg/kg
Holtzman (1974)	rats	1) Locomotor activity	Yes	3, 10, 30	0.1, 0.3, 1, 3, 10
		2) Avoidance responding	Yes	10, 30	0.1, 0.3, 1, 3, 10
Holtzman (1974)	mice	Hyperactivity	No	10, 30, 100	1, 3, 10, 30, 100
Dettmar et al. (1978)	rats	Rotation following unilateral lesions of the substantia nigra	a) Yes	0.3, 3	2
			b) No	10, 30	2
Dettmar et al. (1978)	mice	Locomotor activity	Yes	0.3, 1, 3	2
Haber et al. (1978)	rats	Rearing activity	Yes	10	1.5
Haber et al. (1978)	rats	Hyperactivity	No	10	1.5
Horita & Carino (1978)	rabbits	Analeptic effect	Yes	2	0.5
Segal et al. (1979)	rats	1) Locomotor activity	Yes	0.5, 5, 10	0.5, 2.5
		2) Stereotypy	No	Up to 20	2.5
Rethy et al. (1971)	mice	Locomotor activity	No	10	1 - 10
Perez-Cruet et al. (1979)	rats	1) Locomotor activity	Yes	10	0.5, 2.5
		2) Stereotypy	No	10	0.5, 2.5
Adams et al. (1981)	rats	1) Locomotor activity	Yes	1, 2, 4	2.5 (5, 10)
		2) Stereotypy	No (Potentiated)	1, 2, 4	2.5 (5, 10)

(1980), that levels of endorphins may be lower than normal in depression.

These assumptions are far from being established and, at best, they are too simplistic. However, at least in the case of amphetamine, there is some evidence that opioid mechanisms may be involved or may even modulate the behavioral response to the drug. Several groups (those listed in the Table, and a review by Sawynok et al. 1979) reported that the administration of the opioid antagonist naloxone abolished behavioral response to amphetamine in animals. It seems that this interaction is dose-dependent and probably also species-dependent. This is mainly suggested in view of reports from laboratories where different species were tested with different doses (Dettmar et al. 1978; Holtzman 1975). Furthermore, when naloxone was added to amphetamine, the dose-response curve of the later drug was shifted downward and not to the right as would be expected by a direct competition phenomenon. The downward shift may be the common endpoint achieved through a diversity of mechanisms, because other drugs can alter the dose-response curve of amphetamine for operant behavior and locomotor activity in a manner similar to naloxone (Reviews: Weiss & Laties 1969; Rech & Stolk 1970) but naloxone is unique in that it has no influence on these activities when administered alone.

The involvement of opioid mechanisms with human behavioral response to amphetamine is unclear. It was reported by Cohen et al. (1981) that plasma levels of β-endorphin were increased following infusion of 0.3 mg/kg dextroamphetamine to eight normal monozygotic twins. The increase in levels of β-endorphin was significantly correlated ($r = 0.76$) to the increase in levels of cortisol. However, when amphetamine was administered to schizophrenic patients (Schulz et al. 1981), no increase in levels of β-endorphin was found. This finding, which confirmes previous reports concerning cortisol (Halbreich et al. 1981b), may point to an exclusion of β-endorphin as the opioid involved in the behavioral and mood response to amphetamine. Future studies should probably concentrate on other opioids, like met-enkephalin (Belluzzi & Stein 1977). Such studies should be facilitated once some technical obstacles in the radioimmunoassay of plasma methionine-enkephalin are overcome.

Endorphins also probably interact with, or modulate neurotransmitters and trace amines like phenylethylamine (PEA), whose involvement in the mechanisms of behavioral response to amphetamine has been strongly suggested by several groups (Reviews: Mosnaim & Wolf 1978).

PEA is a naturally occurring amine that mimics amphetamine in its behavioral effects. Amphetamine has been shown to markedly affect PEA levels in the central nervous system. In rabbits it reduces three times the brain content of PEA in the first 30 minutes. In mice and rats it has been shown to increase the turnover of PEA in the brain, markedly augment its synthesis, and accelerate its disposition. Depletion of brain PEA by pretreatment with α-methyldopahydrazine (AMDH) decreases many of the central actions of amphetamine. The time course of changes in stereotype and motor activity of untreated rats in response to PEA also is similar to that of amphetamine.

The role of PEA in the behavioral response to amphetamine has never been adequately demonstrated in humans. In any case, a multivariate approach should be applied to the study of the physiology of the behavioral and mood responses to amphetamine. In future studies an attempt should be made to integrate the various changes in many substances into a comprehensive picture.

References

Adams, P.M., Beauchamp, R., and Alston, C. Naloxone and dopamine agonists. *Life Sci.*, 20:629-634, 1981.

Belluzzi, J.D., and Stein, L. Enkephalin may mediate euphoria and drive-reduction reward. *Nature*, 266:556-558, 1977.

Byck, R. Peptide transmitters: A unifying hypothesis for euphoria, respiration, sleep, and the action of lithium. *Lancet*, 2:72-73, 1976.

Cohen, M.R., Nurnberger, J.I., Pickar, D., Gershon, E., and Bunney, W.E., Jr. Dextroamphetamine infusions in normals result in correlated increases of plasma beta-endorphin and cortisol immunoreactivity. *Life Sci.*, 29:1243-1247, 1981.

Dettmar, P.W., Cowan, A., and Walter, D.S. Naloxone antagonizes behavioral effects of *d*-amphetamine in mice and rats. *Neuropharmacology*, 17:1041-1044, 1978.

Gerner, R.H., Callin, D.H., and Gorelick, D.A. Beta-endorphin intravenous infusion causes behavioral changes in psychiatric inpatients. *Arch. Gen. Psychiatry*, 37:642-648, 1980.

Haber, S., Matsukami, T., Berger, P.A., Barchas, J.D., and Akil, H. Naloxone blocks amphetamine-induced rearing: Potential interaction between catecholamines and endorphins. *Prog. Neuropsychopharmacol.*, 2:425-430, 1978.

Halbreich, U., Asnis, G.M., Halpern, F.S., Tabrizi, M.A., and Sachar, E.J. Diurnal growth hormone responses to dextroamphetamine in normal young men and postmenopausal women. *Psychoneuroendocrinology*, 5:339-344, 1980.

Halbreich, U., Asnis, G.M., Ross, D., and Endicott, J. Amphetamine induced dysphoria in postmenopausal women. *Br. J. Psychiatry*, 138:470-473, 1981a.

Halbreich, U., Sachar, E.J., Asnis, G.M., Nathan, R.S., and Halpern, F.S. Diurnal cortisol responses to dextroamphetamine in normal subjects. *Psychoneuroendocrinology*, 6:223-229, 1981b.

Halbreich, U., Sachar, E.J., Asnis, G.M., Nathan, R.S., and Halpern, F.S. The prolactin response to intravenous dextroamphetamine in normal young men and postmenopausal women. *Life Sci.*, 28:2337-2341, 1981c.

Halbriech, U., Asnis, G.M., Ross, D., and Endicott, J. The behavioral and mood responses to d-amphetamine: Some possible physiological correlates. *Psychopharmacol. Bull.*, 17:83-84, 1981d.

Holtzman, S.G. Behavioral effects of separate and combined administration of naloxone and *d*-amphetamine. *J. Pharmacol. Exp. Ther.*, 189:51-60, 1974.

Horita, A., and Carino, M.A. Analeptic and antianaleptic effects of naloxone and naltrexone in rabbits. *Life Sci.*, 23:1681-1686, 1978.

Mosnaim, A.D., and Wolf, M.E. (eds.) *Noncatecholic Phenylethylamines. Part 1: Biological Mechanisms and Chemical Aspects.* New York and Basel: Marcel Dekker, 1978.

Nurnberger, J., Gershon, E., Jimerson, D.C., Buchsbaum, M., Gold, P., Brown, G., and Ebert, M. Pharmacogenetics of *d*-amphetamine response in man. In: Gershon, E., Matthyse, S., Breakefield, R., and Ciaranello, R.D. (eds.), *Genetic Research Strategies in Psychobiology and Psychiatry.* Pacific Grove, CA: Boxwood Press, 1981, pp. 257-268.

Perez-Cruet, J., Volavka, J., Mallya, A., and Baig, S. Effects of endorphins on motor behavior, striatal dopaminergic activity, and dopaminergic receptors. In: Usdin, E., Bunney, W.E., Jr., and Kline, N. (eds.), *Endorphins in Mental Health Research.* New York: Oxford Press, 1979, pp. 302-324.

Rech, R.H., and Stolk, J.M. Amphetamine-drug interactions that relate catecholamines to behavior. In: Costa, E., and Garrattini, S. (eds.), *Amphetamines and Related Compounds.* New York: Raven Press, 1970, pp. 385-413.

Rethy, C.R., Smith, C.B., and Villarreal, J.E. Effects of narcotic analgesics upon the locomotor activity and brain catecholamine content of the mouse. *J. Pharmacol. Exp. Ther.*, 126:472-479, 1971.

Sawynok, J., Pinsky, C., and LaBella, F.S. On the specificity of naloxone as an opiate antagonist. *Life Sci.*, 25:1621-1632, 1979.

Schulz, S.C., van Kammen, D.P., Rogol, A.D., Ebert, M., Pickar, D., Cohen, M.R., and Naber, D. Amphetamine increases prolactin but neither growth hormone nor beta-endorphin immunoreactivity in schizophrenic patients. *Psychopharm. Bull.*, 17:193-195, 1981.

Segal, D.S., Browne, R.G., Arnsten, A., Derrington, D.C., Bloom, F.E., Guillemin, R., and Ling, N. Characteristics of beta-beta-endorphin-induced behavioral activation and immobilization. In: Usdin, E., Bunney, W.E., Jr., and Kline, D.S. (eds.), *Endorphins in Mental Health Research.* New York: Oxford University Press, 1979, pp. 307-324.

Weiss, B., and Laties, V G. Behavioral pharmacology and toxicology. *Ann. Rev. Pharmacol.*, 9:297-326, 1969.

Where Is the "Lesion" in Patients Who Fail to Suppress Plasma Cortisol Concentrations with Dexamethasone?[1]

Ned H. Kalin, M.D.,[2] Stephen J. Weller, M.D.,[2] William T. McKinney, M.D.,[2] Gary W. Kraemer, M.D.,[2] and Steven E. Shelton[2]

Introduction

The failure to suppress plasma cortisol concentrations after the low-dose dexamethasone suppression test (DST) occurs in up to 50 percent of patients with depressive illness (Brown et al. 1979; Carroll et al. 1981; Sachar et al. 1980; Schlesser et al. 1980). This endocrine abnormality has been studied extensively in psychiatric patients but little is known about its underlying pathophysiology. Using depressed subjects and nonhuman primates, the authors have begun to explore the factors mediating this dysfunction. The following studies were designed to further characterize the role pituitary adrenocorticotropic hormone (ACTH) secretion plays in mediating cortisol nonsuppression in depressed patients.

Materials and Method

Human Studies

Twenty-eight male inpatients, selected for clinical reasons to undergo a DST, were tested by the method of Carroll et al. (1981) within the first week of admission. An 8 a.m. baseline blood sample was drawn, and at 11 p.m. 1 mg of dexamethasone was administered orally. Blood samples were obtained at 8 a.m. and 4 p.m. the following day. Diagnostic and Statistical Manual-III (DSM-III) diagnoses were made from both patient interviews and chart reviews. Data from the human studies will be presented in greater detail in another report (Kalin et al., in press).

Patients were excluded from the study if they suffered from a life-threatening medical illness, poorly controlled diabetes mellitus, alcohol withdrawal, or disease involving the hypothalamic-pituitary-adrenal (HPA) system. Patients taking medications known to interfere with the DST (Kalin et al. 1981) were also excluded. Any patient with a postdexamethasone value of >5 μg/dl in either the 8 a.m. or 4 p.m. sample was considered a cortisol nonsuppressor.

Monkey Studies

The rhesus monkeys used in this study were housed in three peer groups, $N=4$, $N=4$, and $N=3$, and underwent repetitive peer separations as described by McKinney et al. (1972). At the end of the separation week a DST was performed on each animal Blood was drawn by femoral venipuncture at 9 a.m. on the day before and after the 11 p.m. intramuscular administration of dexamethasone sodium phosphate (150 μg/kg).

Blood Collection and RIAs

All blood samples were collected into glass tubes containing 10.5 mg of EDTA and were immediately placed on ice. The samples were then centrifuged for 10 minutes at 3,000 r.p.m. for the separation of plasma; plasma was frozen at −70°C until assayed.

In the human samples, plasma cortisol concentrations were assayed using an RIA kit supplied by Clinical Assays with a sensitivity of 2 μg/dl.

---

[1] This research was supported by the Veterans Administration.

[2] Psychiatry Service, William S. Middleton Memorial Veterans Administration Hospital and the Department of Psychiatry, University of Wisconsin School of Medicine, Madison, WI 53705.

Address correspondence to: Ned H. Kalin, M.D., William S. Middleton Memorial VAH 2500 Overlook Terrace, Madison, WI 53705.

The monkey samples were measured with a kit supplied by New England Nuclear with a sensitivity of 1 µg/dl.

ACTH immunoreactivity was assayed using an RIA kit obtained from Immunonuclear Corp. (Risch et al., in press) with a sensitivity of 37.5 pg/ml, and intraassay variability of ± 10 percent. Samples from human and monkey experiments were assayed separately in one run.

Results

Human ACTH Concentrations

The patients were separated into two groups on the basis of their cortisol response. The suppressors ($N = 17$) consisted of nine patients meeting criteria for major depressive episode and eight patients meeting criteria for other DSM-III diagnoses. The nonsuppressors ($N = 11$) all met criteria for either major depressive episode or bipolar depression. The Table demonstrates that the mean plasma ACTH concentration in the nonsuppressor group was significantly higher than in the suppressors both before and after dexamethasone administration. In the 8 a.m. predexamethasone samples the nonsuppressors' mean ACTH concentration was 93.9 ± 26.16 pg/ml compared to 51.1 ± 6.47 pg/ml in the suppressors ($t = 1.91$, $p < 0.05$, one-tailed t-test). The 8 a.m. postdexamethasone mean ACTH concentration was also significantly greater in nonsuppressors, 83.9 ± 25.80 pg/ml compared to the suppressors' 45.5 ± 5.20 ($t = 1.79$, $p < 0.05$, one-tailed t-test).

Table

Mean Plasma ACTH (pg/ml ± S.E.M.)

	Suppressors ($N = 17$)	Nonsuppressors ($N = 11$)	One-Tailed t-Test
8 a.m. Predexamethasone	51.1 ± 6.47*	93.9 ± 26.16**	$t = 1.91$ $p < 0.05$
8 a.m. Postdexamethasone	45.5 ± 5.20	83.9 ± 25.80	$t = 1.79$ $p < 0.05$
4 p.m. Postdexamethasone	58.4 ± 5.65	76.9 ± 20.05	$t = 1.06$ N.S.

* 8/17 of the suppressors were < 37.5 pg/ml
** 3/11 of the nonsuppressors were < 37.5 pg/ml

Monkey ACTH Concentrations

The Figure demonstrates the ACTH and cortisol concentrations for the 11 rhesus monkeys at the end of their separation week. In the monkeys cortisol nonsuppression was defined as a 9 a.m. postdexamethasone concentration of > 10 µg/dl. Baseline ACTH concentrations were greater in the monkey cortisol nonsuppressors compared to the suppressors. However, this difference did not reach statistical significance. Postdexamethasone ACTH concentrations were similar in cortisol suppressors and nonsuppressors, but the postdexamethasone cortisol concentrations varied significantly.

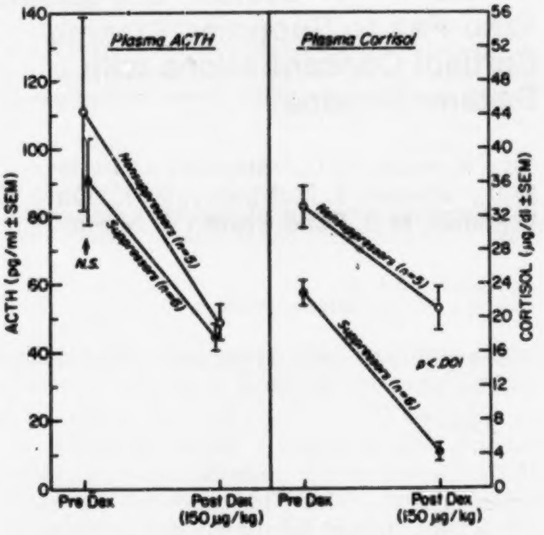


FIGURE. The mean plasma ACTH and cortisol concentrations for 11 rhesus monkeys after peer separation. Cortisol nonsuppression was defined as a postdexamethasone concentration of > 10 µg/dl.

Discussion

Since it has been demonstrated that changing plasma cortisol concentrations are not always directly related to pituitary ACTH secretion (Krieger & Allen 1975; Holaday et al. 1977; Risch et al. in press), it cannot be assumed that the cortisol abnormalities seen in depressed patients reflect hypothalamic and/or pituitary dysfunction.

The authors found that plasma ACTH concentrations are significantly greater in human cortisol nonsuppressors than in suppressors at 8 a.m. before and after dexamethasone administration. The actual differences between the two groups may be even greater than our data show, since 3/11 of the nonsuppressors and 8/17 of the suppressors had predexamethasone ACTH concentrations below the sensitivity of our RIA. In monkeys, baseline ACTH concentrations also tended to be greater in the cortisol nonsuppressors, but postdexamethasone ACTH concentrations did not vary between the suppressors and nonsuppressors as in humans. The similarity in the baseline ACTH concentrations between monkeys and humans supports our earlier suggestion that the rhesus monkey is a reasonable model to use in exploring the regulatory mechanisms of the hypothalamic-pituitary-adrenal system in humans (Kalin et al. 1981).

ACTH concentrations in depressed subjects' have been reported in only two other studies. Fang et al. (1981) found essentially no differences among 8 a.m. predexamethasone ACTH concentrations in normals, depressed cortisol suppressors, and depressed nonsuppressors. They also found no differences at 8 a.m. after dexamethasone; however, ACTH concentrations were significantly greater in their nonsuppressor group at 4 p.m. postdexamethasone.

In a preliminary report Reus et al. (1982) found significantly greater ACTH concentrations after dexamethasone administration in depressed cortisol nonsuppressors compared to depressed suppressors. They also reported a trend for higher predexamethasone 8 a.m. ACTH concentrations in the nonsuppressors compared to the suppressors. The Reus et al. study (1982), as well as the authors' findings, support the hypothesis that the failure to suppress plasma cortisol concentrations after dexamethasone is related to increased pituitary ACTH secretion.

References

Brown, W.A., Johnston, R., and Mayfield, D. The 24-hour dexamethasone suppression test in a clinical setting: Relationship to diagnosis, symptoms, and response to treatment. *Am. J. Psychiatry,* 136:543-547, 1979.

Carroll, B.J., Feinberg, M., Greden, J.F., Tarika, J., Albala, A., Haskett, M.B., James, N., Kronfol, Z., Lohr, N., Steiner, M., De Vigne, J., and Young, E. A specific laboratory test for the diagnosis of melancholia. *Arch. Gen. Psychiatry,* 38:15-22, 1981.

Fang, V.S., Tricou, B.J., Robertson, A., and Meltzer, H.Y. Plasma ACTH and cortisol levels in depressed patients: Relation to dexamethasone suppression test. *Life Sci.* 29:931-938, 1981.

Holaday, J.W., Martinez, H.M., and Natelson, B.H. Synchronized ultradian cortisol rhythms in monkeys: Persistence during corticotropin infusion. *Science,* 198:56-58, 1977.

Kalin, N.H., Cohen, R.M., Kraemer, G.W., Risch, S.C., Shelton, S., Cohen, M., McKinney, W.T., and Murphy, D.T. The dexamethasone suppression test as a measure of hypothalamic-pituitary feedback sensitivity and its relationship to behavioral arousal. *Neuroendocrinology,* 32:92-95, 1981.

Kalin, N.H., Risch, S.C., Janowsky, D.S., and Murphy, D.L. Use of dexamethasone suppression test in clinical psychiatry. *J. Clin. Psychopharm.,* 1:64-69, 1981.

Kalin, N.H., Weiler, S.J., and Shelton, S.E. Plasma ACTH and cortisol concentrations before and after dexamethasone. *Psychiatry Res.* (In press)

Krieger, D.T., and Allen, W. Relationship of bioassayable and immunoassayable plasma ACTH and cortisol concentrations in normal subjects and in patients with Cushing's disease. *J. Clin. Endocrinol. Metab.,* 10:675-687, 1975.

McKinney, W.T., Suomi, S.J., and Harlow, H.F. Repetitive peer separations of juvenile-age rhesus monkeys. *Arch. Gen. Psychiatry,* 27:200-203, 1972.

Reus, V.I., Joseph, M.S., and Dallman, M.F. ACTH levels after the Dexamethasone Suppression Test in depression. *New Engl. J. Med.,* 306:23-24, 1982.

Risch, S.C., Kalin, N.H., Janowsky, D.S., Cohen, R.M. Pickar, D., and Murphy, D.L. Co-release of ACTH and β-endorphin immunoreactivity in human subjects in response to central cholinergic stimulation. *Science.* (In press)

Sachar, E.J., Asnis, G., Halbreich, V., Nathan, S., and Halpern F. Recent studies in the neuroendocrinology of major depressive disorders. *Psychiatr. Clin. No. Am.,* 3:313-325, 1980.

Schlesser, M.A., Winokur, G., and Sherman, B.M. Hypothalamic-pituitary-adrenal axis activity in depressive illness. *Arch. Gen. Psychiatry,* 37:737-747, 1980.

The Epidemiology of Mental Disorders: Results from the Epidemiologic Catchment Area Study (ECA)

Chair: Myrna M. Wiessman, Ph.D.
Department of Psychiatry
Yale University School of Medicine
New Haven, Connecticut

An Epidemiologic Perspective on Senile Dementia—Facts and Fragments

Jacob A. Brody, M.D.,[1] and Lon R. White, M.D., M.P.H.[1]

In 1978 there were 2.5 million Americans 85 years and older. By the year 2000 there will be between 3.3 and 6.7 million people 85 and older in this country, depending upon mortality trends. In this age group the estimated prevalence of dementia exceeds 20 percent. The tragedy and the staggering burden represented by this illness and attendant disability is broadly appreciated.

The characteristic pathologic changes of Alzheimer's disease occur in both its senile and presenile forms. Although multi-infarct dementia (MID) accounts for 20 to 40 percent of the dementias of late life, not all patients have either definite MID or the characteristic neuropathologic changes of Alzheimer's disease (Terry 1978). To further confuse matters, these changes are found so frequently among the elderly (dying of all causes) as to raise the question whether senile dementia of the Alzheimer's type (SDAT) is a disease at all or a part of normal aging. Also unclear is the relationship to these conditions of the entity that Kral refers to as benign scenescent forgetfulness (Kral 1978). It can be persuasively argued that pre-senile Alzheimer's disease and SDAT should be considered one disease entity whose vistims range in age from middle to late life. However, a failure to discriminate pre-senile from senile dementia may obscure true differences in pathogenesis if in fact they are not the same disease. The problem of disease definition illustrated by this observation is probably in part responsible for the failure of clear epidemiologic patterns or discernible risk factors to have emerged from previous research efforts.

Although biochemical and anatomic differences between the brains of patients with SDAT and those of patients dying of unrelated conditions have been and continue to be the subject of elegant research efforts, no clear understanding of pathogenesis exists. Epidemiologists have thus far contributed little to the resolution of the problem, since the only factor definitely associated with increased risk is advanced age. Despite this, age-specific incidence and prevalence curves have not been clearly defined. Such definition would contribute to the determination of whether or not SDAT has a unitary pathogenesis, and to the development of measures of frequency for the comparison of individuals grouped according to characteristics or exposures. The methodologic problems most responsible for this paucity of information involve: a) the need to study entire communities of elderly persons, b) the need for a standardized and valid means of classifying individuals according to cognitive ability/disability, and c) for incidence studies, the need for repeated observations over a period of years. These problems are also responsible for uncertainty as to the effect of dementia on life expectancy as it may be modified by the age of onset of the illness.

Prevalence rates for SDAT throughout the world do not vary greatly. Approximately 4 percent of the population over 65 has what can be called a malignant form of senile dementia, with about 20 percent having a mild form of cognitive disability. As mentioned, the prevalence rises sharply with age to approximately 20 percent with severe dementia at age 80 (Mortimer et al. 1981). A general conformity has been noted for data derived from population surveys and to some extent from regional institutional surveys.

---

[1] Epidemiology, Demography, and Biometry Program, National Institute on Aging, National Institutes of Health, Bethesda, MD 20205.

Clinicians tend to agree that there are more women than men with SDAT. Electroencephalographic findings over time, however, suggest that fast wave activity is better preserved in females than in males (Busse & Obrist 1963). The female excess may be the result of greater longevity, greater likelihood of seeking medical attention, or greater likelihood of being widowed and living alone, hence requiring institutionalization more frequently than would a male.

Although differences by race have not been reported, confidence in the lack of a difference in dementia incidence between black and white elderly persons is limited because of marked differences in survival. The apparent absence of differences in incidence according to race and sex may be interpreted as suggesting that the pathogenesis of senile dementia may not involve those characteristics and factors known to be associated with differential mortality by sex and race.

Professional pugilists represent the only occupational group which seems to be predisposed to dementia, an observation which has thus far led to no insights into the etiology of SDAT.

A neurologic disease which includes dementia is responsible for approximately 10 percent of adult deaths among the Chamorro people of Guam. Although this syndrome, Parkinsonism-dementia of Gual, shares several neuropathologic characterists with SDAT, its pathogenesis remains as obscure as that of SDAT despite many years of vigorous investigation (Brody et al. 1975). No other geographic or ethnic focus of SDAT is known, except for foci related to familial Alzheimer's disease.

The sporadic form of dementia accounts for the vast majority of SDAT cases. Interest in the familial form relates to the implications of the conclusion that the disease can have a genetic causation (Goudsmit et al. 1981). Thus far these implications have led to no greater understanding of the causes of sporadic SDAT, but have served to guide and encourage avenues of research which consider genetic contributions to pathogenesis. Preliminary findings suggested that familial Alzheimer's disease was transmissible to primates by intracerebral innoculation, and thereby resembled the transmissible spongiform encephalopathies, Kuru and Creutzfeldt-Jacob disease. This appears not to be the case, and the balance of evidence fails to support a slow virus etiology (Goudsmit et al. 1980).

No history of earlier life exposure, rural or urban residence, medical illness, or psychiatric condition appears to predispose to the development of senile dementia. A reported increased risk among persons of lower social status is of uncertain significance, since test batteries used to detect dementia certainly discriminate against such persons and since socioeconomic factors might modify the likelihood that a person would come to medical attention (Gurland 1981).

None of the variables mentioned above has been studied by comparing age-specific prevalence or incidence curves. Instead, most were analyzed by examining age adjusted rates or by comparing the frequency of the variable among SDAT patients with that in the general population or in a control group. Nevertheless, the absence of obvious clustering or of clear differences in risk according to these several factors argues against specific exposures (such as to zoonotic agents or aluminum in antacids) as important etiologic factors.

Although epidemiologic studies have unearthed no patterns of disease occurrence which point to definitive pathogeneses, there are two fascinating, not yet fully substantiated, observations. The first is an association with increased familial frequency of Down's syndrome. This observation is made more exciting by the report that the neuropathologic changes of Alzheimer's disease apparently occur in all (or nearly all) Down's syndrome patients who live to be 40 (Heston & Mastri 1977). The second and less well substantiated observation is of advanced maternal age at the time of birth of individuals who eventually develop SDAT (Cohen & Eisdorfer 1981). It appears that this association may hold for some but not for all groups of SDAT patients, since it was not substantiated by another study in which birth order was investigated as a possible risk factor (Akesson 1969).

It may be meaningful that the risk of SDAT, a condition occurring much more commonly among the very old, seems so unaffected by factors differentially related to longevity. Perhaps this suggests that we should direct our attention away from the sort of adult characteristics, life style, and exposure factors which seem to be involved in determining who survives to be old-old, and toward genetic, early life, and late life characteristics and exposures. The alternative view is that the failure to define risk factors has been due to aggregation of cases of heterogeneous pathogenesis (but clinical similarity) or that the methods of factor and/or endpoint definition have been imprecise or inappropriate.

The epidemiologic data most immediately needed involve the age-specific prevalence, incidence, and clinical course of dementia in medically unselected, longitudinally studied populations of elderly persons. There is also an obvious need for research approaches in which correlations are sought between epidemiologic, neuropsychologic, biochemical, clinical, and pathologic observations. Such studies should reflect the recent burgeoning of information relative to cognitive function evaluation and neurotransmitter metabolism (particularly as related to the cholinergic system), and to hypotheses based on biochemical and neuropathological observations. Careful attention should be give to genetic indicators, including the frequency among family members of other conditions (Down's syndrome, leukemia, immune dyscrasias, or certain neurological diseases), and certain genetic markers (especially HLA markers such as the DB7-CW3 Haplotype, and the HP^1 haptoglobin gene product) (Eisdorfer et al. 1980; Walford & Hudge 1980; Stam & Op den Velde 1978). A different approach would involve the in-depth study of kindreds afflicted with familial Alzheimer's disease or sharing an increased risk for the sporadic form of dementia.

It is essential that, while responding to new knowledge generated by clinical and laboratory studies, the epidemiologist bring to bear on the problem of dementia his most rigorous and imaginative methodologies in the hope of accomplishing: 1) the identification of factors associated with either increased or decreased risk for developing dementia, or 2) the delineation of patterns (i.e., disease occurrence, severity, clinical expression, course) which would point to differentiation of groups of dementia patients having different pathogeneses.

References

Akesson, H.O. A population study of senile and arteriosclerotic psychoses. *Human Hered.*, 19:546-566, 1969.

Brody, J.A., Stanhope, J.M., and Kurland, L.T. Patterns of amyotrophic lateral sclerosis and parkinsonism-dementia of Guam. In: Hornabrook, R.W. (ed.), *Topics on Tropical Neurology*. (Contemporary Neurology series). Philadelphia: F.A. Davis Co., 1975, pp. 45-70.

Busse, E.W., and Obrist, W.D. Significance of focal electroencephalographic changes in the elderly. *Postgrad Med.*, 34:179-182, 1963.

Cohen, D., and Eisdorfer, C. Data presented at the White House Conference on Aging, 1982.

Eisdorfer, C., Cohen, D., and Buckley, C.E. III Serum immunoglobulins and cognition in the impaired elderly. In: Katzman, R., Terry, R.D., and Bick, K.L. (eds.), *Aging Vol. 7, Alzheimer's Disease: Senile Dementia and Related Disorders*. New York: Raven Press, 1978, p. 405.

Goudsmit, J., Morrow, C.H., Asher, D.M., Yanagihara, R.T., Masters, C.L., Gibbs, C.J., Jr., Gajdusek, D.C. Evidence for and against the transmittability of Alzheimer's disease. *Neurology.*, 30:945-950, 1980.

Goudsmit, J., White, B.J., Weitkamp, L.R., Keats, B.J.B., Morrow, C.H., and Gajdusek, D.C. Familial Alzheimers disease in two kindreds of the same geographic and ethnic origin: A clinical and genetic study. *J. Neurol. Sci.*, 49:79-89, 1981.

Gurland, B.J. The borderlands of dementia: The influence of sociocultural characteristics on rates of dementia occurring in the senium. In: Miller, N.E., and Cohen, G.D. (eds.), *Clinical Aspects of Alzheimer's Disease and Senile Dementia*. New York: Raven Press, 1978.

Heston, L.L., and Mastri, A.R. The genetics of Alzheimer's disease; Associations with hematologic malignancy and Down's syndrome. *Arch. Gen. Psychiatry*, 34:976-81, 1977.

Kral, V.A. Benign senescent forgetfulness. In: Katzman, R., Terry, R.D., and Bick, K.L. (eds.), *Aging, Vol. 7, Alzheimer's Disease: Senile Dementia and Related Disorders*. New York: Raven Press, 1978, pp. 47-51.

Mortimer, J.A., Schuman, L.M., and French, L.R. Epidemiology of dementing illness. In: Mortimer, J.A. and Schuman, L.M. (eds.), *The Epidemiology of Dementia*. New York: Oxford University Press, 1981, pp. 3-23.

Stam, F.C., and Op den Velde, W. Haptoglobin types in Alzheimer's disease and senile dementia. In: Katzman, R., Terry, R.D., and Bick, K.L. (eds.), *Aging, Vol. 7, Alzheimer's Disease: Senile Dementia and Related Disorders*. New York: Raven Press, 1978, pp. 279-286.

Terry, R.D. Aging, senile dementia, and Alzheimer's disease. In: Katzman, R., Terry, R.D., and Bick, K.L. (eds.), *Aging, Vol. 7, Alzheimer's Disease: Senile Dementia and Related Disorders*. New York: Raven Press, 1978, pp. 11-14.

Walford, R.L., and Hodge, S.E. HLA distribution in Alzheimer's disease. In: Teresaki, P.I. (ed.), *Histocompatibility Testing*. Los Angeles:UCLA Tissue Typing Lab., 1980.

Workshop—

Antipsychotics and Clinical Response: An Overview

John M. Davis, M.D.,[1] Katherin Hendricks, B.S.,[1] and Javaid I. Javaid, Ph.D.[1]

There have been very few methodologically appropriate investigations of the relationship between antipsychotic drug concentrations in plasma and clinical efficacy. One of the complicating matters is that in chronic schizophrenics who show very little symptomatology (so called "burned-out" schizoprenics) it is often difficult to rate improvement. Curry and Marshall (1968) first noted that there were marked individual differences in plasma levels among schizophrenic patients on comparable doses of chlorpromazine. A range of almost 20-fold difference (approximately 25 to 500 ng/ml) in plasma levels was seen in patients on reasonable clinical doses. A few patients who had very low levels of chlorpromazine failed to show side effects or clinical response. One patient with a high chlorpromazine plasma level showed excessive sedation. When the dose was lowered, plasma levels decreased, and this patient showed a clinical response. It is necessary that these exploratory open studies be verified by properly controlled studies.

Sakalis et al. (1972) treated a small number of schizophrenics and manics with 300 mg of chlorpromazine daily. Since they deliberately included patients who were not acutely ill (because they chose patients amenable to psychophysiological studies), it may have been an inappropriate sample to study for therapeutic effects. Lader (1976) extended the study to include a larger group of new patients, many of whom were acutely ill. However, 300 mg is probably lower than the ED_{50} dose of chlorpromazine (the average dose necessary to produce 50 percent of maximal improvement). For this reason, it would be very unlikely that any patient would have plasma levels above the therapeutic window. The expected relationship between plasma level and clinical efficacy would, therefore, be a linear one at this dose. In a recent report of results on the first 32 patients, the investigators found a correlation of -0.32 between clinical efficacy and plasma levels, which is of borderline significance ($p = 0.4$ level, one-tailed).

Wode-Helgodt et al. (1978) did a methodologically valid study on patients who were treated with randomly assigned fixed doses of 200, 400, or 600 mgs of chlorpromazine per day. In 15 male schizophrenics, there was a positive correlation ($r = 0.82$, $p < 0.01$) between improvement and prolactin elevation at 4 weeks. There was a similar correlation between plasma levels and clinical response. May et al. (1981) studied schizophrenic patients generally treated with chlorpromazine (6.6 mg/kg/day) for 28 days. Plasma chlorpromazine and prolactin levels did not correlate with the clinical outcome.

Chlorpromazine can theoretically be metabolized to 168 different metabolites. It is known that many metabolites of chlorpromazine have pharmacological activity. If a chemical assay measures only the unchanged chlorpromazine, and if the clinical effects are produced to a fair extent by metabolites, and if the amount of metabolite is not well correlated with the amount of unchanged drug, then the presence of active metabolites may obscure the correlation between chlorpromazine-plasma levels and therapeutic efficacy. This may complicate the interpretation of chlorpromazine studies.

Other Antipsychotics

Cotes et al. (1978) treated patients with a fixed dose of flupenthixol and noted a correlation between prolactin levels and total symptom changes ($r = 0.56$, $p < 0.05$).

In 29 schizophrenic patients plasma fluphenazine levels had an inverted U-shaped relationship with clinical response (Dysken et al. 1981). Most nonresponders have either very low fluphenazine levels or very high fluphenazine levels. Also patients treated with haloperidol showed an inverted U-shaped relationship (unpublished results). Nonresponders have either very low plasma haloperidol or very high haloperidol levels.

---

[1] Illinois State Psychiatric Institute, Chicago, IL 60612.

Use of Free or RBC Levels

It is the concentration of free drug which is in equilibrium with tissue drug levels. Quantification of free drug is technically impossible at this time, yet potentially quite important. Drugs must cross the blood-brain barrier to reach central receptor sites. These factors of distribution, in addition to rate of metabolism, will determine the amount of drug at receptor site. If some of the mechanisms involved in the drug's distribution across the cell membrane of the red blood cell mimic those governing the passage of drug through the blood brain barrier, then drug levels within RBC (or RBC/plasma ratio) may give additional information. In fact, Manian et al. (1974) have shown similarities between RBC and rat brain synaptosomes-chlorpromazine levels. If the assumption is valid, then RBCs may be a preferred tissue for drug measurement.

Garver et al. (1976) administered butaperazine on a constant dose schedule to acutely symptomatic schizophrenic patients while measuring plasma and RBC levels. Although both plasma and RBC levels vs. response were best characterized by an inverted U-shaped curve, the relationship using RBC levels was more striking. These results support the hypothesis that RBC levels of antipsychotic drugs are a better correlate of clinical response and side effects than plasma levels. These results have been replicated in a completely new sample of patients (Casper et al. 1980).

Blood Levels in Chronic Schizophrenics

Most schizophrenics respond to some degree to neuroleptic drugs and then return home. However, there are occasional patients who show no response to drugs whatsoever and need to be hospitalized in a chronic state hospital. Since some of these very chronic patients are fast metabolizers, failure to respond to drugs might be a possible explanation of their chronicity. Such a chronic population was found to have their plasma and red cell levels substantially below those seen in the acute population (Smith et al. 1979). A similar, very unresponsive group of patients in an acute setting was also studied. Many of these patients had absolutely no clinical response to antipsychotic drugs; many were, indeed, considered for transfer to a chronic facility. In essence, this was the same population as the chronic nonresponders, but identified in an acute setting. These patient also had extremely low plasma and red cell levels. A fair number of these nonresponders did respond when given higher than normal doses of fluphenazine enanthate or decanoate. Since chlorpromazine undergoes first-pass metabolism, an intermuscular formulation may bypass this first-pass effect to achieve an adequate plasma level.

Conclusion

Although all studies do not agree, it appears from the literature that in general, antipsychotics may have a range of drug concentration. Below and above this range the clinical response appears to be less. Measuring blood levels has added an important dimension in treating schizophrenic patients. However, there is a need for more controlled, methodologically valid studies.

References

Casper, R., Garver, D.L., Dekirmenjian, H., Chang, S., and Davis, J.M. Phenothiazine levels in plasma and red blood cells. *Arch. Gen. Psychiatry,* 37:301-305, 1980.

Cotes, P.J., Crow, T.J., Johnstone, E.C., et al. Neuroendocrine changes in acute schizophrenia as a function of clinical state and neuroleptic medication. *Psychol. Med.,* 8:657-665, 1978.

Curry, S.H., and Marshall, J.H.L. Plasma levels chlorpromazine and some of its relatively nonpolar metabolites in psychiatric patients. *Life Sci.,* 7:9-17, 1968.

Dysken, M.W., Javaid, J.I., Chang, S.S., Schaffer, C., Shahid, A., and Davis, J.M. Fluphenazine pharmacokinetics and therapeutic response. *Psychopharmacology (Berlin),* 73:205-210, 1981.

Garver, D., Davis, J.M., Dekirmenjian, H., Jones, F.D., Casper, R., and Haraszti, J. Pharmacokinetics of red blood phenothiazines and clinical effects: Acute dystonic reactions. *Arch. Gen. Psychiatry,* 33:862-866, 1976.

Lader, M. Monitoring plasma concentrations of neuroleptics. *Pharmakopsychiatr. Neuropsychopharmacol.,* 9:170-177, 1976.

Manian, A.A., Piette, L.H., Holland, D., Grover, T., and Leterrier, F. Red blood cell drug binding as a possible mechanism for tranquilization. In: Forrest, I.S., Carr, C.J., and Usdin, E. (eds.), *Advances in Biochemical Psychopharmacology,* Vol. 9. New York: Raven Press, 1974, pp. 149-161.

May, P.R.A., van Putten, T., Jenden, D., Yale, C., and Dixon, W.J. Chlorpromazine levels and the outcome of treatment in schizophrenic patients. *Arch. Gen. Psychiatry,* 38:202-207, 1981.

Sakalis, G., Curry, S.H., Mould, G.P., and Lader, M.H. Physiologic and clinical effects of chlorpromazine and their relationship to plasma level. *Clin. Pharmacol. Ther.,* 13:931-946, 1972.

Smith, R.C., Crayton, J.W., Dekirmenjian, H., Klass, D., and Davis, J.M. Blood levels of neuroleptic drugs in nonresponding chronic schizophrenic patients. *Arch. Gen. Psychiatry,* 36:579-584, 1979.

Wode-Helgodt, B., Borg, S., Fyro, B., and Sedvall, G. Clinical effects and drug concentrations in plasma and cerebrospinal fluid in psychotic patients treated with fixed doses of chlorpromazine. *Acta Psychiatr. Scand.,* 58:149-173, 1978.

Measurement of Antipsychotics in Patients

Javaid I. Javaid, Ph.D.,[1] Robert D. Linden, M.D.,[1] and John J. Davis, M.D.[1]

It is well established that patients treated with similar doses of antidepressants or antipsychotics have pronounced variations of drug concentrations in plasma (Alexanderson 1972; Forsman et al. 1977; Garver et al. 1977; Hammer & Sjoqvist 1967; Javaid et al. 1981). These interindividual differences have emphasized the need for measuring drug concentrations in blood and correlating these with clinical effects. A number of controlled studies with various antidepressants, have demonstrated a significant relationship between antidepressant concentration in plasma and clinical response. This information, particularly for nortriptyline, imipramine, and lithium, can be used as a guideline for antidepressant concentration in plasma in patients being treated with these medications. The therapeutic or toxic concentrations for most of the antipsychotics, however, have not been established. This scarcity of information has, in part, been due to the lack of specific and sensitive methods for measuring low therapeutic levels of high potency antipsychotics. In recent years, however, there has been emphasis on the development of such methods and at present sensitive and specific methods are becoming available.

In the present studies, drug concentrations in plasma from patients treated with different antipsychotics were measured by gas liquid chromatographic (GLC) methods and radioreceptor assay (RRA). The RRA is based upon the assumption that the therapeutic action of antipsychotic drugs is mediated through their ability to block dopamine receptors. The radiolabeled neuroleptics (such as [^{3}H]-spiroperidol) bound to specific membrane receptors can be displaced by compounds binding to the same receptors. Since RRA measures the total pharmacological activity of the sample *in vitro*, it has great potential for clinical efficacy studies. Potentially, RRA may be used to measure all antipsychotics of different chemical structures in the same assay, expressing the results as "activity units" against one standard (such as chlorpromazine or haloperidol).

Table 1

Neuroleptic Levels by Chemical and Radioreceptor Assays

Drug	*N*	GLC	RRA	*r*	RRA Chem
		ng/ml			
Butaperazine	10	152.0	201.0	0.84*	1.3
Haloperidol	20	7.2	10.1	0.62**	1.3
Fluphenazine	20	0.97	7.1	0.85†	7.3
Trifluoperazine	35	0.7	5.7	0.02	8.1

* $p < 0.05$
** $p < 0.01$
† $p < 0.001$

The drug concentrations in plasma from patients treated with four different antipsychotics are shown in Table 1. The parent compounds were used as standards for both the GLC and RRA. The similar values obtained by both methods for butaperazine (RRA/GLC ratio = 1.3) and haloperidol (RRA/GLC ratio = 1.3) suggest that most likely these drugs do not have many active metabolites *in vivo*. On the other hand, RRA values for both fluphenazine and trifluoperazine were 7-8 times greater than the drug concentrations measured by GLC. Higher values by RRA indicate the presence of active metabolites which were not measured by GLC method.

---

[1] Illinois State Psychiatric Institute, Chicago, IL 60612.

Since the RRA measures the total inhibitory activity in the sample, theoretically this would be an advantage in clinical efficacy studies, where the investigator is primarily concerned with the clinical effects of the drug, which may be due to the parent drug and/or the active metabolites. It has been shown that *in vitro* potencies of different antipsychotics in blocking dopamine receptors are linearly correlated to their daily doses required for therapeutic treatment in patients (Seeman & Lee 1975). If a certain degree of dopamine blockade is required for the amelioration of schizophrenic symptoms, then the *in vitro* differences of potencies between antipsychotics could account for the differences in clinical doses. Since RRA measures total dopamine blockade activity, one would expect that at therapeutic doses, all antipsychotics would produce similar dopamine blockade activity. However, this was found not to be true. Table 2 shows that the dopamine blockade activity in plasma samples from patients treated with high potency antipsychotics (haloperidol, perphenazine, fluphenazine, and trifluoperazine) was much smaller than butaperazine and thioridazine. Similar results have been reported by other investigators (Calil et al. 1979; Cohen et al. 1980). One possible explanation for large differences in the dopamine receptor blockade activity (as determined by RRA) in plasma from patients treated with different antipsychotics, may be that some of the active metabolites do not cross blood brain barrier. Another possibility is that the binding affinities of different neuroleptics and their metabolites to plasma proteins may vary widely.

Table 2

Neuroleptic Concentrations (CPZ - Equivalence) In Patients Treated with Therapeutic Doses

Drug	Neuroleptic Activity (Chlorpromazine Equivalence)
Thioridazine	1,974
Butaperazine	1,196
Haloperidol	66
Perphenazine	44
Fluphenazine	71
Trifluoperazine	62

The chemical assays (such as GLC) for antipsychotics require sample extraction and are time-consuming; however, they are specific. On the other hand, RRA and radioimmunoassays (RIA) for antipsychotics do not require any extraction, are simple and expedient. These methods, however, are not specific. It has been shown (Rubin et al. 1980) that antibodies prepared against haloperidol by two different methods had different cross reactivities and gave different values of haloperidol in the same samples. Hence, the choice of the method depends upon the specific aims of the investigator, and the methodological details should be kept in mind.

References

Alexanderson, B. Pharmacokinetics of nortriptyline in man after single and multiple oral doses: The predicability of steady-state plasma concentrations from single-dose plasma level data. *Eur. J. Clin. Pharmacol.*, 4:82-91, 1972.

Calil, H., Avery, D.H., Hollister, C.E., et al. Serum levels of neuroleptics measured by dopamine receptor assay and some clinical observations. *Psychiatry Res.*, 1:39-44, 1979.

Cohen, B.M., Lipinski, J.F., Harris, P.Q., et al. Clinical use of the radioreceptor assay for neuroleptics. *Psychiatry Res.*, 1:173-178, 1980.

Forsman, A., Folsch, G., Larsson, M., and Ohman, R. On the metabolism of haloperidol in man. *Curr. Ther. Res.*, 21:606-617, 1977.

Garver, D.L., Dekirmenjian, H., Davis, J.M., Casper, R., and Ericksen, S. Neuroleptic drug levels and therapeutic response: Preliminary observations with red blood cell bound butaperazine. *Am. J. Psychiatry*, 134:304-307, 1977.

Hammer, W., and Sjoqvist, F. Plasma levels of monomethylated tricyclic antidepressants during treatment with imipramine-like compounds. *Life Sci.*, 6:1895-1903, 1967.

Javaid, J.I., Dekirmenjian, H., Liskevych, U., Lin, R.L., and Davis, J.M. Fluphenazine determination in human plasma by a sensitive gas chromatograph method using nitrogen detector. *J. Chromatogr. Sci.*, 19:439-443, 1981.

Seeman, P., and Lee, T. Antipsychotic drugs: Direct correlation between clinical potency and presynaptic action on dopamine neurons. *Science*, 188:1217-1219, 1975.

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-180/103

The *Psychopharmacology Bulletin* is prepared by the Pharmacologic and Somatic Treatments Research Branch of the National Institute of Mental Health. Its purpose is to facilitate the dissemination and exchange of information among the national and international scientific community. The emphasis is on rapid, informal reporting of work which has not appeared in the more formal literature. We invite contributions such as original articles, brief reports, review articles, letters to the Editor, news items, books for review, and announcements appropriate for the *Bulletin*.

All material published in the *Psychopharmacology Bulletin* is in the public domain unless otherwise noted. Publication in the *Bulletin* therefore does not preclude publication elsewhere.

Individuals interested in submitting material to the *Psychopharmacology Bulletin* should contact:

Allen Raskin, Ph.D.
Editor-in-Chief
Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

We respectfully ask you to adhere to the following guidelines when preparing a paper for the *Psychopharmacology Bulletin:*

1. Manuscript Format: Manuscripts should be typed double-spaced with ample margins, and submitted in triplicate. Do not split paragraphs from one page to another, even if this makes page lengths uneven. Also, do not hyphenate words at the end of a line, even if this makes uneven lines.

Title page should include each author's name, degree, and full address.

Papers should be written in *third* person, e.g., the investigators found, **Not:** I found, we found. Contents should be *substantive,* not indicative, e.g., the investigator used the gas chromatography method to determine the three molecular structures, **Not:** The author described the method for determining the structure of the drug.

2. Figures: Figures, charts, or graphs should be submitted as glossies (photographs printed on smooth shiny paper) or should be professionally prepared using black ink on white paper. Only one copy is needed. Indicate in the text where these figures and their legends should be placed.

3. References: References mentioned in the text should appear as full citations in the **References** following the text with *all* authors cited in the reference list, e.g., Simpson, G.M., Lee, L.H., Zubok, B., and Gardos. A rating scale for tardive dyskinesia. *Psychopharmacology (Berlin),* 64(2): 171-179, 1979.

If a work has two authors, always cite both names every time the reference occurs in the text, e.g., (Swanson & Cole 1974). If more than two authors, cite only the surname of the first author in the text followed by et al., e.g., Williams et al. 1963.

4. Abbreviations: Abbreviations should appear in parentheses after the first time they are mentioned in the paper, i.e., Brief Psychiatric Rating Scale (BPRS).

Use generic names in referring to drugs; trade names may be given in parenthesis the first time a drug is mentioned only.

Journal titles should be abbreviated in the *References* according to the National Library of Medicine's Index Medicus.

5. Brief Reports: Authors wishing very rapid reporting of new work may submit manuscripts of up to five typed double-spaced pages for inclusion as Brief Reports. If accepted, these results would appear in the next issue of the *Bulletin*. In preparing a manuscript for publication as a Brief Report, please follow the format cited above.

DEPARTMENT OF
HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20857

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U. S. DEPARTMENT OF H.H.S.
HHS 396

FOURTH CLASS
BOOK RATE

U.S.MAIL

DHHS Publication No. (ADM) 82 - 173
Printed 1982

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20857

Psychopharmacology Bulletin

Vol. 18, No. 4
October 1982

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service • Alcohol, Drug Abuse, and Mental Health Administration

Contributions and inquiries should be sent to:

Allen Raskin, Ph.D.
Editor-in-Chief

Lillian Altman
Managing Editor

Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

The *Psychopharmacology Bulletin* is available on subscription from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402. Subscription price $11.00 per year for the United States. All other countries add $2.75 for postage. Please make check or money order payable to the Superintendent of Documents. An annual subscription for four quarterly issues begins with the next issue following receipt of the order. Single copies and back issues may also be ordered from the Superintendent of Documents. The expiration date is printed on the top line of the address label. Change of address and complaints about non-receipt of issues should be sent to the Superintendent of Documents, and should include the old address, preferably a mailing label, as well as the new address.

ORDER FORM Mail To: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Enclosed is $______ ☐ check,
(U.S. Currency Only)
☐ money order, or charge to my
Deposit Account No.
☐☐☐☐☐☐☐–☐

Order No.__________

VISA
master charge

Credit Card Orders Only

Total charges $_______ Fill in the boxes below.

Credit Card No. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Expiration Date Month/Year ☐☐☐☐

Please enter my subscription to: **PSYCHOPHARMACOLOGY BULLETIN** [*PSBU*]
@ $11.00 domestic, @ $13.75 foreign.

Name—First, Last

Street address

Company name or additional address line

City **State** **ZIP Code**

(or Country)

PLEASE PRINT OR TYPE

For Office Use Only.

	Quantity	Charges
Enclosed		
To be mailed		
Subscriptions		
Postage		
Foreign handling		
MMOB		
OPNR		
UPNS		
Discount		
Refund		

NEWARK PUBLIC LIBRARY
NOV 17 1982
U. S. GOVT. PUBS.
DEPOSITORY 376

Psychopharmacology Bulletin

CONTENTS

Vol. 18, No. 4

October 1982

Page

Fellowship Program 1
Meeting Announcements 1
Book Reviews 2
New Journal 4
New Books 4
Notice 5
Adverse Drug Reactions 6
  Safe Passage (How Good a Guarantee?)—*Paul Leber* 6

Brief Reports—

  Supersensitivity, Drug Withdrawal, and Open Field Behavior—*João Palermo-Neto* 11
  Tiapride in Tardive Dyskinesia—*D.J. Murphy, G. Hughes, and G.K. Shaw* 13

Articles—

  Haloperidol Plasma/Red Blood Cell Ratios and Clinical Efficacy—*Robert Neborsky, David S. Janowsky, James Perel, Ethan Munson, and Dennis Depry* 17
  Cholinomimetic-Induced Co-Release of Prolactin and Beta-Endorphin in Man—*S. Craig Risch, David S. Janowsky, Larry J. Siever, Lewis L. Judd, Jeffrey L. Rausch, Leighton Y. Huey, Kimberlee A. Beckman, Robert M. Cohen, and Dennis L. Murphy* 21

Review—

  Hormonal and Neurotransmitter Hypotheses of Premenstrual Tension—*Jeffrey L. Rausch, David. S. Janowsky, S. Craig Risch, Lewis L. Judd, and Leighton Y. Huey* 26

Psychopharmacology and the Anxiety Disorders Workshop—

  Diagnostic Classification of Anxiety and Phobic Disorders—*David V. Sheehan and Kathy H. Sheehan* 35
  New Antianxiety Agents—*Jonathan O. Cole* 45
  Animal Models of Anxiety: Implications for Research in Humans—*Thomas W. Uhde, Jean-Phillippe Boulenger, Larry J. Siever, Robert L. DuPont, and Robert M. Post* 47
  Caffeine Consumption and Anxiety: Preliminary Results of a Survey Comparing Patients with Anxiety Disorders and Normal Controls—*Jean-Philippe Boulenger and Thomas W. Uhde* 53
  New Anxiolytics: Are they Really New?—*David J. Greenblatt and Richard I. Shader* 58
  Differentiating Depression from Anxiety: Is It Possible? Is It Useful?—*Edna B. Foa and Uriel G. Foa* 62
  Differentiating Anxiety and Depression in Anxiety Disorders: Use of Rating Scales—*Ronald S. Lipman* 69

Page

Are There Anticompulsive or Antiphobic Drugs? Review of the Evidence—*Isaac Marks* 78
Medication in the Treatment of Panic Attacks and Phobic States—*Donald F. Klein* 85
Agoraphobia: Behavioral and Pharmacological Treatments, Preliminary Outcome, and Process Findings—*Matig Mavissakalian and Larry Michelson* 91
Comparison of Generalized Anxiety Disorder With Panic Disorder Patients—*Rudolf Hoehn-Saric* 104
Unresolved Issues in the Treatment of Agoraphobia With Panic Attacks—*Michael R. Liebowitz and Donald F. Klein* 109
Antiobsessional and Antidepressant Effects of Clomipramine in the Treatment of Obsessive-Compulsive Disorder—*Thomas R. Insel, Ina Alterman, and Dennis L. Murphy* 115

20th Annual Meeting of the ACNP—Poster Sessions—

Evaluation of Alpha-Adrenergic Responsiveness to Clonidine Challenge and Noradrenergic Metabolism in the Affective Disorders and Their Treatment—*Larry J. Siever, Thomas W. Uhde, Edward K. Silberman, Charles R. Lake, David C. Jimerson, S. Craig Risch, Ned H. Kalin, and Dennis L. Murphy* 118
Biological Markers for Depressive Illness—*Alan G. Robertson, Betty Jo Tricou, Victor S. Fang, and Herbert Y. Meltzer* 120
Relationship of Dexamethasone (2 mg) and Plasma Cortisol Hypersecretion in Depressive Illness: Clinical and Neuroendocrine Parameters—*Gregory M. Asnis, Uriel Halbreich, Edward J. Sachar, R. Swami Nathan, Mark Davies, Hana Novacenko, Lynn C. Ostrow, Jean Endicott, and Joaquim Puig-Antich* 122
Melatonin Secretion as a Neurobiological "Marker" and Effects of Light in Humans—*Alfred J. Lewy, Thomas A. Wehr, Norman E. Rosenthal, John I. Nurnberger, Larry J. Siever, Thomas W. Uhde, David A. Newsome, Leslie E. Becker, Sanford P. Markey, Irvin J. Kopin, and Frederick K. Goodwin* 127
The Relationship of Plasma-Free MHPG to Anxiety and Psychophysical Pain in Normal Volunteers—*Thomas W. Uhde, Larry J. Siever, Robert M. Post, David C. Jimerson, Jean-Philippe Boulenger, and Monte S. Buchsbaum* 129
Current Knowledge of Tricyclic Antidepressant Response Indicators—*David H. Tilley, Solomon C. Goldberg, and Robert O. Friedel* 132
Effects of Membrane Fluidity on Secretion and Receptor Stimulation—*Fulton T. Crews* 135
A Study of the Metabolism of Des-Tyrosine-γ-Endorphin Using an Improved HPLC System—*Hans Schoemaker, Andrew Chen, Thomas P. Davis, and Henry I. Yamamura* 144
The Central Nervous System Control of the Immune System—Enkephalins: Antitumor Activities—*Nicholas P. Plotnikoff* 148
A Behavioral Study of the Changes in the CNS of Mice After Subchronic Treatment with the Dopamine Autoreceptor Agonist 3-PPP—*Stephan Hjorth, David Jackson, Arvid Carlsson, and Per Lindberg* 149
Studies of Plasma Homovanillic Acid as an Index of Brain Dopamine Function—*Kenneth S. Kendler, John Y-K. Hsieh, and Kenneth L. Davis* 152
Plasma Haloperidol Levels and Clinical Response in Acute Schizophrenia—*Irl Extein, K.A. Augusthy, Mark S. Gold, A.L.C. Pottash, David Martin, and William Z. Potter* 156
Abnormal Immune Regulation in Schizophrenic Patients—*Lynn E. DeLisi and Richard Jed Wyatt* 158
Abnormal Scans in Young Schizophrenics—*S. Charles Schulz, Miriam Koller, Pulla R. Kishore, Robert M. Hamer, and Robert O. Friedel* 163
Computer EEG Drug Data Base in Psychopharmacology and in Drug Development—*Turan M. Itil, Gopi N. Menon, and Kurt Z. Itil* 165

Page

The First Clinical Study of BW-234U in Schizophrenia—*Jonathan Davidson, Robert Miller, Martha Wingfield, William Zung, and Anthony T. Dren* 173

Does Long-Acting Injectable Neuroleptic Protect Against Tardive Dyskinesia?—*Solomon C. Goldberg, Ramakrishnan S. Shenoy, Demetrios Julius, Robert M. Hamer, Beverly Ross, Teena Minton, and Marilyn Spiro* 177

Combined MAOI-Tricyclic Antidepressant Treatment: A Controlled Trial—*Kerrin White, Javad Razani, George Simpson, Ronald Rebal, R. Bruce Sloane, Judith O'Leary, and Ruby Palmer* ... 180

Differential Efficacy of L-Deprenyl, a Selective MAO Type-B Inhibitor, in Endogenous and Nonendogenous Depression—*J. John Mann, Allen Frances, Eric D. Peselow, and Samuel Gershon* 182

Pharmacological Treatment of Delusional Depressives—*Duane G. Spiker, Israel Hanin, James M. Perel, Jane E. Cofsky, Albert J. Rossi, and Denise Sorisio* 184

Erythrocyte and Plasma Choline in Bipolar Psychiatric Patients: A Followup Study—*Israel Hanin, Bruce M. Cohen, Ursula Kopp, and Joseph R. Lipinski* 186

Relationship Between Cognition and Mood in Geriatric Depression—*Barry Reisberg, Steven H. Ferris, Anastase Georgotas, Mony J. de Leon, and Michael K. Schneck* 191

Cerebrospinal Fluid Acetylcholine, Choline, and Senile Dementia of the Alzheimer's Type—*Kenneth L. Davis, John Y-K. Hsieh, Michael I. Levy, Thomas B. Horvath, Bonnie M. Davis, and Richard C. Mohs* 193

Cognitive and Performance Deficits in Depression—*Allen Raskin, Alfred S. Friedman, and Alberto DiMascio* 196

Desglycinamide-9-Arginine-8-Vasopressin (DGAVP, Organon 5667) in Cognitively Impaired Patients—*Jared R. Tinklenberg, Robert Pigache, Philip A. Berger, and Bert Kopell* 202

How Does Methylphenidate (MP) Affect Information Processing in Man?—*Enoch Callaway, Roy Halliday, Shirley Peeke, and Victor Reus* 205

Parental Reports of Adverse Responses to Food Substances in Child Psychiatry Patients and Normal Controls—*Jovan G. Simeon, H. Bruce Ferguson, Carole Anne Ralph, and D. Mistry* 206

Classical Conditioning of Cocaine's Stimulatory Effects—*Wagner H. Bridger, Stanley R. Schiff, Stanley S. Cooper, William Paredes, and Gordon A. Barr* 210

Naloxone Potentiates Cocaine Effect in Man—*Robert Byck, Alan Ruskis, James Ungerer, and Peter Jatlow* 214

Rapid Acquisition of Conditioned Responses to Hydromorphone in Detoxified Heroin Addicts—*Joseph W. Ternes, Charles P. O'Brien, and Thomas T. Testa* 215

Lofexidine in Abrupt Methadone Withdrawal—*Arnold M. Washton and Richard B. Resnick* 220

Effects of Desipramine on Diurnal Rhythms of Plasma 3-Methoxy-4-Hydroxyphenylglycol (MHPG) in Depressed Patients—*Edward M. DeMet, Angelos E. Halaris, Harry E. Gwirtsman, Rochelle M. Reno, and Phyllis I. Becker* 221

β-Endorphin, Cortisol, and Prolactin in Serum of Schizophrenic Patients During Long-Term Neuroleptic Treatment and After Withdrawal: Relationships to Psychopathology—*Dieter Naber, Margot Albus, Franz Müller, Horst Burke, Doris Welter, Manfred Ackenheil, and Hanns Hippius* 224

Psychopharmacology—A Recurring Bibliography—
  Subject Section S-1
  Author Section A-59

Fellowship Program

The University of Texas Health Sciences Center announces the third year of their Clinical Psychopharmacology Fellowship Program for physicians who have completed psychiatric residency training. Two positions are open for the 1983-1984 year. The fellow will be eligible for an appointment as Instructor in the Department of Psychiatry and will receive a commensurate stipend.

The program inclues: a) clinical research experiences in several of the ongoing studies in the department; b) clinical psychopharmacological preceptorial work; c) participation in one of the ongoing studies of biological disturbances in major psychiatric illness; d) wet laboratory experience in analytical methods; e) an integrative tutorial series to provide an overview of neuropharmacology, biological hypotheses of psychiatric disorders, and clinical investigative techniques; f) participation in graduate school and other Health Science Center courses and seminars pertinent to the learning needs of the fellow; and g) opportunity to emphasize study and training in a selected clinical area.

For further information, please contact: Charles L. Bowden, M.D., Nancy U. Karren Professor of Psychiatry, Dept. of Psychiatry, The University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284.

* * * * *

Meeting Announcements

The 1983 meeting of the **Society of Behavioral Medicine** will be held at the Hyatt Regency in Baltimore, Maryland on March 2-5, 1983. There will be a special track for the Fourth Annual Meeting on the topic of Behavioral Medicine in Industry. For further information, please contact: Thomas J. Coates, Ph.D., Program Chair, Society of Behavioral Medicine, P.O. Box 8530, University Station, Knoxville, TN 37996.

* * * * *

Announcement and call for papers for the VIIth World Congress of the **International College of Psychosomatic Medicine** to be held in Hamburg, Federal Republic of Germany, July 17-22, 1983. This Congress will take place immediately after the World Congress of Psychiatry in Vienna. Topics for the plenary session will be: early identification and prevention of psychosomatic disorders; maintaining health despite stress and adverse circumstances; the effectiveness of psychotherapy on specified psychosomatic disorders; integrational models of psychosomatic pathogenesis; taxonomic subgroups within psychosomatic diseases; the psychosomatic problems involved in somatic treatment; integration of psychosomatics into hospital treatment; and the influence of social change and economic factors on psychosomatic disorders.

Epidemiology, original points of view, theoretical viewpoints, pain, sleep and dreams, hypnosis, behavioral therapy, psychosomatic illness in the elderly, and various other topics will be discussed in the symposia.

For further information, contact Psychosomatics 83, Hamburg Messe und Congress GmbH, Congress Organization, P.O. Box 302360, D-2000 Hamburg 36, Federal Republic of Germany.

* * * * *

The **Canadian College of Neuropsychopharmacology** will be holding its Sixth Annual Scientific Meeting in Saskatoon, Saskatchewan on May 25-28, 1983. The sponsors are various departments of the University of Saskatchewan. The meeting will include an academic lecture by the 1982 Heinz Lehmann award winner, Dr. T. L. Sourkes; plenary lectures; symposia; roundtables; workshops; oral communications; and poster sessions.

For further information, please write to 1983

CCNP Meeting, c/o Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan S7N OXO, Canada.

* * * * *

The Second International Congress on Drugs and Alcohol will be held December 18-22, 1983 in Tel-Aviv, Israel. This multidisciplinary congress is being organized by the Society for Medicine and Law in Israel and the Israel Medical Association, and will provide an excellent opportunity for researchers, intervention agents, and policymakers to exchange their views, concerns, and future plans.

Those interested should contact: Congress Secretariat, Peltours Ltd., Congress Department, P.O. Box 394, Tel Aviv, 61003 Israel.

Book Reviews

- **The Psychobiology of Affective Disorders,** edited by Joseph Mendels, M.D. and Jay D. Amsterdam, M.D., presents the proceedings of a symposium held in February 1980. The symposium gathered a group of experts to review current knowledge of psychobiologic factors associated with clinical depression. The presentations and discussions focused on biological factors in the etiology of depression and as predictors of differential response to psychopharmacologic treatment.

The 14 papers presented represent a wide range of research efforts and attempt to summarize relevant data on the interaction of specific factors as neurotransmitters, receptors, hormones, and genes with the psychologic and environmental components of depression. The volume expresses an optimistic view that significant progress is being achieved in understanding the psychobiology of affective disorders. Although considerable research is required to fully understand the complexities of this problem, the contributors are encouraged that this psychobiological avenue of investigation has great potential for the development of a rational approach for the diagnosis and therapy of affective disorders.

In the opening chapter, Martin Katz discusses the epidemiology of depression and explanations for its apparent increasing incidence, including increased awareness of its presence. Next, David Dummer presents recent clinical, biologic, and genetic data supporting the subclassification of affective disorders into unipolar, bipolar I, and bipolar II subtypes.

Elliot Gershon's paper reviews the evidence that genetic factors are of importance in determining vulnerability to major affective disorder. The usefulness of information about affective disorders in first-degree relatives for treatment and prevention of these disorders is presented.

Three chapters by James Maas and Yung Huang, Jay Amsterdam and Joseph Mendels, and David Janowsky provide an in-depth review of noradrenergic, serotonergic, and cholinergic neuronal system functioning and depression. Alan Fraser and Joseph Mendels focus on evidence that repeated administration of antidepressant drugs leads to compensatory neuronal processes that modify the initial effects of an enhanced noradrenergic response. Each of these contributions skillfully delineates the currently conceptualized role of these neurotransmitters in the complex regulation of affect and the pathophysiology of affective disorders.

The theoretical and clinical significance of the neuroendocrine aspects of depression is presented by Bernard Carroll. Carroll describes the utility of the dexamethasone suppression test (DST) as a measure of neuroendocrine disinhibition. About 50 percent of endogenously depressed patients show this phenomenon.

In Boyd Hartman's presentation, depression is conceptualized as one component of a dysregulation of general central homeostatic mechanisms. This research indicates that tricyclic antidepressants have pharmacologic effects on cerebral vascular permeability mediated by the central adrenergic regulatory system. Thus, he believes these drugs may have biologically important central effects on non-neuronal tissues.

In two additional chapters, recent pharmacologic and clinical studies and sleep and circadian rhythm disturbance in depression are reviewed by David Hawkins. In the concluding three chapters, George Winokur, Morris Lipton, and Jay Amsterdam and Joe Mendels discuss the advances in clinical psychiatric practice resulting from psychiatric research, and attempt to summarize new psychobiological strategies in affective illness.

This book is valuable as an wide-ranging review of the psychobiology of affective disorders. Generally, the contributions are concise, readable, and informative reviews of past and current work in the area. Several of the authors present provocative new theories and hypotheses. The inclusion of the open discussion following each presentation provides additional perspectives on the topic. The book contains valuable information and extensive references for both clinicians and psychopharmacologic researchers.

The book may be ordered directly from the publisher, S. Karger, Basel, Switzerland. Price: SFr. 39./DM47./U.S. $23.50. 220 pp. soft cover.

Jack Blaine, MD.,
National Institute of Mental Health
Rockville, Maryland

* * * * *

• **The Missing Link,** by Walter J. Garre, is a philosophical and psychological attempt to explain the "transition from animal instinct to the human mind." The main result of this transition, Dr. Garre states, is man's sense of self-glory. All human motivation stems from this need to feel important, resulting in unrealistic rationalizations and beliefs about other humans and nature. Included are the beliefs that man can control nature, that mankind has a specific purpose, and that there is a God who is aware of the existence of each individual.

The one recurring theme in this book is that of strict determinism. Each human being is physically and emotionally the product of his genetic endowment and environmental experiences. Free will is an unrealistic creation to enable the individual to feel special.

Dr. Garre attempts to explain a wide range of topics through his deterministic theory. Some of these topics are evolution, personality disorders, depression, violence, anxiety, sexual disorders, love, and art. Most personality traits, claims Garre, arise as a result of the degree of acceptance and importance felt by the child in early years. The reader is continuously reminded, however, that the parents themselves are only as adequate as their parents prepared them to be.

The Missing Link is a thorough discussion of determinism. It also serves as a primer on Darwinian theory as well as Freudian and Jungian theories of personality. Unfortunately, this book does not provide any insights on the transition from animal instincts to the human mind, as the title claims. It does discuss the differences or lack of differences between humans and animals. The book also does not provide "scientific proof," as the author states, of his theory. Rather, Dr. Garre explains contradictions between determinism and various twin studies by pointing out the inadequacies of the studies cited; he does not provide evidence, scientific or otherwise, to substantiate his beliefs.

Despite its shortcomings, the book does make interesting and, at times, provocative reading.

The book may be ordered directly from Philosophical Library, 200 West 57th Street, New York, NY 10019. Price:$15.00; 293 pp.

Sarah Raskin
Johns Hopkins University
Baltimore, Maryland

• **Compendium of Current Source Materials for Drugs,** compiled by Eutychia Londos, is an annotated bibliography of sources where librarians, health professionals, and interested lay persons can find information on drugs. The 12 sections of this text include the following types of materials: standard reference books for both prescription and nonprescription drugs; dictionaries and encyclopedias; evaluative and comparative sources; sources for laws and regulations, including names and addresses of national and international enforcement agencies; books and pamphlets for general reading, including alcoholism, drug abuse, and drug therapy; directories of education information; treatment centers and agencies, with national information centers for smoking listed; bibliographies on drug sources; journal and newsletters; reports; audiovisual catalogs and indexes, including names and addresses of pharmaceutical companies providing free loan film services; and computers and on-line databases, annotating the most recent developments in this new area of drug information retrieval. A combined author and title index is provided.

The author, Eutychia Londos, is a librarian working primarily with audiovisual materials and computerized literature retrieval services. Updates or supplements to this compendium are planned as new source materials become available.

The book may be ordered directly from the publisher, Scarecrow Press, Inc., 52 Liberty Street, P.O. Box 656, Metuchen, N.J. 08840. Price: U.S. $12.50; 146 pp. Size: 8 1/2 x 11.

Allen Raskin, Ph.D.
National Institute of Mental Health
Rockville, Maryland

New Journal

Clinical Gerontologist, a new journal in the field of aging and mental health, edited by T.L. Brink, Ph.D., is now being published by The Haworth Press, Inc., 28 East 22nd Street, New York, NY 10010. The Journal is written and refereed by and for mental health practitioners. The editor is interested in topics such as organic brain syndrome, depression, paranoia, hypochondriases, psychosomatic disorders, suicide, multidisciplinary teams, alcoholism in later life, and helping families of dependent elders.

New Books

- **The Handbook of Biological Psychiatry.** Edited by Prof. Dr. Herman van Praag, Malcolm Lader, Ole Rafaelsen, and Edward Sachar. Individual titles are: Disciplines Relevant to Biological Psychiatry; Brain Mechanisms and Abnormal Behavior (Psychophysiology); Brain Mechanisms and Abnormal Behavior (Genetics and Neuroendocrinology); Brain Mechanisms and Abnormal Behavior (Chemistry); Drug Treatment in Psychiatry-Psychotropic Drugs; and Practical Applications of Psychotropic Drugs and Other Biological Treatments. The books can be purchased individually or in a set. The entire set price (6 volumes) is $370.75 (Twenty percent higher outside the U.S. and Canada). New York: Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 10016.

* * * * *

- **The Biology of Anxiety.** Edited by Roy J. Mathew, M.D., D.P.M. Brunner/Mazel Publishers, 19 Union Square, New York, NY 10003. Price: $30.00; 312 pp.

* * * * *

- **The Substance Abuse Problems.** Sidney Cohen, M.D. (ed.). The Haworth Press, 149 Fifth Avenue, New York, NY 10010. Price: $19.95, softcover; $29.95, hardcover.

* * * * *

- **Biological Treatments in Psychiatry.** Lothar Kalinowsky, M.D., (ed.). Grune & Stratton, Inc., 111 Fifth Avenue, New York, NY 10003. $49.50.

* * * * *

Lithium and Manic Depression: A Guide. Written by John Bohn, R.Ph. and James Jefferson, M.D., with assistance from other staff members at the Lithium Information Center, Department of Psychiatry, University of Wisconsin-Madison, 600 Highland Avenue, Madison, WI 53792. Price: $3.00 per copy (1 to 10 copies); $2.00 per copy (more than 10 copies).

Notice

Use of Approved Drugs of Unlabeled Indications*

The appropriateness or the legality of prescribing approved drugs for uses not included in their official labeling is sometimes a cause of concern and confusion among practitioners.

Under the Federal Food, Drug, and Cosmetic (FD&C) Act, a drug approved for marketing may be labeled, promoted, and advertised by the manufacturer only for those uses for which the drug's safety and affectiveness have been established and which FDA has approved. These are commonly referred to as "approved uses." This means that adequate and well-controlled clinical trials have documented these uses, and the results of the trials have been reviewed and approved by FDA.

The FD&C Act does not, however, limit the manner in which a physician may use an approved drug. Once a product has been approved for marketing, a physician may prescribe it for uses or in treatment regimens of patient populations that are not included in approved labeling. Such "unapproved" or, more precisely, "unlabeled" uses may be appropriate and rational in certain circumstances and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature.

The term "unapproved uses" is, to some extent, misleading. It includes a variety of situations ranging from unstudied to thoroughly investigated drug uses. Valid new uses for drugs already on the market are often first discovered through serendipitous observations and therapeutic innovations, subsequently confirmed by well-planned and executed clinical investigations. Before such advances can be added to the approved labeling, however, data substantiating the effectiveness of a new use or regimen must be submitted by the manufacturer to FDA for evaluation. This may take time and, without the initiative of the drug manufacturer whose produce is involved, may never occur. For that reason, accepted medical practice often includes drug use that is not reflected in approved drug labeling.

With respect to its role in medical practice, the package insert is informational only. FDA tries to assure that prescription drug information in the package insert accurately and fully reflects that data on safety and effectiveness on which drug approval is based.

---

*Reprinted from the *FDA Drug Bulletin*, Vol. 12, No. 1, 1982.

Adverse Drug Reactions

Safe Passage (How Good a Guarantee?)

Paul Leber, M.D.

In the author's first three contributions to this column, he examined aspects of two alleged causal relationships between drug exposure and untoward events (lithium and leukemia; neuroleptics and sudden death), and the more general problem of common untoward clinical events falsely attributed to drug exposure.

In this column, the author will address another class of problem which is frequently encountered in the process of conducting drug safety assessments. What is the significance of failing to detect any untoward events during drug exposure? In other words, what conclusions may be drawn from a report of "safe passage?"

Clearly, safe passage by several persons on a particular voyage does not guarantee that all travelers will be kept out of harm's way on similar trips. Any assurance that can be drawn from reports of safe passage must be qualified by a consideration of how many individuals have attempted the voyage, and the qualities and character of those who enjoyed safe passage.

Consideration of each of these caveats is especially critical when a report of "safe passage" is likely to lead to an increased use of a potentially toxic drug in what may be called a "physiologically disadvantaged" population.

A case in point is a recent and reassuring *New England Journal of Medicine* article on the apparent safe use of two tricyclic antidepressant drugs in ambulatory patients with heart disease (Veith et al. 1982). Before discussing the article and its relationship to safe passage, however, some background on the risks attributed to the use of tricyclics in patients with cardiovascular disease is necessary.

The cardiotoxic effects of large overdoses of tricyclics were recognized by 1959 (Mann et al.). Concern about the danger they may pose to cardiac patients (when used at therapeutic doses) can be traced to 1) a 1961 report of severe postural hypotension and associated myocardial infarctions (Muller et al.), and 2) a 1970 report of an increased incidence of sudden death (Coull et al.). Other evidence about tricyclics in heart disease, however, is more comforting. One widely quoted hospital based epidemiological survey by the Boston Collaborative Drug Surveillance Program (1972), for example, suggests that the short term outcome of hospitalized patients with "cardiovascular disease" was not affected by treatment with tricyclics. The usefulness of this report has been questioned, however. In the view of one of the preeminent groups in the field, the Boston study has many shortcomings and is not as reassuring as it may seem at first reading (Glassman & Bigger 1981). In particular, the study's sanguine outcome must be evaluated in light of the following information: 1) the average dose of tricyclic administered was below 81 mg per day, and 2) the mean observation period was 2 weeks or less for the two largest specific drug groups (amitriptyline and imipramine).

On the other hand, not all the evidence is negative: one of the pharmacologic properties of tricyclic drugs may offer protection to some patients with heart disease. Bigger and Glassman's

---

Note: This article was written by Dr. Leber in his private capacity. No official support or endorsement by the Food and Drug Administration is intended or should be inferred.

group have documented that the quinidine-like, anti-arrhythmic effect of imipramine may, under selected conditions, prove beneficial to the patient with heart disease (Bigger et al. 1977).

Given this background, the potential significance of the investigation by Veith and his colleagues can be readily understood. Clinicians are often confronted with significantly depressed patients who have serious heart disease. Aside from the dysphoria and suffering associated with the depressed state, depression may interfere with successful physical, social, and vocational rehabilitation of the patient. Thus, a direct examination of the risk of antidepressant drug use in depressed cardiac patients is an important undertaking which commands the interest of the medical community. When the results of such a study support the relative safety of antidepressants, one may anticipate a change in tricyclic use in clinical practice. Indeed, one may expect the influence of the article to be fairly widespread, given the large readership of the *New England Journal of Medicine.* In light of these considerations, it seems important to examine, critically, the message of safe passage conveyed in the article, be it explicitly intended by its authors or not.

The paper is entitled, "Cardiovascular Effects of Tricyclic Antidepressants in Depressed Patients with Chronic Heart Disease." Below the title, set in bold type, is the synopsis of the study which states, in part, "Our findings underscore the need for a reappraisal of the cardiovascular risks of tricyclic antidepressants and suggest that in the absence of severe impairment of myocardial performance, depressed patients with preexisting heart disease can be effectively treated with these agents without an adverse effect on ventricular rhythm or hemodynamic function." It seems possible that a reader may interpret this statement as a more or less unqualified endorsement of tricyclic use in heart disease.

Admittedly, the discussion section of the paper presents a more comprehensive analysis of the study's limitations. The authors note that their patient sample contained relatively few patients with seriously impaired cardiac performance (i.e., ejection fractions below 0.35). They comment that their paper cannot resolve that issue of the relationship between sudden death and tricyclics. Nevertheless, they are fairly sanguine about the safety of tricyclics in "patients considered at high risk for cardiovacular side effects. . ."

How was this conclusion reached in a study involving 17 drug-treated patients? More important, is the conclusion reasonable? A fair response to these questions must begin with a detailed examination of the study.

Twenty-four patients (outpatients?) from the psychiatric and medical services of the Seattle V.A. Medical Center took part in this double-blind, parallel-control design, clinical trial. All subjects were males with heart disease who were catagorized as suffering from "secondary major depressive disorder, endogenous subtype, according to research diagnostic criteria." All participants had scores of 18 or more on the 17-item Hamilton Depression Scale and had been depressed for a mean of 7 months prior to treatment. Twenty-three of the patients had had a previous myocardial infarction (none within 2 months of the study). Although no patients had "evidence of overt congestive heart failure," "many" were taking cardiac medications throughout the trial.

Patients were assigned to one of three treatment groups (imipramine, doxepin, or placebo) for a period of 4 weeks by a "modified randomization" procedure. Subjects were not stratified on measures of ventricular performance. Consequently, although the differences among the group means were not significant (small "n"?), four of the five subjects with the lowest baseline ejection fraction values were distributed to the placebo group. In characterizing the patient sample, it is important to note that only one of the eight imipramine recipients had an ejection fraction at rest of less than 0.40. Indeed, it appears that eight drug-treated patients had ventricular performance, at rest and upon exercise, which fell in the normal range (N.B., "appears" because the individual results can only be estimated by extrapolation from a graph.) Indeed, on average, the sickest patients were assigned to placebo (i.e., the mean duration of baseline exercise was significantly lower in the placebo than in the imipramine group).

Patients on active treatment were begun on 50 mg p.o., h.s., and advanced on an every 3-day fixed schedule to the maximum dose permitted by side effects. A maximum dose limitation of 150 mg that had been imposed initially was removed because of good experience with the first eight drug-treated patients. Dosage, however, was held constant in the last week of treatment in an attempt to reach steady-state conditions. At the end of week 4, plasma levels of imipramine ranged from 34 to 468 nanograms per ml (mean of 147) and plasma levels of doxepin ranged from 21 to 646 nanograms per ml (mean of 174).

The authors evaluated the patients over the course of the trial on several measures of depression and cardiac function. Put succinctly, the results showed that the drug-treated groups enjoyed a significant within-group improvement from their baseline depression assessments, and a two-way Analysis of Variance (ANOVA) demonstrated a significant (?overall) drug-placebo treatment difference.

The assessments of cardiac function did not reveal any adverse effect of antidepressant treatment. Specifically, there were no statistically significant changes in left ventricular function as measured by a change in the mean ventricular ejection fraction (CVEF) at rest or with exercise.*

Evidence of ventricular irritability based upon the number of premature ventricular contractions per hour was difficult to assess because of the very high within, subject variability observed between repeated observations. Estimates of cardiac electrical activity based upon weekly 12 lead EKG recordings (i.e., heart rate, PR interval, QRS interval, and corrected QT interval) also showed no clinically important differences between the groups.

Finally, recorded blood pressures did not identify a statistically significant change in the extent of orthostatic hypotension observed pre- and post-treatment in the three treatment groups. Nevertheless, it is important to note that postural dizziness associated with documented orthostatic hypotension did occur in one patient given imipramine and in three given doxepin. One patient on doxepin had a syncopal episode.

Returning to the original question posed by this author, given the results of the Veith study, can one reasonably conclude that it is "safe" to use tricyclics in depressed patients with cardiovascular disease?

The answer, of course, depends upon what one is willing to accept as evidence of "safety" for this particular indication and population. Clearly, because "safety" is an abstraction, safety can never be demonstrated directly. Instead, one estimates the risk of injury associated with drug exposure and equates the relative absence of risk with some degree of relative safety. Thus, for practical purposes, the drug safety assessment process is directed at making a reliable estimate of the incidence of untoward events in the population upon drug exposure. Then, based upon some undefined process, personal beliefs about the magnitude of the risk, the benefit of the drug's effect, and the gravity of the condition being treated, are integrated to reach a judgment about the drug's relative safety.

Viewed from this perspective, the value of the Veith study as a predictor of tricyclic safety depends upon the precision of the estimate of the risk of serious injury that can be obtained from its results.

Judged by these standards, the Veith study, involving merely 17 drug-treated patients, can be expected to detect only relatively common risks and to be rather imprecise in estimating the bounds of these risks. This should not be especially surprising, as large multicenter studies involving hundreds of patients are known to be relatively insensitive to untoward events that occur at frequencies below 2 or 3 percent. The limitation that a small sample size places on the ability to detect a significant risk can be illustrated for the sample size used in the Veith study, 17.

To make the argument clear, let us assume that the population actually contains two classes of individuals: 1) those who will and 2) those who will not come to grief if treated with tricyclics. Given this assumption, how large a proportion of the depressed cardiac patient population might be at risk despite the safe passage of the 17 individuals observed in Seattle?

This question can be answered using the binomial distribution as a model. The question is formally stated in the following manner. How large must "p," the proportion of subjects who will suffer harm, be to be 95 percent certain that at least one patient in a sample of 17 will suffer the event? If no events are observed in the sample of 17 patients, then we can be equally certain that the true proportion, "p," must be less than the one calculated. For the binomial distribution, the probability of detecting one or more events is unity minus the probability of detecting none in a sample of 17 individuals. Setting the probability of the statement at 95 percent, the equation can be solved for the value of "p": $[0.95 = 1-(1-p)^{17}]$. The calculated value of "p" is approximately 0.16. Thus, the failure of Veith and his colleagues to detect even a single instance of tricyclic-induced ventricular impairment among 17 patients can only be considered unlikely if more than 16 percent of the depressed cardiac population were going to suffer a serious impairment of ventricular performance when treated with tricyclics. This is not a very reassuring result regardless of one's vantage point.

---

*Ventricular ejection fraction (VEF) is now widely used as a measure of ventricular performance. The VEF is a dimensionless index, obtained by detecting radiation over the precordium following the intravascular injection of radioactive material. It reflects the average fraction of the end-diastolic volume ejected during systole. It is presumed that the difference between two successive measurements of the ejection fraction (i.e., the change in VEF or CVEF) reflects a change in ventricular performance. Thus, if no change in performance occurs, the CVEF is zero; if performance worsens, the CVEF will be less than zero (i.e., it will be negative).

If 17 counts of safe passage offer little reassurance, what can account for the Seattle groups' belief that the outcome of their study "underscore(s) the need for a reappraisal of the cardiovascular risks of tricyclic antidepressants. . .?"

The problem may lie in the deceptive appeal of average change scores with values close to zero. Indeed, a change score measurement close to zero conveys virtually the same information as a report of safe passage. Unfortunately, such scores may lend themselves to overinterpretation.

To illustrate the point, consider the change in baseline ventricular ejection fraction (CVEF) associated with tricyclic use. As mentioned earlier, if tricyclics have no effect on the ventricular performance, the mean value of the CVEF (VEF on drug-VEF baseline) in the population of depressed patients with heart disease will be zero. Of course, it will not be zero for every patient. In fact, for purposes of assessing safety, the variability of the CVEF is as important a measure as the mean itself. Specifically, even if the mean is zero, a substantial proportion of patients might still be at considerable risk if variability in the population is great. Thus, the assurance given by Veith and associates that their study had an 84 percent chance to detect a change of 10 percent in the mean VEF (i.e., a negative CVEF equal or greater than one-tenth of the baseline VEF) is not as comforting as it appears at first reading. This is because we are not so much interested in the mean value of the CVEF (as it is essentially zero) as we are in the relative proportion of the population that will have clinically important CVEF values (i.e., ones with larger negative values).

A more appropriate goal of a safety assessment, therefore, is to construct statistical tolerance limits for the CVEF. Because we are only interested in decrements in ventricular performance, we wish to find one-sided limits. Specifically, we wish to find a value, A, above which at least a proportion P, of the population will lie (Natrella 1963).

Tables for calculating such limits exist. Using resting CVEF data for the nine sickest drug-treated patients (mean CVEF was 0.01; sample standard deviation reported as 0.03) the following may be stated with a 90 percent confidence: assuming normality, at least 90 percent of the distribution will have a CVEF greater than a value equal to the sample mean minus the product of the tabled value of K (2.133 for a sample size of nine) and the sample standard deviation. $[\text{Lower limit of CVEF} = 0.01-(2.133 \times 0.03) = -.054]$. (*See* Table A-7 in Natrella 1963.) In other words, 10 percent of the population can reasonably be expected to have a 0.05 or greater fall in their VEF at rest when treated with tricyclics. Even this estimate, however, may be too optimistic. The tolerance limit calculations are based upon the assumption that the patient sample is a random one from the population (i.e., that it is representative) and upon the assumption that CVEF scores follow a normal distribution. Neither of these assumptions need be correct.

Assuming, however, that the tolerance limits are reasonably accurate, how clinically significant will a fall of 0.05 units in resting VEF be for 10 percent of depressed patients with serious heart disease? Obviously, there is no ready answer. It does seem reasonable, however, that a fall of this sort is more likely to be important to the patient with marginal cardiac reserves than it is to the typical patient in the Seattle study who had VEFs in the normal range.

These calculations have been presented to illustrate the limits of safe passage arguments. From the perspective of the public health, 17 patients is very few indeed. It is of interest to this author that Veith and his associates recognized the problem when they noted that their results could not provide an estimate of the risk of sudden death. They clearly recognized that failure to detect an event in a small number of subjects is not especially reassuring. However, when Veith and his colleages were able to measure a variable, they behaved as though they had additional information which permitted them to make stronger inferences about safety than they might had they interpreted their experience as 17 counts of safe passage. In this author's view, it is more appropriate (i.e., conservative) to treat the measurements of cardiovascular performance as merely "hard data" corroboration (i.e., an independent check) of each count of safe passage.

Viewed in this light, the more or less uneventful passage of 17 mildly ill cardiac patients would not justify a reappraisal of the risks of tricyclic drugs. Indeed, syncope, a major recognized risk of tricyclic treatment for the patient with cardiovascular disease, did occur. Incidentally, this clinically significant event would not have been identified by examining the mean values for increments in orthostatic hypotension observed in each drug-treated group.

Before ending the column, this author wants to emphasize that his concern is not with the work nor with the results of the investigative team that conducted this very well-designed and interesting clinical trial. We will all be well served if the work in Seattle is continued, and if other studies, of similar design, are conducted. This author's concern is with the relatively strong implication of relative safety presented by the paper, especially in its lead abstract. While the author hopes that the implication is warranted, he fears that it may not be. Until larger samples of more severely ill cardiac patients are studied, wisdom suggests that tricyclics be used with caution in patients with compromised cardiovascular function.

References

Bigger, J.T., Giardina, E.G.V., Perel, J.M., Kantor, S.H., and Glassman, A.H. Cardiac antiarrhythmic effect of imipramine hydrochloride. *N. Engl. J. Med.*, 296:206-208, 1977.

Boston Collaborative Drug Surveillance Program. Adverse reactions to the tricyclic-antidepressant drugs. *Lancet*, 1:529-531, 1972.

Coull, D.C., Crooks, J., Dingwall-Fordyce, I., Scott, A.M., and Weir, R.D. Amitriptyline and cardiac disease. *Lancet*, 2:590-591, 1970.

Glassman, A.H., and Bigger, J.T. Cardiovascular effects of therapeutic doses of tricyclic antidepressants. *Arch. Gen. Psychiatry*, 38:815-820, 1981.

Mann, A.M., Catterson, A.G., and MacPherson, A.S. Toxicity of imipramine: Report on serious side effects and massive overdosage. *Can. Med. Assoc. J.*, 81:23-27, 1959.

Muller, O.F., Goodman, N., and Bellet, S. The hypotensive effect of imipramine hydrochloride in patients with cardiovascular disease. *Clin. Pharmacol. and Ther.*, 2:300-307, 1961.

Natrella, M.G. *Experimental Statistics*, Section 2-5, Statistical Tolerance Limits, National Bureau of Standards Handbook 91, 1963.

Veith, R.C., Raskin, M.A., Caldwell, J.H., Barnes, R.F., Gumbrecht, G., and Ritchie, J.L. Cardiovascular effects of tricyclic anidepressants in depressed patients with chronic heart disease. *N. Engl. J. Med.*, 306:954-959, 1982.

Brief Reports—

Supersensitivity, Drug Withdrawal, and Open Field Behavior

João Palermo-Neto, M.S., Ph.D.[1]

The open field has been used to study withdrawal from long-term drug treatment (Bernardi & Palermo-Neto 1979; Bernardi et al. 1981; Capaz et al. 1981; De Lima & Palermo-Neto 1980; Palermo-Neto & De Lima, in press). Thus, abrupt withdrawal from long-term haloperidol administration in increasing doses enhanced general activity of rats in an open field (Bernardi & Palermo-Neto 1979). Identical findings were observed after withdrawal from long-term treatment with diphenylhydantoin (De Lima & Palermo-Neto 1980), ethanol (Capaz et al. 1981), and sodium barbital (Palermo-Neto & De Lima 1982). The open field was also used to compare the effects of single and long-term haloperidol administration (Bernardi et al. 1981). The effects of withdrawal from the neuroleptics were explained by a development of supersensitivity in the central dopaminergic receptors. Indeed, a significant displacement to the left of the dose-response curve for apomorphine-induced stereotypy in rats on abrupt haloperidol withdrawal was observed (Bernardi et al. 1981). Central nervous system (CNS) supersensitivity was also used to explain withdrawal effects for the remaining drugs employed. Thus, in ethanol-withdrawn mice a positive correlation was found between locomotion plus rearing frequencies and audiogenic-induced seizure susceptibility (Capaz et al. 1981). Equal results were detected after withdrawal from long-term diphenylhydantoin (De Lima & Palermo-Neto 1981) and sodium barbital (Palermo-Neto & De Lima 1982). In these latter two studies, drug removal also made rats more sensitive to convulsions elicited by maximal transcorneal electroshock.

There is a close relation between CNS supersensitive phenomena and the "withdrawal syndrome" observed after withdrawal from long-term administration of CNS-depressant drugs (Collier 1966, 1968; Sharpless 1964, 1969, 1975). In rats, the main characteristic of this syndrome is a hyperexcitability state characterized by a greater tendency to convulsions independent of the pattern and nature of the elicitor stimuli (Essig 1967; Kalant et al. 1971). Thus, it seems that both the increase in seizure susceptibility and the increment in general activity of withdrawn rats are simply a manifestation of CNS supersensitivity induced by the long-term drug depression (Sharpless 1969). According to Sharpless (1964), this phenomena is probably a compensatory mechanism developed against the long-term depressant effect of the drug, induced perhaps to maintain homeostasis. Indeed, withdrawal signs were not detected in rats after gradual withdrawal from long-term haloperidol treatment (Bernardi & Palermo-Neto 1979). Furthermore, comparing the effects of single and long-term haloperidol administration, the author observed a correlation between the impairment of motor function induced by different doses of haloperidol, singly administered, and the increment of general activity observed after withdrawal from long-term neuroleptic administration (Bernardi et al. 1981).

It is important to emphasize concern that the author is referring to postsynaptic supersensitivity, also named "denervation" or "disuse" supersensitivity, where the major synaptic change involved is at the postsynaptic receptors (Tarsy & Baldessarini 1974). Specificly, the author believes that, in his experiments, the long-term interrup-

---

[1] Laboratory of Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of São Paulo, SP, Brazil.

Send correspondence to Dr. Palermo-Neto at Faculdad de Medicina Veterinaria USP, Farmacologia Aplicado e Toxicologia, Av. Corifeu de Azevedo Marques, 2720, 05340 São Paulo, SP, Brazil.

tion of synaptic transmission resulted in supersensitive receptors to the endogenously released neurotransmitter or to its related agonists. This hypothesis seems true. Indeed, haloperidol blocks postsynaptic dopaminergic receptors (Ljungberg & Ungerstedt 1977) and diphenylhydantoin, ethanol, and sodium barbital interfere with synaptic transmission in presynaptic terminals blocking different processes of Ca^{++}-dependent neurotransmitter release, such as noradrenaline (Blaustein 1976; Pincus & Lee 1973; Williams et al. 1975). In this respect, catecholaminergic systems are related both to general activity (Dunstan & Jackson 1976) and to convulsion spread (Jobe et al. 1973). Further, it was shown that noradrenaline plays an important role in barbiturates withdrawal (Morgan et al. 1978; Tabakoff et al. 1977).

Thus, it seems that hyperactivity, a classic and insufficiently explored symptom of early drug withdrawal (Martin 1977), is one of the many behavioral manifestations of CNS supersensitivity. So, quantification of these behaviors in an open field displays the phenomena. Indeed, as sound or high levels of illumination inside the apparatus were not used, it is supposed that the subject will habituate to, and hence be minimally influenced by, aspects of test situations other than the specific stimulus component being used as the independent variable, in the author's studies, drug withdrawal.

References

Bernardi, M.M., and Palermo-Neto, J. Effects of abrupt and gradual withdrawal from long-term haloperidol treatment on open-field behavior of rats. *Psychopharmacology (Berlin),* 65:247-250, 1979.

Bernardi, M.M., De Souza, H., and Palermo-Neto, J. Effects of single and long-term haloperidol administration on open-field behavior of rats. *Psychopharmacology (Berlin),* 73:171-175, 1981.

Blaustein, M.F. Barbiturates block calcium uptake by stimulated and potassium depolarized rat sympathetic ganglia. *J. Pharmacol. Exp. Ther.,* 196:80-86, 1976.

Capaz, F.R., Vasconcellos, L.E., De Moralis, S., and Palermo-Neto, J. The open-field: A simple method to show ethanol withdrawal symptoms. *Arch. Int. Pharmacodyn. Ther.,* 251:228-236, 1981.

Collier, H.O.J. Tolerance, physical dependence, and receptors. *Adv. Drug Res.,* 3:171-188, 1966.

Collier, H.O.J. Supersensitivity and dependence. *Nature,* 220:228-231, 1968.

De Lima, T.C.M., and Palermo-Neto, J. The effects of diphenylhydantoin on rat behavior. *Psychopharmacology (Berlin),* 69:183-185, 1980.

De Lima, T.C.M., and Palermo-Neto, J. Effects of withdrawal from long-term diphenylhydantoin treatment on audiogenic and maximal electroshock-induced seizures in rats. *Acta Neurol. Scand.,* 63:189-196, 1981.

Dunstan, R., and Jackson, D.M. The demonstration of a change in adrenergic receptor sensitivity in the central nervous system of mice after withdrawal from long-term treatment with haloperidol. *Psychopharmacology (Berlin),* 48:105-114, 1976.

Essig, C.F. Clinical and experimental aspects of barbiturate withdrawal convulsions. *Epilepsia (Boston),* 8:21-30, 1967.

Jobe, P.C., Picchioni, A.L., and Chin, L. Role of norepinephrine in audiogenic seizure in the rat. *J. Pharmacol. Exp. Ther.,* 184:1-10, 1973.

Kalant, H., Le Blanc, A.E., and Gibbins, R.J. Tolerance to and dependence on some nonopiate psychotropic drugs. *Pharmacol. Rev.,* 23:135-191, 1971.

Ljungberg, T., and Ungerstedt, U. Different behavior patterns induced by apomorphine: Evidence that the method of administration determines the behavioral response to the drug. *Eur. J. Pharmacol.,* 46:41-50, 1977.

Martin, W.R. *Drug Addiction I.* New York:Springer Verlag 1977.

Morgan, W.W., Hufman, R.D., Pfeil, K.A., and Gonzales, E.G. Behavioral supersensitivity to apomorphine following chronic treatment with drugs that interfere with synaptic function of catecholamines. *Psychopharmacology (Berlin),* 56:41-44, 1978.

Palermo-Neto, J., and De Lima, T.C.M. Effects of withdrawal from long-term barbital treatment on open-field behavior and seizure susceptibility of rats. *Neuropharmacology.,* 25:277-281, 1982.

Pincus, J.H., and Lee, S.H. Diphenylhydantoin and calcium: Relation to norepinephrine release from brain slices. *Arch. Neurol.,* 29:239-244, 1973.

Sharpless, S.K. Reorganization of function in the nervous system: Use and disuse. *Ann. Rev. Physiol.,* 28:357-388, 1964.

Sharpless, S.K. Isolated and deafferented neurons: Disuse supersensitivity. In: Jasper, H.H., Ward, A.A., and Pope, A. (eds.), *Basic Mechanisms of the Epilepsies.* Boston: Little Brown, 1969, pp. 329-348.

Sharpless, S.K. Supersensitivity-like phenomena in the central nervous system. *Fed. Proc.,* 34:1990-1997, 1975.

Tabakoff, B., Ritzmann, F., and Hoffman, P.L. Role of catecholamines in the development of tolerance to barbiturates and ethanol. *Adv. Exp. Biol.,* 85:155-168, 1977.

Tarsy, D., and Baldessarini, R.J. Behavioral supersensitivity to apomorphine following chronic treatment with drugs which interfere with synaptic function of catecholamines. *Neuropharmacology,* 13:927-940, 1974.

Williams, J.W., Tada, M., Katz, A.M., and Rubin, E. Effect of ethanol and acetaldehyde on the (Na$^+$, K$^+$) activated adenosine triphosphatase activity of cardiac plasma membranes. *Biochem. Pharmacol.,* 24:27-32, 1975.

Vol. 18, No. 4, October 1982

Tiapride in Tardive Dyskinesia

D.J. Murphy, M.R.C. Psych.,[1] G. Hughes, M.B. B.Sc.,[1] and G.K. Shaw, F.R.C. Psych.[1]

Introduction

Tardive dyskinesia is manifested by a wide variety of involuntary movements including orolingual dyskinesia, chorea, athetosis, dystonia, tics, and facial grimacing, but excluding rhythmic tremor (APA Task Force Report, 1980). There is substantial evidence that the pathogensisi of tardive dyskinesia relates to chronic dopamine receptor blockade produced by long-term administration of antipsychotic drugs (Gardos & Cole 1980).

Drug treatment of tardive dyskinesia has been ineffective (Editorial, *Br. Med. J.* 1981). Many clinical trials demonstrate improvement in a proportion of patients but few patients in any given trial have shown more than 50 percent improvement (Gardos & Cole 1980).

Tiapride (N-diethylaminoethyl methoxy-2-methyl sulphonyl-5-benzamide hydrochoride) is closely related structurally to both metoclopramide and the antipsychotic drug sulpiride. It differs from typical neuroleptics in animals models for neuroleptic activity: it fails to induce catalepsy, displays weak sterotypy antagonism, weak ability to displace neuroleptic ligands, and inactivity in inhibiting dopamine sensitive adenylate cyclase (Jenner et al. 1978).

It inhibits perioral dyskinesias induced by the striatal injection of dopamine in animals (Costall & Naylor 1977), reduces levodopa-induced peak dose involuntary movements (Lees et al. 1979), and produced a marked improvement in buccofacial dyskinesia in the elderly (Courrier et al. 1978). In the present study the antidyskinetic potential of tiapride was examined on chronic psychiatric patients with tardive dyskinesia.

Method

Eight patients were selected from the wards of a large psychiatric hospital. They all had a casenote diagnosis of chronic schizophrenia. Their clinical features and medication history are summarized in Table 1. It was not possible to discover the length of time for which dyskinesia had been present, but it was not less than 5 years in any patient. Likewise, exact duration of neuroleptic therapy was difficult to establish but was never less than 20 years. All patients displayed involuntary movements of the orolingual or facial musculature. While the authors were inexperienced in neurological practice, efforts were made by casenote perusal and clinical evaluation to exclude patients with a neurological disorder (other than tardive dyskinesia) or those displaying stereotyped movements of schizophrenia. Baseline psychotropic medication remained unchanged for the 6-week trial period, and during the trial no patient received any other medication affecting dopaminergic or cholinergic neurotransmission. Tiapride was administered in three daily doses at 8:00 a.m., 1:00 p.m., and 6:00 p.m. Dosage is recorded in Table 2. The dose was increased after a week if response was not marked.

Movements were recorded by video-filming in a standardized manner as described by Kidger et al. (1980) at the same time of day (afternoon) each week. The scoring format for abnormal movements by Kidger et al. (1980) was used by the authors who jointly viewed the tapes. Filming was done before tiapride was introduced and thereafter at weekly intervals before dosage was

---

[1] Bexley Hospital, Bexley, Kent, England.

Address for reprint requests and correspondence: Dr. D.J. Murphy, University of Michigan Hospital, Department of Psychiatry, Clinical Studies Unit, Ann Arbor, MI 48104.

increased and at the conclusion of the trial. Parkinsonian effects were measured using the rating scale of Simpson and Angus (1970) before the start and at the conclusion of the study.

Results

The effects of treatment are summarized in Table 2. At the conclusion of week 6, when all but one patient were on 600 mg of tiapride per day, one patient was worse, three were marginally worse, one remained the same, two were marginally improved, and one was improved. Mean dyskinesia score before treatment was 4.13 ± 1.81 S.D.: at maximum dosage of tiapride was 4.25 ± 1.83 S.D. (not statistically significant). During the course of the trial, seven of the eight patients did show improvement on initial ratings but this was not maintained. One patient was noticed to have ceased a grunting sound which he was accustomed to make which initially we had not considered to be a dyskinetic phenomenon but in retrospect might have been due to diaphragmatic dyskinesia. Another patient not rated as improved was reported by nursing staff to be able to hold a cigarette in her mouth which she had not been capable of previously. In patients 2, 6, and 7, the dose of tiapride was increased to 800 mg per day for 2 days only after week 6 with marginal improvement in one patient only. The mean parkinsonism score rose from 8.75 ± 5.50 S.D. to 10.86 ± 4.74 S.D. at maximum dose of tiapride (not significant: Student's *t*-test), but this did not seem to impair everyday activities. One patient dropped out of the trial because of transfer to a hostel and in another the full dosage increase was not possible because of hypotension. No marked changes in mental state were noted in any patient.

Discussion

The results of the investigation suggest that tiapride does not have a clinically significant antidyskinetic action in patients with chronic tardive dyskinesia. The work was prompted by the theory that there are two different populations of dopamine receptors in the striatum (Jenner & Marsden 1979), those whose blockade caused neuroleptic-induced parkinsonism and those whose hypersensitivity is responsible for dyskinetic movements (Costall & Naylor 1977). The failure of tiapride to influence these receptors

Table 1

Patient Data and Baseline Medication

Patient No.	Sex	Age	Approximate Duration of Previous Neuroleptic Treatment (years)	Neuroleptics During Investigation	Anticholinergics During Investigation
1	M	56	20	Clopenthixol 800 mg I/M 2-weekly	Procyclindine 10 mg daily
2	M	53	20	Haloperidol 12 mg daily	Procyclidine 15 mg daily
3	M	66	24	None	Procyclidine 5 mg daily
4	M	64	20	Clopenthixol 100 mg I/M 3-weekly	Procyclidine 10 mg daily
5	M	61	25	Clopenthixol 200 mg I/M 3-weekly	Procyclidine 10 mg daily
6	F	65	25	None	None
7	M	65	20	Fluphenazine Decanoate 75 mg I/M 3-weekly	Procyclidine 10 mg daily
8	M	74	25	Thioridazine 225 mg daily	None

in the dose-dependent manner expected from a mechanism of postsynaptic blockade poses some questions. Was this a condition in which irreversible changes had taken place? This seems likely. Marsden et al. (1975) reported that the risk of permanent tardive dyskinesia was around 30 percent of those developing the problem and the general ineffectiveness of treatment has been alluded to previously. However, sulpiride, which is similar to tiapride, was reported to reduce tardive dyskinetic movements in a dose-dependent manner by Casey et al. (1979). Differences between Casey's group and that of the authors' study were that his subjects had a lower mean length of neuroleptic treatment, and only 5 of his 11 subjects had a diagnosis of schizophrenia.

The finding of a nonsignificant increase in parkinsonism is in accordance with Casey et al.'s results with sulpiride lending indirect support to the theory of subpopulations of striatal dopamine receptors. However, at variance with the findings are those of Lees et al. (1979) and L'Hermitte et al. (1977) who found a marked increase in parkinsonism with smaller doses of tiapride albeit in patients with idiopathic parkinson's disease. The finding that levodopa induced peak dose movements were reduced in the studies of Lees et al. (1979) and L'Hermitte et al. (1977) underlines differences in the pathophysiology of the two conditions.

Reservations about the general applicability of the findings are as follows. A small group of elderly subjects were used, most of whom remained on neuroleptic and anticholinergic medication which may have affected the action of tiapride. A rating scale was used which measured the site and duration of movements and not the intensity. Perhaps the dose was increased too rapidly. A greater response might have been obtained at higher doses than were used. The investigators feel that further preliminary studies are warranted, particularly on a less chronic population.

Table 2

Dosage, Tardive Dyskinesia, and Parkinsonism Scores

Patient No.	Dose[a] T.D. Score[b]	Before Tiapride	Duration of Treatment (Weeks)						Parkinsonism Score[c]	
			1	2	3	4	5	6	Before Tiapride	At Maximum Dose of Tiapride
1	Dose		76	150	150	150	300	600	1	8
	T.D. Score	5	7	2	2	6	2	6		
2	Dose		75	150	300	600	600	600	13	17
	T.D. Score	7	1	4	4	2	3	3		
3	Dose		75	150	300	600	600	600	8	11
	T.D. Score	2	2	6	5	2	2	6		
4	Dose		75	75	75	150	300	75	8	15
	T.D. Score	2	0	1	2	1	3	3		
5	Dose		75	150	300	300			16	—
	T.D. Score	4	4	1	3	3				
6	Dose		75	150	300	600	600	600	6	7
	T.D. Score	6	7	6	5	4	5	7		
7	Dose		75	150	300	600	600	600	3	4
	T.D. Score	4	3	6	1	2	4	4		
8	Dose		75	75	75	150	300	600	15	14
	T.D. Score	3	0	2	2	3	1	2		

[a] Total daily dose of tiapride (mgs)

[b] On scale of Kidger et al.

[c] On scale of Simpson and Angus.

Conclusion

Tiapride, a substituted benzamide derivative closely related to metoclopramide, failed to have a marked beneficial effect in seven of eight patients in a 6-week open study on patients with chronic tardive dyskinesia. Despite the use of high doses, increase in parkinsonian symptoms was not significant, lending support to the notion of separate groups of dopamine receptors. The authors' results underline the intractability and possible irreversibility of the syndrome.

Acknowledgment: Thanks are due to Drs. T. Kidger and T.R.E. Barnes for helpful advice, to Mrs. J. Johns, and to Mr. G. Samuel of Chemitechna, Ltd., who supplied medication.

References

APA Task Force Report. The task force on late neurological effects of antipsychotic drugs. Tardive dyskinesia. *Am. J. Psychiatry,* 10:1163-1172, 1980.

Casey, D.E., Gerlach, J., and Simmerlsgaard, H. Sulpiride in tardive dyskinesia. *Psychopharmacology (Berlin),* 66:73-77, 1979.

Costall, D., and Naylor, R.J. Neuropharmacological indications of an anti-dyskinetic potential for tiapride. *Semaines des Hopitaux de Paris,* 53:72-76, 1977.

Courrier, A., Dury, P., and Arbogast, J. The use of tiapride in internal medicine. *Semaines des Hopitaux de Paris,* 54:733-737, 1978.

Editorial. Tardive dyskinesia. *Br. Med. J.,* 282:1257-1258, 1981.

Gardos, G., and Cole, J.O. Overview: Public health issues in tardive dyskinesia. *Am. J. Psychiatry,* 137(7):776-781, 1980.

Jenner, P., Elliott, P.N.C., Clow, A., Reavill, C., and Marsden, C.D. A comparison of *in vitro* and *in vivo* dopamine receptor antagonism produced by substituted benzamide drugs. *J. Pharm. Pharmacol.,* 30:46-48, 1978.

Jenner, P., and Marsden, C. Mecanisme d'action des benzamides substitutes. (Mechanism of action of substituted benzamides.) *Psychologie Medicale,* 11(13):2775-2793, 1979.

Kidger, T., Barnes, T.R.E., Trauer, T., and Taylor, P.J. Sub-syndromes of tardive dyskinesia. *Psychol. Med.,* 10:513-520, 1980.

Lees, A.J., Lander, C.M., and Stern, G.M. Tiapride in levodopa-induced involuntary movements. *J. Neuro. Neurosurg. Psychiatry,* 42:380-383, 1979.

L'Hermitte, F., Signotet, J.L., and Agid, Y. Study of the effects of an original molecule, tiapride, in the treatment of abnormal movements of extrapyramidal origin. *Semaines des Hopitaux de Paris,* 53(N.39B):9-15, 1977.

Marsden, C.D., Jarsy, D., and Baldessarini, R.J. Spontaneous and drug-induced movement disorders in psychotic patients. In: Benson, D.F., and Blumer, D. (eds.), *Psychiatric Aspects of Neurologic Disease.* New York: Grune & Stratton, 1975, pp. 219-266.

Simpson, G., and Angus, J. A rating scale for extrapyramidal side effects. *Acta Psychiatr. Scand.,* Suppl. 212, 1970.

Articles—

Haloperidol Plasma/Red Blood Cell Ratios and Clinical Efficacy[1]

Robert Neborsky, M.D.,[2] David S. Janowsky, M.D.,[2] James Perel, Ph.D.,[3] Ethan Munson, D.O., B.A.,[2] and Dennis Depry, M.D.[2]

Introduction

Although the ability to accurately measure serum and red blood cell (RBC) levels of antipsychotic agents and their metabolites by a variety of techniques has advanced greatly during the past decade (Clark et al. 1977; Cohen & Hershel 1979; Creese & Snyder 1977; Hornbeck et al. 1979; Rubin et al. 1980), utilization of these analytic techniques to assess which dose of a given neuroleptic is indicated in a specific patient has been less useful than originally hoped for, although several studies have suggested some relationship between serum and/or RBC levels of neuroleptics and clinical efficacy (Casper et al. 1980; Davis 1980).

The present study is part of a previously reported experiment designed to evaluate the relationship of high- and relatively low-dose haloperidol administration to outcome in acutely ill psychotic inpatients (Neborsky et al. 1981). In this study, the relationship of plasma and RBC levels of haloperidol, as well as the relationship of the ratio of plasma to RBC haloperidol levels to antipsychotic efficacy, has been studied.

Method

In a study (Neborsky et al. 1981) intended to investigate the effects of rapid neuroleptization and subsequent short-term maintenance with low- and high-dose haloperidol, a total of 20 acutely psychotic male inpatients were utilized. Although originally diagnosed by Diagnostic and Statistical Manual-II (DSM-II) criteria, these subjects were later diagnosed retrospectively by DSM-III criteria. Based on the later criteria, the following was found: schizophreniform disorder, $N=11$; brief reactive psychosis or schizophreniform disorder, $N=1$; schizophrenic disorder, paranoid type, $N=1$, schizophrenia, undifferentiated type, $N=5$; major affective disorder, manic episode, $N=2$.

Of these 20 subjects, 10 were randomly assigned to a 10 mg dose haloperidol treatment group and 10 patients were assigned to a 2 mg dose haloperidol treatment group. Each patient then received a series of double-blind haloperidol administrations in a three-phase sequence. Treatment Day 1 was subdivided into two phases (Phases I and II). During Phase I, which consisted of an intramuscular rapid neuroleptization phase, patients received at least 1 and up to 5 hourly injections of haloperidol, given until tolerance for oral medication was possible. During Phase II, the oral rapid neuroleptization phase, the patients received the same 2 mg dose or 10 mg dose of oral haloperidol, respectively, as they had received in Phase I, up to a maximum of four additional doses. At 8:00 a.m. the following day, the patients were entered into Phase III, the oral maintenance phase, which lasted for 6 more days. During this phase, the patients received a total number of 2 or 10 mg doses each day. This data is equal to the total administered during Phase I plus II. However, the treating physician was permitted to blindly alter the number of dosages based on behavioral observations. Table 1 displays the mean milligrams of haloperidol administered during each of the three phases.

---

[1] This work was supported in part by the Medical Research Service of the San Diego Veterans Administration Medical Center (MRIS #4576) and USPHS Grant MH-30914 from the National Institute of Mental Health.

[2] Departments of Psychiatry, University of California, San Diego and San Diego Veterans Administration Medical Center, La Jolla, CA 92093.

[3] Western Psychiatric Institute and Clinic, Pittsburgh, PA 15261.

Table 1

Milligrams Haloperidol Administered During Three Experimental Phases Expressed as Mean ± SEM

Dosage	Phase I[a]	Phase II[b]	Total of Phase I + II	Average Daily Dose During Phase III[c]
2 mg/dose	8 ± 0.6	2 ± 0.5	10 ± 0.6	12 ± 0.7
10 mg/dose	29 ± 2.0	14 ± 4.0	45 ± 3.0	38 ± 4.0

[a] Phase I = Rapid Intramuscular Neuroleptization Phase
[b] Phase II = Rapid Oral Neuroleptization Phase
[c] Phase III = Oral Maintenance Phase

Behavioral responses to treatment were measured in part using the Brief Psychiatric Rating Scale (BPRS) of Overall and Gorham (1962). The BPRS was completed at baseline, and at the end of Phase III. Daily 9:00 a.m. bloods were drawn in heparinized tubes, centrifuged, separated into plasma and RBC fractions (which were allowed to lyze), and frozen at −40°C. Selected plasma and RBC samples were measured for haloperidol levels from the same sample by the radioimmunoassay technique of Perel et al. (1981) and Shostak and Perel (1976). Although the majority of the blood samples analyzed for this report were drawn on the last day of Phase III, certain samples analyzed were drawn on other days due to sample loss (mean day ± SEM = 6.85 ± .27).

Results

As described previously, there was no difference in overall clinical outcome between the high- and low-dose haloperidol treatment groups (Neborsky et al. 1981). Regardless of dosage, early clinical improvement during the first day of treatment (Phases I and II) predicted eventual improvement at the end of Phase III (Neborsky et al. 1982). Despite no overall dose-related differences in improvement between treatment groups in clincial outcome, there were substantial differences in improvement within groups (Neborsky et al. 1982). Some patients' symptoms nearly returned to a remitted baseline state, while others were completely refractory to treatment.

In examining the relationship between measured haloperidol levels, plasma and RBC haloperidol levels were found to differ significantly between the high- and low-dose groups. The high-dose group's plasma levels averaged 33.9 ± 5.0 ng/ml (mean ± SEM) and the high-dose RBC levels averaged 40.8 ± 5.7 ng/ml, whereas the low-dose groups averaged 8.2 ± 0.8 ng/ml and 9.3 ± 1.0 ng/ml, respectively. The average oral dose administered to each patient correlated significantly with the average plasma ($r = .639$, $p < .001$), and RBC concentrations ($r = .759$, $p < .001$), and a strong correlation between plasma and RBC haloperidol concentrations ($r = .975$, $p < .001$) was also found.

As shown in Table 2, there was no significant correlation of either plasma or RBC haloperidol levels with either baseline, or absolute or percent

Table 2

Correlations of Haloperidol Plasma Levels, Red Blood Cell Levels, and Plasma/Red Blood Cell Ratios with Clinical Improvement After 7 Days of Treatment in 20 Acutely Psychotic Psychiatric Inpatients

	Baseline BPRS Scores	Absolute Improvement in BPRS	Percent Improvement in BPRS
Plasma Concentration of Haloperidol	.061	.109	.101
Red Blood Cell Concentration	.085	−.023	−.064
Plasma/Red Blood Cell Ratio	−.126	.496[a]	.640[c]
Red Blood Cell/Plasma Ratio	.141	−.560[b]	−.715[c]

[a] = $p < .05$
[b] = $p < .01$
[c] = $p < .001$

improvement in psychopathology, as measured by the BPRS change scores between the baseline an the end of the maintenance phase. In contrast, the ratio of either plasma to RBC or RBC to plasma haloperidol concentrations demonstrated a strong and statistically significant correlation with both the absolute BPRS change scores and the percent change in the BPRS from the beginning to the end of the study, but did not correlate at all with baseline BPRS scores. The ratios showed a range from 0.907 to 1.599 for the RBC/plasma ratio, and from 0.625 to 1.103 for the plasma/RBC ratio. The range of the plasma/RBC haloperidol ratios and their relationship to improvement on the BPRS are displayed in the Figure.

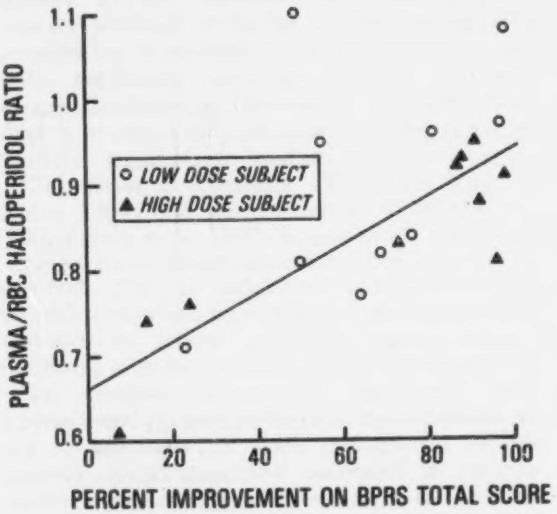


FIGURE. The relationship of plasma/RBC haloperidol ratios to percent improvement in the BPRS following 7 days of treatment in 20 acutely psychotic inpatients.

Discussion

The results are unsupportive, at least in acutely ill psychotic psychiatric inpatients, of the assertion that haloperidol dose and plasma and RBC haloperidol levels as such are useful indicators of clinical efficacy, at least when clinically accepted doses of haloperidol are utilized. This observation is different from that of some others who reported dose-effect relationship between haloperidol levels and efficacy (Calil et al. 1979; Ericksen et al. 1978; Forsman et al; 1977; Magliozzi et al. 1981; Tune et al. 1980). The reason for this difference is difficult to accurately appraise, because of study design variations and patient sampling differences between studies, but it is clear that the study was of very short duration, lasting only 7 days. If the study had been carried out for a longer time, or with a larger number of patients, a more classic dose response curve might have become apparent. Another difficulty with the study is that it was not a fixed-dose study, so that with each dosage group, respectively, an artificial triphasic relationship could have been produced (Cohen & Baldessarini 1981; Neborsky et al. 1981). A further difficulty in the design is the fact that the patients may not have reached steady-state blood levels, so that the oral dose to blood level correlations may be misleading (Forsman & Ohman 1975, 1976). A final weakness of this study is the fact that the patient group, although all psychotic, was diagnostically mixed, and was generally acute, rather than chronic schizophrenics. It is conceivable that a more homogenous group of subjects, or subjects with a poorer prognosis, would not have shown the significant correlations between plasma/RBC haloperidol ratios and clinical outcome.

Nevertheless, the observation that plasma/RBC haloperidol ratios may reflect clinical efficacy, regardless of dose, may have potential theoretical and practical implications. If plasma/RBC haloperidol ratios, analyzed early in treatment of a patient are found to eventually predict efficacy data, a valuable clinical tool may be developed. Furthermore, it is possible that *in vitro* techniques for examining plasma/RBC neuroleptic level ratios, prior to initiating neuroleptic treatment, may offer a clinical tool for prediction of response to neuroleptic therapy beyond the trial and error methods currently in use.

References

Calil, H.M., Avery, B.H., and Hollister, L.E. Serum levels of neuroleptics measured by dopamine radioreceptor assay and some clinical observations. *Psychol. Res.*, 1:39-44, 1979.

Caspar, R., Garver, D.L., Dekirmenjian, H., Chang, S., and Davis, J. Phenothiazine levels in plasma and red blood cell. *Arch. Gen. Psychiatry*, 37:301, 1980.

Clark, B.R., Tower, B.B., and Robin, R. Radioimmunoassay of haloperidol in human serum. *Life Sci.*, 20:319-326, 1977.

Cohen, B.M., and Baldessarini, R.J. Haloperidol levels and clinical response. *Am. J. Psychiatry,* 138:1513-1514, 1981.

Cohen, B.M., and Herschel, M. Neuroleptic, antimuscarinic, and antiadrenergic activity of chlorpromazine, thioridazine, and their metabolites. *Psychol. Res.*, 1:199-208, 1979.

Creese, I., and Snyder, S.H. A simple and sensitive radioreceptor assay for antipsychotic drugs in blood. *Nature,* 279:180-182, 1977.

Davis, T.M., Schaffer, C.B., Killian, G.A., Kinard, C., and Chan, C. Important issues in the drug treatment of schizophrenia. *Schizophren. Bull.*, 6:70-87, 1980.

Ericksen, S.E., Hurt, S.W., and Chang S. Haloperidol dose, plasma levels, and clinical response. A double-blind study. *Psychopharmacol. Bull.*, 14(2):15-16, 1978.

Forsman, A., Folsch, G., Larsson, M., and Ohman, R. On the metabolism of haloperidol in man. *Curr. Ther. Res.*, 21:606-617, 1977.

Forsman, A., and Ohman, R. Some aspects of the distribution and metabolism of haloperidol in man. In: Sedvall, G. (ed.), *Antipsychotic Drugs: Pharmacodynamics and Pharmacokinetics.* Oxford: Pergamon Press, 1975, pp. 359-365.

Forsman, A., and Ohman, R. Pharmacokinetic studies in haloperidol in man. *Curr. Ther. Res.*, 20:319-336, 1976.

Hornbeck, C.L., Griffiths, J.C., Neborsky, R.J., and Faulkner, M.A. A gas chromotograph mass spectrometric chemical ionization assay for haloperidol with selected ion monitoring. *Biomed. Mass Spec.*, 6(10):427-430, 1979.

Magliozzi, J.R., Hollister, L.E., and Arnold, K.V. Relationship of serum haloperidol levels to clinical response in schizophrenic patients. *Am. J. Psychiatry,* 138:365-367, 1981.

Neborsky, R., Janowsky, D., and Munson, E. Behavioral prediction of response to haloperidol: A test dose strategy. *J. Clinical Psychiatry,* 43:157-158, 1982.

Neborsky, R.J., Janowsky, D.S., Munson, E., and Depry, D. The rapid treatment of acute psychotic symptoms with high- and low-dose haloperidol behavioral considerations. *Arch. Gen. Psychiatry,* 38:195-199, 1981.

Overall, J.E., and Gorham, D.P. The Brief Psychiatric Rating Scale (BPRS). *Psychol. Rep.*, 10:799-812, 1962.

Perel, J.M., Pajerski, J., and Steller, R.L. Specific method for the analysis of haloperidol, comparison with gas chromatographic techniques. (In preparation)

Rubin, R.T., Forsman, A., and Heykants, J. Serum haloperidol determinations in psychiatric patients. *Arch. Gen. Psychiatry,* 37:1069-1074, 1980.

Shostak, M., and Perel, J.M. Radioaminoassay for haloperidol. *Fed. Proc.*, 35:531, 1976.

Tune, L.E., Creese, I., Depaulo, J.R., Slavney, P.R., Coyle, J.T., and Snyder, S.H. Clinical state and serum neuroleptic levels measured by radioreceptor assay in schizophrenia. *Am. J. Psychiatry,* 137:187-190, 1980.

Cholinomimetic-Induced Co-Release of Prolactin and Beta-Endorphin in Man[1]

S. Craig Risch, M.D.,[2,4] David S. Janowsky, M.D.,[2,4] Larry J. Siever, M.D.,[3] Lewis L. Judd, M.D.,[2] Jeffrey L. Rausch, M.D.,[2] Leighton Y. Huey, M.D.,[2,4] Kimberlee A. Beckman,[2] Robert M. Cohen, M.D.,[3] and Dennis L. Murphy, M.D.[3]

The endorphins have been mechanistically implicated in the hypothalamic modulation of anterior pituitary prolactin release, presumably by affecting hypothalamic neurotransmitter activity regulating anterior pituitary prolactin release mechanisms (Meites et al. 1979; Van Vugt & Meites 1980). In animal studies (Gold et al. 1979; Grandison & Guidotti 1977; Rivier et al. 1977b; Shaar & Clemens 1980; Van Vugt & Meites 1980) and human studies (Catlin et al. 1980; Extein et al. 1980; Schulz et al. 1980), the intravenous or intraventricular administration of beta-endorphin or exogenous opioids, such as morphine or methadone, produce dose-dependent increases in plasma prolactin concentrations. Similarly, in animal studies, administration of the opiate receptor antagonist, naloxone, may depress basal plasma prolactin concentrations, as well as attenuate or block endogenous or exogenous opioid-associated increases in plasma prolactin concentrations (Grandison & Guidotti 1977; Guidotti & Grandison 1978; Meites et al. 1979; Rivier et al. 1977b; Shaar & Clemens 1980; Van Vugt & Meites 1980).

These studies suggest that the endogenous opioid peptides may be important in the normal physiological regulation of anterior pituitary prolactin release.

It is believed that endogenous opioid peptide effects on anterior pituitary prolactin release are probably not due as such to direct effects on hypothalamic hormones regulating pituitary function (Meites et al. 1979), nor are they believed to be due to a direct opioid effect on the pituitary, since beta-endorphin does not stimulate prolactin release from hemipituitaries (Shaar et al. 1977) or from cultured pituitary cells (Rivier et al. 1977a, 1977b). Rather, it is currently hypothesized that endogenous opioid peptides modulate anterior pituitary prolactin release via actions on hypothalamic neurotransmitters such as dopamine and serotonin, which in turn regulate the release of hypothalamic hormones into the hypothalamic pituitary portal vasculature. Specifically, beta-endorphin has been demonstrated to reduce medial basal hypothalamic concentrations of dopamine, both *in vivo* (Deyo et al. 1979; Van Loon et al. 1980a; 1980b; Van Vugt et al. 1979) and *in vitro* (Enjalbert et al. 1979; Wilkes & Yen 1980). In addition, other studies have suggested that endorphins and enkephalins may increase brain serotonin turnover (Algeri et al. 1978; Van Loon & De Souza 1978), and may thereby modulate anterior pituitary prolactin release (Cusan et al. 1977; Spampinato et al. 1979).

In addition, considerable evidence, albeit conflicting, suggests a relationship between central acetylcholine and plasma prolactin activity. In a series of animal experiments by Grandison et al. (1974) and Grandison & Meites (1976), centrally or systemically administered cholinomimetics reduced basal prolactin levels, reduced the daily nocturnal surge of prolactin, reduced prolactin rises in female rats or estrogen-treated male rats

---

[1] This work was supported in part by the Medical Research Service of the San Diego Veterans Administration Medical Center (MRIS #4576) and USPHS Grant MH-30914 from the National Institute of Mental Health.

[2] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

[3] Clinical Neuropharmacology Branch, National Institute of Mental Health, Bethesda, MD 20205.

[4] Psychiatry Services, San Diego Veterans Administration Medical Center, San Diego, CA 92161.

at proestrus, and reduced prolactin rises subsequent to stress, ether, or 5-hydroxytryptamine (5-HTP) administration. Subramanian and Gala (1976) also report that both nicotinic and muscarinic cholinergic agonists prevent the afternoon circadian surge in ovariectomized, estrogen-treated rats. However, in the same study (Subramanian & Gala 1976), these investigators noted that high doses of atropine also attenuated this afternoon surge of prolactin in ovariectomized, estrogen-treated rats. McLean and Nikitovich-Winer (1975) also reported that high-dose atropine in animal studies inhibited the nocturnal rise in prolactin secretion, an effect which could be blocked by pretreatment with physostigmine. Libertun and McCann (1973) similarly reported that intraventricular or subcutaneous atropine could inhibit prolactin release in rats. In contrast, Lawson and Gala (1975), using cholinergic receptor agonists and antagonist pharmacological probes in animal studies, were unable to demonstrate any effect of these agents on basal prolactin levels.

In spite of the varying effects of cholinomimetic drugs on plasma prolactin levels in animals, the intravenous administration of centrally active cholinomimetics, such as physostigmine, an acetylcholinesterase inhibitor with both nicotinic and muscarinic cholinomimetic properties, or arecoline, a relatively selective muscarinic agonist, consistently produces significant increases in plasma prolactin, as well as beta-endorphin immunoreactivity in human subjects (Risch et al. 1980, 1981).

From these human results, these investigators have hypothesized that the cholinomimetic-induced increases in prolactin concentrations, observed in these investigators' previous studies, might reflect cholinergic activation of hypothalamic beta-endorphin release mechanisms as described above.

These investigators now describe three separate studies in three groups of human volunteer subjects in which centrally active cholinomimetic agents and placebo controls are used to define correlations between cholinomimetic-stimulated increases in hypothalamic-pituitary release of beta-endorphin and increases in plasma prolactin concentrations.

Method

In three separate experiments, the relationship of physostigmine as well as arecoline-induced increases in plasma prolactin and beta-endorphin immunoreactivity was studied. In the first experiment, nine normal volunteers (5 male, 4 female, ages 18-29) at the National Institute of Mental Health (NIMH) received physostigmine salicylate 33 μg/kg and saline placebo. In the second experiment, eleven normal volunteers (all male, ages 21-30) at the University of California at San Diego received physostigmine salicylate 22 μg/kg and saline placebo. In the third experiment, six normal volunteers (2 male, 4 female, ages 19-28) at the NIMH received arecoline hydrobromide (3 mg) and saline placebo.

All three studies were conducted under a Food and Drug Administration-approved investigational new drug (IND) and with local Human Subjects Committee approval, and all subjects gave written informed consent. Studies were conducted between the hours of 8:00 a.m. and 11:00 a.m. under randomized, double-blind conditions in which subjects, after pretreatment with methscopolamine 1.0 mg intramuscular (i.m.) or glycopyrrolate 0.2 mg intravenously (i.v.) received either placebo (normal saline) or active drug (physostigmine 22 μg/kg or physostigmine 33 μg/kg or arecoline 3.0 mg), as described above, on 1 day and received the other condition at least 2 days later, given over a 10-minute period. In each study, after an adaptational period of 30 minutes subsequent to the insertion of an indwelling heparin lock catheter, subjects had blood samples for neuroendocrine measurements drawn at 30, 15, and 0 minutes prior to active drug or placebo infusion, and at 10, 20, 35, and 50 minutes subsequent to each 10-minute infusion.

Plasma concentrations of beta-endorphin and prolactin were determined by radioimmunoassay as previously described (Kalin et al. 1981; Risch et al. 1980, 1981). The antibody for beta-endorphin demonstrates a 50 percent cross-reactivity, with beta-lipotropin, but less than 0.01 percent with alpha-endorphin, alpha-MSH, and less than 0.004 percent with leucine enkephalin and methionine enkephalin. Within-assay variability for beta-endorphin is approximately 56 percent and sensitivity is 25-50 pg/ml. The antibody for prolactin has cross-reactivities of hTSH <0.3 percent, hLH <0.1 percent, hFSH <1 percent, and hGH <0.03 percent. Within assay, variability for prolactin is approximately 5 percent and sensitivity is 5 ng/ml. In each of the three studies, all samples for plasma beta-endorphin or prolactin determinations were assayed within the same assay.

Significance of changes in plasma beta-endorphin and prolactin immunoreactivities were determined by repeated measures analysis of variance. Linear regression analyses were performed to determine the relationships and significance of cholinomimetic-induced changes in plasma prolactin and beta-endorphin immunoreactivities within individual subjects.

Results

In Experiments 1 and 2, highly significant increases in plasma beta-endorphin and prolactin immunoreactivity occurred after physostigmine infusion, but not after placebo, similar to those previously reported by these investigators (Risch et al. 1980, 1981). Changes in plasma concentrations of beta-endorphin and prolactin immunoreactivities subsequent to physostigmine were highly correlated, as described in Figures 1 and 2.

Similarly, in Experiment 3, significant increases in plasma beta-endorphin and prolactin immunoreactivities also occurred after arecoline, but not after saline placebo. As with the physostigmine infusions, changes in plasma concentrations of beta-endorphin and prolactin immunoreactivities subsequent to arecoline infusion were highly correlated, as illustrated in Figure 3.

Discussion

In three separate studies, changes in plasma concentrations of beta-endorphin were highly correlated with changes in plasma concentrations of prolactin. In addition, as depicted in Figures 1, 2, and 3, there were no increases in plasma prolactin concentrations in the absence of increases in plasma beta-endorphin concentrations. Although high correlations between exogenously administered opioids and subsequent prolactin release have been previously reported, this is the first report of such an association between endogenously stimulated opioids and changes in plasma prolactin concentrations.

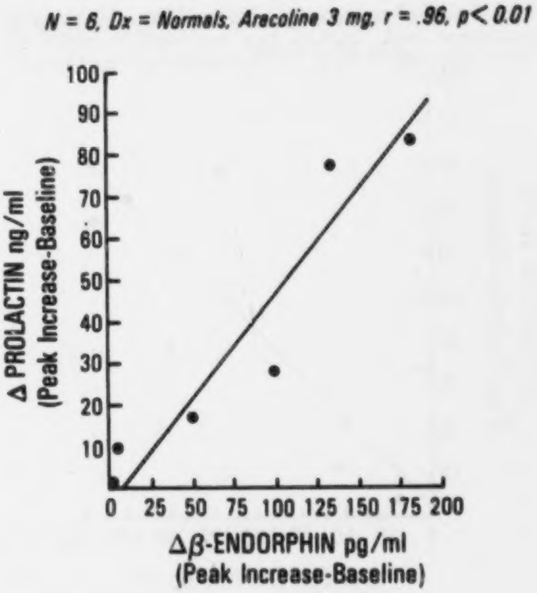


FIGURE 1

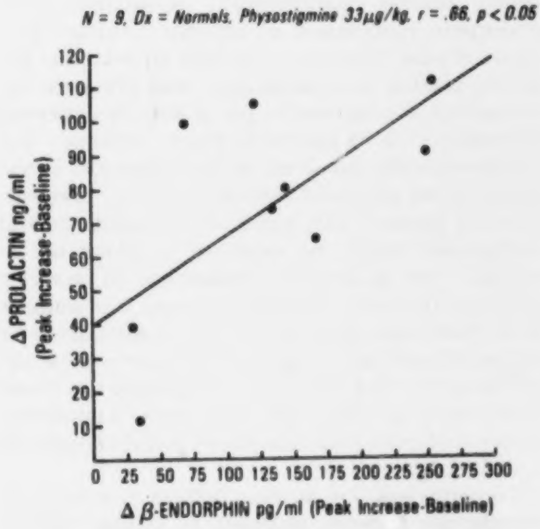


FIGURE 2

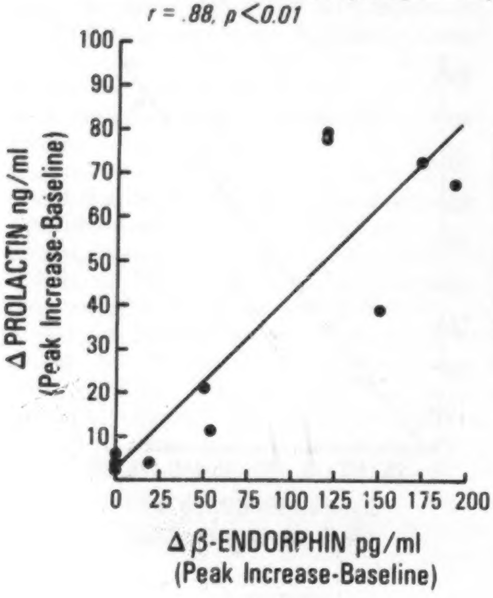


FIGURE 3

As reviewed above, these high correlations may reflect central cholinergically stimulated beta-endorphin modulation of anterior pituitary prolactin release. However, the high correlations between plasma beta-endorphin and prolactin increases do not necessarily prove that the observed increases in beta-endorphin release are mechanistically involved in the prolactin elevations. If the proposed model is correct, pretreatment of subjects with naloxone, a specific opioid antagonist, might be expected to block or attenuate the endorphin stimulation of anterior pituitary prolactin release. However, the authors have been reluctant to use the combination of naloxone and physostigmine because a pilot experiment in their laboratory suggested increased cholinergic toxicity, although three subsequent larger studies in their laboratory failed to replicate this finding.

Nevertheless, the authors believe that the high correlations between increases in plasma concentrations of beta-endorphin and prolactin observed in their studies provide a useful heuristic model for understanding the effects of centrally active cholinergic agents on anterior pituitary prolactin regulation. Furthermore, if the proposed model is correct, these findings may provide an interesting example of peptidergic modulation of primary neurochemical mechanisms involved in hypothalamic-pituitary prolactin regulation.

References

Algeri, A., Consolaizrone, A., Calderini, G., Achilli, G., Puche Canas, E., and Garattini, S. Effect of the administration of (D-Ala)-methionine-enkephalin on the serotonin metabolism in rat brain. *Experientia*, 34:1488-1489, 1978.

Catlin, D.H., Poland, R.E., Gorelick, D.A., Gerner, R.H., Hui, K.K., Rubin, R.T, and Li, C.H. Intravenous infusion of β-endorphin increases serum prolactin, but not growth hormone or cortisol, in depressed subjects and withdrawing methadone addicts. *J. Clin. Endocrinol. Metab.*, 50(6):1021-1025, 1980.

Cusan, L., Dupont, A. Kledzik, G.S., Labrie, F., Coy D.H., and Schally, A.V. Potent prolactin and growth hormone releasing activity of more analogues of met-enkephalin. *Nature (London)*, 268:544-547, 1977.

Deyo, S.N., Swift, R.M., and Miller, R.J. Morphine and endorphins modulate dopamine turnover in rat median eminance. *Proc. Natl. Acad. Sci. USA*, 74:3006-3009, 1979.

Enjalbert, A., Ruberg, M., Arancibia, S., Priam, M., and Kordon, C. Endogenous opiates block dopamine inhibition of prolactin secretion *in vitro*. *Nature*, 280:595-597, 1979.

Extein, I., Pottash, A.L.C., Gold, M.S., Sweeney, D.R., Martin, D.M., and Goodwin, F.K. Deficient prolactin response to morphine in depressed patients. *Am. J. Psychiatry*, 137(7):845-846, 1980.

Grandison, L., Gelato, M., and Meites, J. Inhibition of prolactin secretion by cholinergic drugs (37988). *Proc. Soc. Exp. Biol. Med.*, 145:1236-1239, 1974.

Grandison, L., and Meites J. Evidence for adrenergic mediation of cholinergic inhibition of prolactin release. *Endocrinology*, 99:775-779, 1976.

Grandison, L. and Guidotti, A. Regulation of prolactin release by endogenous opiates. *Nature (London)* 270:357-359, 1977.

Gold, W.S., Redmond, D.E., and Donabedian, R.K. The effects of opiate agonist and antagonist on serum prolactin in primates: Possible role for endorphins in prolactin regulation. *Endocrinology*, 105(1):284-289, 1979.

Guidotti, A., and Grandison, L. Participation of hypothalamic endorphins in the control of prolactin release. In: Costa, E., and Trabucchi, M. (eds.). *Advances in Biochemical Psychopharmacology. Vol. 18*. New York: Raven Press, 1978, pp. 191-198.

Kalin. N.H., Insel, T.R., Cohen, R.M., Risch, S.C. and Murphy, D.L. Diurnal variation in CSF prolactin concentration of the rhesus monkey. *J. Clin. Endocrinol. Metab.*, 52(5):857-858, 1981.

Lawson, D.M., and Gala, R.A. The influence of adrenergic, dopaminergic, cholinergic, and serotoninergic drugs on plasma prolactin levels in ovariectomized, estrogen-treated rats. *Endocrinology*, 96:313-319, 1975.

Libertun, C., and McCann, S.M. Blockade at the release of gonadotrophins and prolactin by subcutaneous or intraventricular injection of atropine in male and female rats. *Endocrinology,* 92:1714-1724, 1973.

McLean, B.K., and Nikitovitch-Winer, M.B. Cholinergic control of the nocturnal prolactin surge in the pseudopregnant rat. *Endocrinology,* 97:763-770, 1975.

Meites, J., Bruni, J.F., Van Vugt, D.A., and Smith, A.F. Relation of endogenous opioid peptides and morphine to neuroendocrine functions. *Life Sci.,* 24:1325-1336, 1979.

Rivier, C., Brown, M., and Vale, W. The effect of neurotensin substrate P and morphine sulfate in the secretion of prolactin and growth hormone in the rat. *Endocrinology,* 100:751-754, 1977a.

Rivier, E., Vale, W., Ling, N., Brown, M., and Guillemin, R. Stimulation *in vivo* of the secretion of prolactin and growth hormone by β-endorphin. *Endocrinology,* 100:238-241, 1977b.

Risch, C.C., Cohen, R.M., Janowsky, D.S., Kalin, N.H., and Murphy, D.L. Mood and behavioral effects of physostigmine on humans are accompanied by elevations in plasma β-endorphin and cortisol. *Science,* 209:1545-1546, 1980.

Risch, S.C., Kalin, N.H., Cohen, R.M., and Murphy, D.L. Muscarinic cholinergic influences on ACTH and β-endorphin release mechanisms in human subjects. *Peptides,* 2:Suppl. 1, 95-97, 1981.

Schulz, S.C., Wager, R., Van Kammen, D., Rogol, A.D., Davis, G.C., Wyatt, R.J., Pickar, D., Bunney, W.E., Jr., and Li, C.H. Prolactin response to β-endorphin in man. *Life Sci.,* 27(17):1735-1741, 1980.

Shaar, C.J., Frederickson, C.A., Dininger, N.B., and Jackson, L. Enkephalin analogues and naloxone modulate the release of growth and hormone and prolactin—Evidence for regulation by an endogenous opioid peptide in brain. *Life Sci.,* 21:853-860, 1977.

Shaar, C.J., and Clemens, J.A. The effects of opiate agonists on growth hormone and prolactin release in rats. *Fed. Proc.,* 39(8):2539-2543, 1980.

Spampinato, S., Locatelli, V., Cocchi, D., Vincentini, L., Bajusz, S., Ferri, S., and Muller, E.E. Involvement of brain serotonin in the prolactin-releasing effect of opioid peptides. *Endocrinology,* 105(1):163-170, 1979.

Subramanian, M.G., and Gala, R.R. The influence of cholinergic, adrenergic, and serotonergic drugs on the afternoon surge of plasma prolactin in ovariectomized, estrogen-treated rats. *Endocrinology,* 98:842-848, 1976.

Van Loon, G.R., and De Souza, E.B. Effect of β-endorphin on brain serotonin metabolism. *Life Sci.,* 23:971-978, 1978

Van Loon, G.R., De Souza, E.B., and Shin, S.H. Dopaminergic mediation of β-endorphin induced prolactin secretion. *Neuroendocrinology,* 31:292-296, 1980.

Van Loon, G.R., Ho, D., and Kim, C. β-endorphin induced decrease in hypothalamic dopamine turnover. *Endocrinology,* 106:76-80, 1980.

Van Vugt, D.A., Bruni, J.F., Sylvester, P.W., Chen, H.T., Teiri, T., and Meites, J. Interaction between opiates and hypothalamic dopamine on prolactin release. *Life Sci.,* 24:2361-2368, 1979.

Van Vugt, D.A., and Meites, J. Influence of endogenous opiates on anterior pituitary function. *Fed. Proc.,* 39(8):2533-2538, 1980.

Wilkes, M.M., and Yen, S.S.C. Reduction by β-endorphin of efflux of dopamine and DOPAC from superfused medial basal hypothalamus. *Life Sci.,* 27:1387-1391, 1980.

Review

Hormonal and Neurotransmitter Hypotheses of Premenstrual Tension[1]

ffrey L. Rausch, M.D.,[2] David S. Janowsky, M.D.,[2] S. Craig Risch, M.D.,[2] Lewis L. Judd, M.D.,[2] and Leighton Y. Huey, M.D.[2]

Introduction

The incidence of premenstrual-menstrual psychologic symptoms (premenstrual tension) has been estimated as between 25 and 100 percent of all women (Janowsky et al. 1971), with severity ranging from mild irritability to frank psychotic episodes (Endo et al. 1978; Smith et al. 1976). Symptoms are usually confined to the 5 days prior to menstruation, and abate with the onset of menses or shortly thereafter (Smith 1971). However, increases in negative affect have been found to occur as early as 11 days prior to menstruation, and to continue well into the menstrual phase (Janowsky et al. 1973), although these symptoms are to be distinguished from dysmenorrhea, a syndrome of menstrual pain etiologically associated with prostaglandin levels (Chan & Dawood 1980; Pickels 1979). A variety of hypotheses have been employed to explain the etiology of premenstrual tension (PMT) syndrome. Speculations have ranged from the psychosocial to the biochemical, but to date no single hypothesis has proven altogether satisfactory. This article reviews several of the major biological hypotheses concerning the etiology of premenstrual tension.

The Ovarian Hormone Hypothesis

In 1931, Frank first described the premenstrual tension syndrome and postulated its hormonal pathogenesis, a hypothesis now widely accepted, and deriving considerable support from animal as well as human studies. The ovarian hormones, progesterone and estrogen, are the two hormones which have been most widely studied with respect to premenstrual tension. Various theories have been proposed as to how alterations in these hormones may be etiologic.

Low progesterone levels have been considered etiologic of premenstrual tension. Mundy et al. (1977) studied 16 women, half of whom suffered from premenstrual tension. At 5 to 8 days prior to menstruation, the mean plasma progesterone for the premenstrual tension groups was 31 ± 10 nanomoles per liter as compared with the 45 ± 14 nanomoles per liter for the control group. These findings are comparable with those of Bäckström and Carstensen (1974), who found that in women with predominately psychological premenstrual symptoms, progesterone levels were reduced and estrogen levels increased, as compared with normal women during the week prior to menstruation. Smith (1976) reported small but significant differences in progesterone levels in sufferers of premenstrual depression, with the symptomatic group showing slightly lower progesterone levels, as compared with those of normal women during the week preceding menstruation. O'Brien et al. (1979), however, reported significantly higher levels of progesterone 10 days prior to menstruation in symptomatic women, as compared with controls although, at 4 days prior to menstruation in that study, the symptomatic group's mean progesterone level was nonsignificantly lower than the mean for the control group.

---

[1] This work was supported in part by the Medical Research Service of the San Diego Veterans Administration Medical Center (MRIS #4576) and USPHS Grant MH-30914 from the National Institute of Mental Health.

[2] Departments of Psychiatry, University of California, San Diego and San Diego Veterans Administration Medical Center, La Jolla, CA 92093.

Premenstrual-menstrual emotional symptoms may be related to falling levels of progesterone. Dysphoric emotional symptoms often begin in the luteal phase but intensify as progesterone drops from its highest levels during the luteal peak to its relatively low premenstrual level. Also, induction of depressive symptoms have been reported following withdrawal of exogenous progesterone treatment (Hamburg 1966). Dysphoria occurs in the third trimester of pregnancy, when progesterone is elevated, and increases postpartum as progesterone levels fall (Helmer & Judson 1967; Treadway et al. 1969).

It has also been suggested that premenstrual-menstrual psychologic symptoms may be related to high estrogen levels per se. As with progesterone, an increased occurrence of psychologic symptoms occurs during the luteal phase of the cycle, when estrogen levels are high. Morton (1950) reported production of a premenstrual tension-like syndrome after intramuscular injection of estrogen. However, against this hypothesis, psychologic symptoms do not consistently increase at mid-cycle, when estrogen is most elevated, nor is there evidence of increased premenstrual symptomatology in women with endogenously prolonged or increased estrogen levels, such as occurs in metropathia hemorrhagia (Taylor 1977).

As with progesterone, estrogen withdrawal has been postulated as etiologic of premenstrual tension (Steiner & Carroll 1977) with increases in emotionality occurring in the premenstrual phase correlating with falling estrogen levels (Baird & Guevara 1969). However, the premenstrual fall in serum estrogen levels may not reflect central nervous system estrogen activity, since estrogen is selectively bound and concentrated in the limbic system and hypothalamus (Anderson & Greenward 1969).

It may be that absolute or falling levels of estrogen and/or progesterone are less important in the etiology of premenstrual tension than is the ratio of estrogen to progesterone. Greene and Dalton (1953) have specifically hypothesized a high estrogen/progesterone ratio as etiologic of premenstrual tension. They supported this hypothesis by noting that intramuscular progesterone alleviates the premenstrual syndrome (Dalton 1964; Rees 1953), a finding later challenged in a well-controlled study (Smith 1976).

As further support for an estrogen/progesterone ration hypothesis Bäckström and Carstensen (1974) noted that women with anxiety as the main premenstrual symptom had significantly higher estrogen levels premenstrually, as compared to a group of healthy women. In a later publication by Bäckström and Mattsson (1975), in 15 women with premenstrual tension, a positive correlation was found between the estrogen/progesterone ratio and anxiety.

Studies of the mood effects of oral contraceptives tend to associate irritability and anxiety with a high estrogen/progesterone ratio and depressive symptoms with a low estrogen/progesterone ratio (Culberg 1972). Indeed, these two hormones often have opposite central nervous system (CNS) effects with estrogen increasing running and mating behavior (Colvin & Sawyer 1969), increasing dorsal hippocampal excitability (Timiras 1971), and lowering seizure threshold (Wooley & Timiras 1962), and progesterone counteracting these effects, at least to some extent (Selye 1942, 1969).

In summary, the ovarian hormone hypothesis holds that premenstrual symptomatology is etiologically related to the ratios of progesterone and estrogen in the late luteal phase, or directly related to absolute or falling levels of progesterone or estrogen.

Several considerations make it difficult to completely implicate estrogen and progesterone in the ovarian-linked emotional disorders. Greene and Dalton (1953) found 17 percent of their 84 premenstrual tension sufferers attributing the onset of cyclic menstrual symptoms to the menopause—a time when estrogen and progesterone are relatively low. Also, any estrogen/progesterone ratio hypothesis must account for the relative absence of symptomatology present during the pre-ovulatory period, when serum estrogen levels are markedly higher than progesterone.

Mineralocorticoid Hypothesis

A major and enduring endocrine hypothesis as to the etiology of premenstrual tension implicates the mineralocorticoids. From studies of normal women, there is some evidence that fluctuations of aldosterone may parallel the emotional fluctuations of the menstrual cycle. Aldosterone levels increase during the mid and late luteal phases, often to about twice that occurring during the follicular phase (Katz & Romth 1972; Reich 1962; Schwartz & Abraham 1975; Sundsfjord & Aakvaag 1972;), and at least one investigator has demonstrated premenstrual aldosterone peaks (Reich 1962).

The stimulus for increased aldosterone in the late luteal phase is not completely understood, but progesterone and the ovarian hormones have been implicated. Progesterone has been found to antagonize aldosterone and to cause a sodium diuresis, with a secondary increase in plasma renin activity and aldosterone secretion rates (Crane & Harris 1978). Sundsfjord and Aakvaag (1972), for example, found the pattern of increase and decrease in the plasma levels of aldosterone and plasma renin activity to be similar to those of plasma progesterone, suggesting that these fluctuations are causally related.

Aldosterone secretion may be altered in women suffering from premenstrual tension. Two early studies reported markedly increased premenstrual aldosterone excretion in symptomatic women (Janowsky et al. 1977; Perrini & Piliego 1959). However, more recent studies have failed to support these findings, in that Munday et al. (1977) found that the levels of plasma aldosterone in eight premenstrual tension patients were not consistently different from those of eight controls, despite a small surge of aldosterone in the late luteal phase. O'Brien et al. (1979), in a larger series of 28 women, found that the aldosterone level of symptomatic women on Day 24 was nonsignificantly lower than that of the control group's.

In a study indirectly measuring mineralocorticoid activity, Janowsky et al. (1973) evaluated changes in mood, weight, and urinary potassium/sodium (K^+/Na^+) ratio over a total of 15 menstrual cycles in 11 women in order to investigate whether these changes correlated in the same patients. The urinary K^+/Na^+ ratio was measured since there is evidence that, when dietary factors are controlled, this variable may in part reflect aldosterone and other mineralocorticoid effects. The data indicated that increases in negative affect, weight, and K^+/Na^+ ratio follow similar patterns in normal women when studied longitudinally. Thus, a statistically significant increase in urinary K^+/Na^+ ratio and negative affect occurred in the premenstrual phase of the cycle. The changes in the K^+/Na^+ ratio noted in this study strikingly paralleled the aldosterone excretion curve noted by Reich (1962).

Similarly, in a study of salivary samples from 30 menstruating females, DeMarchi and Tong (1972) found ovulatory and premenstrual increases in the K^+/Na^+ ratio. They noted that changes in salivary sodium and potassium composition have been observed in depressive illness, and that increased intraocular pressure has been found in women suffering from marked premenstrual tension. Finally, in support of a mineralocorticoid hypothesis of premenstrual tension, the aldosterone antagonist spironolactone has been reported to be more effective than placebo in decreasing symptoms of premenstrual tension (O'Brien et al. 1979).

In spite of the above information, some data do not support an aldosterone hypothesis of premenstrual tension. For example, as mentioned above, there is little evidence that the aldosterone activity in women with premenstrual tension is elevated. Also, other diseases such as Conn's Syndrome, associated with increased aldosterone levels, are not necessarily associated with emotional upsets.

It may thus be reasonable to hypothesize that a substance which fluctuates in parallel with aldosterone may cause the cyclic behavioral changes. Angiotensin may be a reasonable candidate for this substance, since angiotensin is an endogenous compound which probably stimulates aldosterone secretion, being activated itself in turn by renin. Angiotensin is elevated during the luteal phase of the menstrual cycle (Janowsky et al. 1971). Increases in renin activity are also found during the second half of the luteal phase (Kaulhausen et al. 1973).

Angiotensin exerts effects on animal behavior, central neurotransmitters, and autonomic functioning (Janowsky et al. 1971). It causes increased drinking behavior when given by vertegral artery infusion or intraventricularly (Fitzsimons & Simons 1969). This appears to be a cholinergic effect which can be antagonized by atropine (Janowsky et al. 1977). Angiotensin counteracts the anesthetic effects of amobarbital (Paliac & Khairallah 1967), and decreases exploratory activity in mice when given intraventricularly (Capek et al. 1969). It disrupts learned passive avoidance responses in rats, possibly from an effect on memory (Morgan & Routtenberg 1977). Furthermore, a central hypertensive effect has also been reported which appears to have cholinergic and adrenergic components (Severs et al. 1967, 1970). Immunohistochemical studies have revealed nerve fibers containing angiotensin in several different parts of the brain (Fuxe et al. 1976; Printz & Lewicki 1977), and a brain enzyme with a renin-like activity has been demonstrated (Genten & Speck 1978). The latter enzyme may be brain renin.

Prolactin Hypotheses

Like estrogen and progesterone, the pituitary hormone prolactin has been proposed as causative of the premenstrual tension syndrome (Andersen et al. 1977; Graham et al. 1978; Halbreich et al. 1976). It appears likely that prolactin levels fluctuate through the menstrual cycle, with peaks occurring at ovulation and later in the mid and late luteal phases (Tamura & Igarashi 1973). However, in some women, there appears to be little change throughout the cycle (McNeilly et al. 1973). Increased levels of prolactin have been reported in premenstrual tension patients as compared with normal controls (Halbreich et al. 1976).

Several pilot studies have suggested that bromocriptine, a dopamine agonist which decreases prolactin, may ameliorate premenstrual tension syndrome as well as premenstrual weight gain and breast enlargement (Graham et al. 1978). However, at least one well-controlled study has shown bromocriptine only equal to placebo in its efficacy in treating premenstrual tension, and others have shown no efficacy (Andersen et al. 1977; Graham et al. 1978). Furthermore, at least one study (Tamura & Igarashi 1973) suggests that prolactin does not increase in the luteal phases of anovulatory women, and Adamopoulos et al. (1972) have noted that premenstrual tension continues to occur during anovulatory cycles.

Monoamine Neurotransmitter Hypothesis

The monoamine neurotransmitters serotonin, norepinephrine, and dopamine have been widely implicated in psychiatric disorders (Barchas et al. 1978). Evidence is also available which implicates these monoamines in the pathophysiology of premenstrual tension.

Animal studies indicate that ovarian hormones and monoamines show overlapping behavioral effects. Like certain antidepressants, estrogen induces running behavior in rats (Colvin & Sawyer 1969) and, like reserpine, progesterone induces sedation in rats and other mammals (Selye 1969).

Brain monoamines and sex steroids show overlapping effects in the regulation of sexual behavior in rats. Reserpine and tetrabenazine, both monoamine depletors, may be substituted for progesterone in activating sexual behavior in estrogen-primed castrated female rats. In contrast, tricyclic antidepressant drugs and monoamine oxidase inhibitors (MAOIs) decrease sexual activation in estrogen/progesterone-primed castrated female rats, especially when brain serotonin is selectively increased (Meyerson & Sawyer 1968). Furthermore, selective depletion of rat brain serotonin induces sexual excitation, especially when brain catecholamines such as dopamine and norepinephrine are simultaneously elevated (Tagliamonte et al. 1969).

Ovarian hormones and monoamines also exhibit overlapping functions in regulating ovulation. Elevation of brain serotonin blocks superovulation in immature rats (Krodon 1969), and decreased norepinephrine levels inhibit physiological estrus as determined by vaginal smears (Airaksinen & McIsaac 1968). Norepinephrine administration into the third ventricle in large doses induces ovulation. Reserpine administration inhibits ovulation in the rat, and this effect is antagonized by the administration of MAOIs or dopamine (Sawyer 1952). Reserpine induces pseudopregnancy in rats when given systematically and following local hypothalamic administration, and this effect is also prevented by treatment with MAOI (Meyerson & Sawyer 1968; Sawyer 1952).

Dopamine appears to exhibit a very important role in the regulation of gonadotropin secretion. Small doses of dopamine, incubated *in vitro* in the presence of pituitary and hypothalamic tissue, induce the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) (Kamberi 1970; Meyerson & Sawyer 1968). Kamberi (1970) and Schneider and McCann (1969) have recently found that administration of small doses of dopamine or relatively high doses of norepinephrine or epinephrine significantly increase blood LH levels, while serotonin causes an opposite effect (Tagliamonte et al. 1969).

Evidence is available to indicate that ovarian hormones exert an influence on MAO activity. Pharmacologic doses of estradiol are associated with decreased tissue MAO activity in rats (Collins et al. 1970; Wurtman & Axelrod 1963). Progesterone appears to increase tissue MAO activity in rats (Collins et al. 1970), and increase plasma MAO activity in amenorrheic females (Klaiber et al. 1971). Increased endometrial monoamine oxidase occurs in the late luteal phase of the menstrual cycle and in direct proportion to the progestin content of oral contraceptives (Grant & Pryse-Davies 1968). Conversely, Belmaker et al. (1974) have noted a decrease in platelet monoamine oxidase premenstrually, and these findings have been replicated by Wirz-Justice et al. (1975).

Changes in brain monoamine levels have been found to cyclically occur throughout the rat estrus cycle. Greengrass and Tounge (1971) reported that the concentration of all three monoamines decreased in the rat during estrus, a time when ovulation is being stimulated by luteinizing hormone. During metaestrus, under the influence of luteal progesterone, the monoamine neurotransmitters begin to rise toward their maximum, achieved at dioestrus when estrogen and progesterone are low.

Thus, there is evidence that alterations in monoamines may be linked to ovarian and adrenal hormone fluctuations, as well as to behavioral changes. On this basis, a catecholamine (norepinephrine/dopamine) hypothesis, and a serotonin hypothesis of premenstrual tension have evolved.

The effects of angiotensin, estrogen, and progesterone on catecholamine neurotransmitter activity have been demonstrated in a number of *in vitro* studies using neurophysiological preparations. Angiotensin can inhibit the uptake of tritiated norepinephrine by brainstem slices, perfused rat brain ventricles (Paliac & Khairallah 1967), and synaptosomes (Janowsky et al. 1971). Further, endogenous rat brain norepinephrine is lowered by intraventricular angiotensin administration (Capek et al. 1969). Estrogen itself decreases the amount of labeled pre-equilibrated tritiated norepinephrine released by electrically stimulated rat brain slices by more than 25 percent (Vogel et al. 1970).

Janowsky and Davis (1970) also reported that progesterone and estradiol block the uptake of labeled norepinephrine by synaptosomes, and that the passive efflux of pre-equilibrated norepinephrine from synaptosomes, which is slightly slowed by estradiol, is increased by progesterone. Estradiol and progesterone inhibited the uptake of tritiated dopamine and norepinephrine by synaptosomes. Progesterone (1×10^{-4}M) increased the rate of passive efflux of labeled dopamine and norepinephrine from synaptosomes, whereas estradiol (1×10^{-6}M) did not affect dopamine efflux.

In the intact female rat, exogenous estrogen has been shown to decrease hypothalamic norepinephrine. Increased norepinephrine and decreased dopamine turnover rates have been shown in the rat after castration, these effects being reversible with large doses of estradiol and progesterone. Increased dopamine turnover has been shown in the tuberoinfundibular region after estradiol (Fuxe et al. 1970). In the striaturm, chronic estradiol administration increased the density of rat dopamine receptors, and increased behavioral sensitivity to amphetamine and apomorphine stereotypy, one of many effects estrogen can have on neurotransmitter receptors (*see* McEwen et al. 1981).

Norepinephrine and dopamine are metabolized enzymatically, in part, by catechol-o-methyltransferase (COMT), and this enzyme's activity has been inhibited *in vitro* by estrogen, progesterone, and deoxycorticosterone (Kalsner 1969). In the rat midbrain, COMT has been found to decrease during estrus (Salseduc et al. 1966).

In humans, several studies have investigated various peripheral measures of catecholamine metabolism during the menstrual cycle. Wiener and Elmadjian (1962), and Patkai et al. (1974) reported increases in urinary norepinephrine excretion during the premenstruum. A later study also measured urinary epinephrine excretion and found small nonsignificant decreases during the 5 days prior to menstruation. A more recent study (DeLeon-Jones et al. 1978) measured the urinary metabolite of central norepinephrine, 3-methoxy-4-hydroxyphenylglycol (MHPG), daily in four healthy women. A statistically significant increase in MHPG was found during the late luteal phase, followed by a rapid decline 2 days prior to menstruation, with a subsequent elevation during the menses. This premenstrual drop in MHPG excretion is interesting in view of previous findings of decreased MHPG in some individuals with depressive illness (Beckman & Goodwin 1975).

During the premenstrual-menstrual phase of the cycle, sensitivity to tyramine increased, this probably being either a measure of increased noradrenergic receptor sensitivity or increased presynaptic neuronal norepinephrine activity (Chose & Turner 1977). In view of the above noted premenstrual decreases in urinary MHPG, it may be that sensitivity to tyramine is reflective of increased receptor sensitivity, complimenting decreased norepinephrine turnover and activity.

There are several lines of evidence, in addition to that described above, that would support an indoleamine role in premenstrual tension. Rats treated with a series of injections of progesterone showed increased brain serotonin uptake (Hackman et al. 1973) and turnover (Ladisich 1977) in several areas of the brain. After withdrawal of the progesterone injections, there was a decrease in brain serotonin uptake found 24 hours after withdrawal of the last progesterone injection (Hackman et al. 1973).

The uptake of serotonin into platelets has been found to be decreased in patients with depressive illness (Rausch et al. 1982), and decreases in platelet serotonin uptake have been found to occur in the premenstrual phase of the cycle (Rausch, unpublished; Taylor et al. 1981; Wirz-Justice & Chappius-Arntt 1976). The amino acid precursor of serotonin, tryptophan, has shown menstrual variations in the plasma, with increases seen premenstrually (Wirz-Justice et al. 1975).

The urinary metabolite of serotonin, 5-hydroxyindoleacetic acid (5-HIAA), has been measured across the menstrual period in normal women, and 5-HIAA excretion has been found to be higher during the secretory phase as compared to the proliferative phase, with the final descent occurring during the premenstrual phase (Lerdo de Tejada et al. 1978). This data could be consistent with the notion that luteal progesterone secretion increases serotonin turnover, with subsequent premenstrual progesterone withdrawal resulting in lowered serotonin turnover.

The serotonin hypothesis may bear some relevance to the mineralocorticoid hypothesis discussed above, since administration of the serotonin precursors tryptophan and 5-hydroxytryptophan have been found to stimulate renin in dogs, and stress can lead to increases in both plasma renin and brain serotonin (Check 1980). Furthermore, corticosterone itself can increase or decrease serotonergic function, depending on the dose (Aubert et al. 1971).

Acetylcholine Hypothesis

Some evidence exists that cholinergic mechanisms may be etiologic in the premenstrual-menstrual emotional upsets. Angiotensin increases brain acetylcholine content in rat and mouse and causes an increase in the output of acetylcholine from the parietal cortex of cats. It causes an increase in the secretion of antidiuretic hormone, which appears to be cholinergically mediated and itself is water retaining. Consistent with these observations, it has been noted that the uterine hyperemia which precedes menstruation is due to increased acetylcholine activity, and neostigmine, a cholinesterase inhibitor, can induce menstruation in nonpregnant women who have delayed menstruation, presumably by increasing uterine acetylcholine activity. Furthermore, a variety of ovarian hormones and other steroids can increase acetylcholine activity in physiologic preparations and can increase sensitivity to acetylcholine in muscle preparations.

Menstrually related remission of symptoms has been demonstrated in patients suffering from myasthenia gravis, and are asssociated with cyclic variations of red cell acetylcholinesterase activity, suggesting a hormonal influence on acetylcholinesterase activity (Vijayan et al. 1977). Physostigmine, a centrally acting cholinomimetic drug, alleviates manic symptoms and causes withdrawal, lethergy, dysphoria, psychomotor retardation and, in some cases, depression in normals, remitted patients, schizophrenics, and manics (Janowsky et al. 1972). Possibly, then, the premenstrual-menstrual emotional upsets in part represent a relative predominance of central cholinergic activity, caused by angiotensin or a variety of endogenous steroid compounds. Finally, there is some evidence that a proprietary combination drug containing an ergot, a barbiturate, and an anticholinergic agent can alleviate premenstrual tension better than placebo can (Robinson et al. 1977). If this finding is valid, and if the effects are due to the anticholinergic agent, this would support a role for acetylcholine in the ovarian-linked emotional disorders.

Summary

In the above paragraphs, the authors have reviewed several of the major hypotheses proposed to explain the etiology of premenstrual tension. Although there is evidence that premenstrual tension is linked to changes in hormones and/or neurotransmitters, the need for further research to confirm or refute the various hypotheses exists, and represents a challenge for the future.

References

Adamopoulos, D.A., Loraine, J.A., Lunn, S.F., Coppen, A., and Daly, R. Endocrine profiles in premenstrual tension. *Clin. Endocrinol.*, 1:282-292, 1972.

Airaksinen, M.M., and McIsaac W.M. Estrus cycle in rats: The role of serotonin and norepinephrine. *Life Sci.*, 7:471-476, 1968.

Andersen, A.N., Larsen, J.F., Steenstrup, O.R., Svendstrup, B., and Nielsen, J. Effect of bromocriptine on the premenstrual syndrome. A double-blind clinical trial. *Br. J. Obstet. Gynec.*, 84:370-374, 1977.

Anderson, C.H., and Greenward, G.S. Autoradiographic analysis of estradiol uptake in the brain and pituitary of the female rat. *Endocrinology,* 85:1160-1165, 1969.

Aubert, M.L., Lemarchand-Beraud, T., Peguillaume, R., and Desaulles, P. Cortisol secretion during the normal menstrual cycle. *Acta. Endocrinol., (Copenh.),* 155:78, 1971.

Bäckström, T., and Corstensen, H. Estrogen and progesterone in plasma in relation to premenstrual tension. *J. Steroid Biochem.*, 5:257-260, 1974.

Bäckström, T., and Mattsson, B. Correlation of symptoms in premenstrual tension to oestrogen and progesterone concentrations in blood plasma. *Neuropsychobiology,* 1:80-86, 1975.

Baird, D.T., and Cuevara, A. Concentration of unconjugated estione and estradiol in peripheral plasma in nonpregnant women throughout menstrual cycle, castrate, and post-menopausal women and men. *J. Clin. Endocrinol.*, 28:149-156, 1969.

Barchas, J.D., Akil, H., Elliot, G.R., Holman, R., and Watson, S. Behavioral neurochemistry: Neuroregulators and behavioral states. *Science,* 200:964-978, 1978.

Beckman H., and Goodwin, F.K. Antidepressant response to tricyclics and urinary MHPG in unipolar patients. *Arch. Gen. Psychiatry,* 32:17-21, 1975.

Belmaker, R.H., Murphy, D.L., Wyatt, R.J., and Loriaux, L. Human platelet monoamine oxidase changes during the menstrual cycle. *Arch. Gen. Psychiatry,* 31:553-556, 1974.

Capek, R., Masek, K.M., Sramka, M., Krsiak, M., and Svec, P. The similarities of the angiotensin and bradykinin action on the central nervous system. *Pharmacology (Basel),* 2:161-170, 1969.

Chan, W.Y., and Dawood, M.Y. Prostaglandin levels in menstrual fluid of nondysmenorrheic and of dysmenorrheic subjects with and without oral contraceptive or ibuprofen therapy. *Adv. Prostaglandin Thromboxane Res.*, 8:1443-1447, 1980.

Check, W.A. Old hormones reveal new surprises. *JAMA,* 243(6):499-500, 1980.

Chose, K., and Turner, P. The menstrual cycle and the tyramine pressor response test. *Br. J. Clin. Pharmacol.,* 4(4):500-502, 1977.

Collins, G.G.S., Pryse-Davies, J., Sandler, M., and Southgate, J. Effect of pretreatment with oestradiol, progesterone, and DOPA on monoamine oxidase activity in the rat. *Nature,* 226:642-643, 1970.

Colvin, G.B., and Sawyer, C.H. Induction of running activity by intracerebral injections of estrogen in ovarectomized rats. *Neuroendocrinology,* 4:309-320, 1969.

Cox, B.D., and Culame, D.P. Changes in plasma amino acid levels during the human menstrual cycle and in early pregnancy. A preliminary report. *Horm. Metab. Res.,* 10:428-433, 1978.

Crane, M.G., and Harris, J.J. Estrogens and hypertension. *Am. J. Med. Sci.*, 276(1):33-54, 1978.

Cullberg, J. Mood changes and menstrual symptoms with difficult gestagen/estiogen combination. *Acta Psychiatr. Scand. (Suppl.),* 236:1-86, 1972.

Dalton, K. *The Premenstrual Syndrome.* London:William Heineman Medical Books, 1964.

DeLeon-Jones, F.A., Steinburg, J., Dekirmenjian, H., and Garver, D. MHPG-excretion during the menstrual cycle of women. *Comm. Psychopharmacol.*, 2:267-274, 1978.

DeMarchi, G.W., and Tong, J.E. Menstrual, diurnal, and activation effects on the resolution of temporarily paired flashes. *Psychophysiology,* 9:362-367, 1972.

Endo, M.M., Daiguji, M., Asano, Y., Yamashita, I., and Takahasi, S. Periodic psychosis recurring in association with menstrual cycle. *J. Clin. Psychiatry,* 39:456-466, 1978.

Fitzsimons, J.T., and Simons, B.J. The effect of drinking in the rat of intravenous infusion of angiotensin. *J. Physiol.,* 203:45-57, 1969.

Frank, R.T. The hormonal causes of premenstrual tension. *Arch. Neurol. Psychiatry,* 26:1053, 1931.

Fuxe, K., Ganten, D., Hökfelt, T., and Bolme, P. Immunohistochemical evidence for the existence of angiotensin II-containing nerve terminals in the brain and spinal cord in the rat. *Neurosci. Lett.*, 2:229-234, 1976.

Fuxe, K., Hökfelt, T., and Jonsson, C. The effect of gonadal steroids on the tuberoinfundibular dopamine neurons. In: *Hormonal Steroids.* Hamburg:Excerpta Medica, 1970.

Ganten, P., and Speck G. The brain renin-angiotensin system: A model for the synthesis of peptides in the brain. *Biochem. Pharmacol.*, 27:2379-2389, 1978.

Graham, J.J., Hardin, P.E., Wise, P.H., and Berriman, H. Prolactin suppression in the treatment of premenstrual tension syndrome. *Med. J. Aust.*, 2(3 Suppl.):18-20, 1978.

Grant, E.C.G., and Pryse-Davies, J. Effects of oral contraceptives on depressive mood changes and on endometrial monoamine oxidase and phosphatases. *Br. Med. J.,* 111:777-780, 1968.

Greene, R., and Dalton, K. The premenstrual syndrome. *Br. Med. J.*, 1:1007-1013, 1953.

Greengrass, P M., and Toungue, S.R. Changes in brain monoamine concentrations during the oestrus cycle in the mouse: Possible pharmacologic implications. *J. Pharm. Pharmacol.*, 23:897-898, 1971.

Hackman, E., Wirz-Justice, A., and Lichsteiner, M. The uptake of dopamine and serotonin in the rat brain during progesterone decline. *Psychopharmacologia (Berlin),*

32:183-191, 1973.

Halbreich, V., Ben-David, M., Assael, M., and Bornstein, R. Serum prolactin in women with premenstrual syndrome. *Lancet,* 2:654-656, 1976.

Hamburg, D. Effects of progesterone on behavior. *Res. Publ. Ass. Res. Nerv. Ment. Dis.,* 43:251-265, 1966.

Helmer, O.M., and Judson, W.E. Influence of high renin substrate levels on the renin-angiotensin system in pregnancy. *Am. J. Obstet. Gynec.,* 99:9-17, 1967.

Israel, S.L. Premenstrual tension. *JAMA,* 110(21):1721-1723, 1938.

Janowsky, D.S., Berens, S.C., and Davis, J.M. Correlations between mood, weight, and electrolytes during the menstrual cycle: A renin-angiotensin-aldosterone hypothesis of premenstrual tension. *Psychosom. Med.,* 35(2):143-152, 1973.

Janowsky, D.S., and Davis, J.M. Progesterone-estrogen effects on uptake and release of norephinephrine by synaptosomes. *Life Sci.,* 9:525, 1970.

Janowsky, D.S., El-Yousef, M.K., Davis, J.M., and Sekerke, H.H. A cholinergic-adrenergic hypothesis of mania and depression. *Lancet,* 1:632-635, 1972.

Janowsky, D.S., Fann, W.E., and Davis, J.M. Monoamines and ovarian hormone-linked sexual and emotional changes. *Arch. Sex. Behav.,* 1(3):205-218, 1971.

Janowsky, D.S., Gorney, R., and Mandell, A.J. The menstrual cycle. *Arch. Gen. Psychiatry,* 17:459-469, 1977.

Kalsner, S. Steroid potentiation of responses to sympathomimetic amines in aortic strips. *Br. J. Pharmacol.,* 36:582-593, 1969.

Kamberi, I.A. Effect of anterior pituitary perfusion and intraventricular injections of catecholamines and indolamines on LH release. *Endocrinology,* 87:1-12, 1970.

Katz, F.H., and Komth, P. Plasma aldosterone and renin activity during the menstrual cycle. *J. Clin. Endocrinol.,* 34:819-821, 1972.

Kaulhausen, H., Oehm, W., and Breuer, H. Plasma renin activity during the normal menstrual cycle. *Acta Endocrinol. (Copenh.),* 173(Suppl):160, 1973.

Klaiber, E.L., Kobayaski, Y., Broverman, D.M., and Hall, F. Plasma monoamine oxidase activity in regularly menstruating women and in amenorrheic women receiving cyclic treatment with estrogens and a progesten. *J. Clin. Endocrinol.,* 33:630-638, 1971.

Krodon, C. Effects of selective experimental changes in regional hypothalamic monoamine levels on superovulation in the immature rat. *Neuroendocrinology,* 4:129-138, 1969.

Ladisich, W. Influence of progesterone on serotonin metabolism: A possible causal factor for mood changes. *Psychoneuroendocrinology,* 2:257-266, 1977.

Lerdo de Tejada, A., Carreno, Q.F.B. Ma. Estela, Lopez, Q.F.I., Leonila, Wionczek, C., and Karchmen, S. Eliminacion urinaria de acido 5-hidroxiindol acetico durante el cicle menstrual humano. (Urinary elimination of 5-hydroxyindoleaetic acid during the human menstrual cycle.) *Genicol. Obstet. Mex.,* 44(262):85-91, 1978.

McEwen, B., Biegon, A., Rainbow, T., Paden, C., Snyder, L., and DeGroff, V. The interactions of estrogens with intracellular receptors and with neurotransmitter receptors: Implications for the mechanism of activation of sexual behavior and ovulation. In: *Steroid Hormone Regulation of the Brain.* Oxford:Pergamon Press, 1981.

McNeilly, A.S., Evans, G.E., and Chard, T. Observations on prolactin levels during the menstrual cycle. In: *Human Prolactin.* Amsterdam:Excerpta Medica, 1973.

Meyerson, B.J., and Sawyer, C.H. Monoamines and ovulation in the rat. *Endocrinology,* 83:170-176, 1968.

Morgan, J.M., and Routtenberg, A. Angiotensin injected into the neostriatum after learning disrupts retention performance. *Science,* 196(4285):87-89, 1977.

Morton, J.H. Premenstrual tension. *Am. J. Obstet. Gynec.,* 60:343-352, 1950.

Munday, M., Brush, M.G., and Taylor, R.W. Progesterone and aldosterone levels in the premenstrual tension syndrome. *J Endocrinol.,* 73:21P, 1977.

O'Brien, P.M.S., Craven, D., Selby, C., and Symonds, E.M. Treatment of premenstrual syndrome by spironolactone. *Br. J. Obstet. Gynec.,* 86:142-147, 1979.

Paliac, D.J., and Khairallah, P.A. Effect of angiotensin on uptake and release of norepinephrine by brain. *Biochem. Pharmacol.,* 16:2291-2298, 1967.

Patkai, P., Johannson, G., and Post, B. Mood, alertness, and sympathetic-adrenal medullary activity during the menstrual cycle. *Psychosom. Med.,* 36(6):503-512, 1974.

Perrini, N., and Piliego, N. The increase of aldosterone in the premenstrual syndrome. *Minerva Med.,* 50:2897-2899, 1959.

Pickels, V.R. Prostaglandins and dysmenorrhea. *Acta. Obstet. Gyncecol. Scand. (Suppl.),* 87:7-12, 1979.

Printz, M.P., and Lewicki, J.A. *Central Actions of Angiotensin and Related Hormones.* New York:Pergamon Press, 1977.

Rausch, J.L., Shah, N.S., Burch, E.A., and Donald, A.G. Platelet serotonin uptake in depressed patients: Circadian effect. *Biol. Psychiatry,* 17(1):121-123, 1982.

Rees, L. The premenstrual tension syndrome and its treatment. *Br. Med. J.,* 1:1014-1016, 1953.

Reich, M. The variations in urinary aldosterone levels of normal females during the menstrual cycle. *Aust. Ann. Med.,* 11:41-49, 1962.

Robinson, K., Huntington, K.M., and Wallace, M.G. Treatment of the premenstrual syndrome. *Br. J. Obstet. Gynec.,* 84:784-788, 1977.

Salseduc, M.M., Jofre, I.I., Izquierdo, J.A. Monoamine oxidase and catechol-o-methyl transferase activity in cerebral structures and sexual organs of rats during their sexual cycle. *Med. Pharmacol. Exp.,* 14:113-119, 1966.

Sawyer, C.H. Stimulation of ovulation in the rabbit by intraventricular injection of epinephrine or norepinephrine. *Anat. Rec.,* 112:385, 1952.

Schneider, H.P.G., and McCann, S.M. Possible role of dopamine as transmitter to promote discharge of LH-releasing factor. *Endocrinology,* 85:121-132, 1969.

Schwarz, U.D., and Abraham, G.E. Corticosterone and aldosterone levels during the menstrual cycle. *Obstet. Gynecol.,* 45(3):339-342, 1975.

Selye, H. Correlations between the chemical structure and pharmacological actions of the steroids. *Endocrinology,* 30:437-453, 1942.

Selye, H. Sprinolactone actions independent of mineralocorticoid blockade. *Steroids,* 13:803-808, 1969.

Severs, W.B., Daniels, A.E., and Buckley, J.P. On the central hypertensive effect of angiotensin II. *Int. J. Neuropharmacol.,* 6:199-205, 1967.

Severs, W.B., Summy-Long, J., Taylor, J.S., and Connor,

J. A central effect of angiotensin: Release of pituitary pressor material. *J. Pharmacol. Exp. Ther.*, 174:27-34, 1970.

Smith, S.L. The menstrual cycle and mood disturbances. *Clin. Obstet. Gynecol.*, 19(2):391-397, 1976.

Steiner, M., and Carroll, B.J. The psychobiology of premenstrual dysphoria: A review of theories and treatment. *Psychoneuroendocrinology*, 2:321-335, 1977.

Sundsfjord, J.A., and Aakvaag, A. Plasma renin activity, plasma renin substrate, and urinary aldosterone excretion in the menstrual cycle in relation to the concentration of progesterone and oestrogens in the plasma. *Acta Endocrinol.*, 71:519-529, 1972.

Tagliamonte, A., Tagliamonte, P., and Gessa, G.L. Compulsive sexual activity induced by *p*-cholorophenylalanine in normal and pinealectomized male rats. *Science*, 166:1433-1435, 1969.

Tamura, S., and Igarashi, M. Serum prolactin levels during ovulatory menstrual cycle and menstrual disorders in women. *Endocrinol. Jpn.*, 20(5):483-488, 1973.

Taylor, D., Mathew, R.J., Ho, B.T., and Weinman, M.L. Serotonin levels and platelet uptake during premenstrual tension. Serotonin in biological psychiatry. Paper read at the 15th Annual Symposium, Texas Research Institute of Mental Sciences, Houston, Texas 1982.

Taylor, R.W. The treatment of premenstrual tension with dyprogesterone. *Curr. Med. Res. Opin.*, 4(Suppl 4):35-40, 1977.

Timeras, P.S. Estrogen as 'organizers' of CNS function. In: *Influences of Hormones on the Nervous System*. Basel:Karger, 1971.

Treadway, R.C., Kane, F.J., Jarreh-Zadeh, A., and Lipton, M.A. A psychoendocrine study of pregnancy and puerperium. *Am. J. Psychiatry*, 125:1380-1386, 1969.

Vijayan, N., Vijayan, V.K., and Dreyfus, P.M. Acetylcholinesterase activity and menstrual remissions in myasthemia gravis. *J. Neurol. Neurosurg. Psychiatry*, 40:1060-1065, 1977.

Vogel, S.A., Janowsky, D.S., and Davis, J.M. Effect of estradiol stimulus-induced release of ^{3}H-norepinephrine and ^{3}H-serotonin from rat brain slices. *Res. Comm. Chem. Pathol. Pharmacol.*, 1(4):451-459, 1970.

Wiener, J.S., and Elmadjian, F. Excretion of epinephrine and norepinephrine in premenstrual tension. *Fed. Proc.*, 21:184, 1962.

Winston, F. Oral contraceptives, pyridoxine, and depression. *Am. J. Psychiatry*, 130(11):1217-1221, 1973.

Wirz-Justice, A., and Chappius-Arntt, E. Sex-specific differences in chlorimipramine inhibition of serotonin uptake in human platelets. *Eur. J. Pharm.*, 40:21-25, 1976.

Wirz-Justice, A., Pühringer, W., Hole, G., and Menzi, R. Monoamine oxidase and free tryptophan in human plasma. *Pharmacopsychiatry*, 8:310-317, 1975.

Wooley, D.E., and Timeras, P.S. The gonad-brain relationship. Effects of female sex hormones on electroshock convulsions in the rat. *Endocrinology*, 70:196-209, 1962.

Wurtman, R.J., and Axelrod, J. Sex steroids, cardiac, ^{3}H-norepinephrine, and tissue monoamine oxidase levels in the rat. *Biochem. Pharmacol.*, 12:1417-1419, 1963.

Vol. 18, No. 4, October 1982

Psychopharmacology and the Anxiety Disorders Workshop

This special section of the *Psychopharmacology Bulletin* is devoted to proceedings at a workshop entitled, "Psychopharmacology and the Anxiety Disorders," held in Washington, D.C. on February 8-9, 1982. This was a relatively small meeting with 17 panelists and 15 guest scientists or staff from the National Institute of Mental Health. The workshop provided a forum for investigators to present their latest findings in this rapidly developing field and to try to resolve points of disagreement. There is now no question that psychoactive drugs, principally the antidepressants, are effective treatments for panic attacks and for obsessive-compulsive disorders. Evidence is also accumulating that the antidepressants are effective treatments for generalized anxiety disorders.

A major theme of the workshop was the possible mechanism(s) of action of the antidepressants as treatments for these disorders.

The articles that follow are expanded versions of papers presented at this workshop.

Allen Raskin, Ph.D., and
Jerome Levine, M.D.
Section Editors

Diagnostic Classification of Anxiety and Phobic Disorders

David V. Sheehan, M.B., B.Ch., B.A.O.[1] and Kathy H. Sheehan, M.S.[2]

In order to understand and investigate anxiety disorders and correctly assign patients to treatment, it is helpful to have a diagnostic classification system. Such a diagnostic classification is like a map to a traveller: without it he may get quite lost, with it he is guided to any destination and his journey is eased considerably.

The multiaxial diagnostic system, recently introduced by Diagnostic and Statistical Manual-III (DSM-III), eliminates much of the confusion of past diagnostic systems. In this system each patient receives a diagnosis at five levels—one diagnosis for each axis.

Axis 1 - A diagnosis of the clinical psychiatric syndrome based on the clinical description of symptoms and signs.

Axis 2 - A personality disorder diagnosis based on the individual's character structure and mode of interaction with his environment.

Axis 3 - A diagnosis of medical (nonpsychiatric) disorder.

Axis 4 - Severity of psychosocial stressors.

Axis 5 - Highest levels of adaptive functioning in the past year.

This paper will focus on an Axis 1 diagnostic classification for anxiety disorders, i.e., the diagnosis of clinical psychiatric syndrome based on a description of the symptoms and signs. This is the preeminant, central axis to which the others are secondary.

Goals of Classification

The immediate goal of a classification system is to organize phenomena in a systematic way into categories in which members of each category have common characteristics, e.g., symptoms, signs, demography, pathophysiology, etiology, natural history, family history, and treatment

---

[1] Hypnosis and Psychosomatic Medicine Clinic, Massachusetts General Hospital, Boston, MA 02116.

[2] Massachusetts General Hospital, Institute of Health Professions, Boston, MA 02116.

response. This is not intended as an obsessive academic exercise. The long-range purpose of having a good classification guide is to:

1) help predict what will happen to a patient who falls into one class based on the past experience with other patients in that class;

2) help control the symptoms by being able to predict and manipulate what will happen in several contingencies; and

3) clarify the relationship between the phenomena, e.g., the symptoms observed.

Classification is useful insofar as it helps to predict, clarify, and control what is going to happen.

Criteria for Classification

A good classification system satisfies the following criteria:

1) The classes are inherently mutually exclusive, i.e., each class is clearly distinct from the other classes; no class overlaps with another class;

2) the classes are internally homogenous, i.e., each class is internally consistent and homogenous within itself;

3) the classification system is comprehensive, i.e., it has a category for all cases;

4) it helps to clarify the relationship between the phenomena in question;

5) it permits better prediction and control; and

6) it is simple, economical, and clear.

The authors' comments will focus on the special importance of having classes that are inherently mutually exclusive and the proscription of significant category overlap. For if that first criterion is not satisfied, the classification system breaks down and the other criteria are meaningless.

Methods of Classification

There are many methods of setting up a classification system. The theological approach is to consult a consortium of experts and distill their collective wisdom. A more scientific approach involves two exploratory stages and a final testing or confirmatory stage. The first exploratory stage involves a cluster analysis of presenting symptoms in a large population to separate the symptoms into distinct groups. The second stage involves a discriminant analysis on these clusters to determine the symptoms (or criteria) with the highest discriminatory power between the clusters. These discriminating variables now become the diagnostic criteria for each class in the classification. The final confirmatory stage calls for a test of these new discriminating variables on a fresh patient population for their ability to a) comprehensively assign all cases into b) mutually exclusive groups.

The authors took the position that existing classification schemes for the anxiety disorders had completed the exploratory stages in arriving at the diagnostic criteria for each category. What remained was to test the existing classification systems to see how well their diagnostic criteria could comprehensively assign patients into mutually exclusive groups.

Table 1

Diagnostic Labels Synonymous with Endogenous Anxiety

Anxiety Hysteria Hysteria (early descriptions) Globus Hystericus	**Atypical Depression** Grand Hysterie Hysterical Neurosis Vertigo Hysterique
Anxiety Neurosis Anxiety Syndrome Pseudo Neurosis Borderline States (Klein, 1964) Locomotor Anxiety	Anxiety States (*Lancet*,1952) Severe Mixed Neurosis Pseudoneurotic Schizophrenia Non-Specific Insecurity Fears Street Fear
Phobic Anxiety State	**Agoraphobia**
Phobic Anxiety Depersonalization Syndrome Separation Anxiety Effort Syndrome	Phobophobia Severe School Phobia Irritable Heart Syndrome
Da Costa's Syndrome Cardiac Neurosis Hyperdynamic B Adrenergic Circulatory State Nervous Tachycardia	Neurocirculatory Asthenia Soldier's Heart Antonomic Epilepsy Vasomotor Neurosis Vasoregulatory Asthenia Hypogylcemic Syndrome
Hyperventilation Syndrome Panic Disorder Autonomic Epilepsy	**Hypochondriacal Neurosis** Depersonalization Neurosis Depressive Anxiety States

Deficits in Existing Classifications of Anxiety Disorders

In one study, a list of diagnostic labels was collected from the past records of approximately 60 patients (Sheehan et al. 1980). All patients described the same set of symptoms. All had spontaneous panic attacks and all were polyphobic. The diagnostic labels had been given for the same set of symptoms, over a period of 20 years. Table 1 illustrates the range of diagnoses given to these patients. The diagnostic confusion reflected in this table suggested two possible explanations. One explanation reflected negatively on the diagnostic abilities of the evaluating psychiatrists. The second explanation was that the classification system for anxiety disorders was itself the source of the confusion. Obviously the second explanation was preferable, since it was more flattering to Boston psychiatrists. The list in Table 1 included many labels in DSM-II (1950) as well as others that had found historical favor with various groups.

In an effort to test the mutual exclusivity of existing diagnostic categories, symptom checklist, scale, and interview data were analyzed on 100 consecutive patients who sought treatment for anxiety attacks and multiple phobias at a Massachusetts General Hospital Psychiatry Clinic (Sheehan & Sheehan, in press-a,b,c). Because of the multitude of labels, it was necessary to choose for the testing phase only those for which there were precisely defined, replicable, diagnostic criteria and for which there was some consensual validation. The criteria of Feighner et al. (1972) and the Research and Diagnostic Criteria (RDC) (Spitzer et al. 1975) and DSM-III criteria (1980) satisfied this demand. The diagnostic criteria of Feighner et al. (1972) had three diagnostic labels which were relevant to this patient population: 1) hysteria 2) anxiety neurosis, and 3) phobic neurosis. Others including Perley and Guze (1962) had also proposed earlier variations of diagnostic criteria for hysteria. Table 2 shows the percentage of patients who satisfied the Feighner et al. diagnostic criteria for each diagnostic category. The majority of patients simultaneously fulfilled all of the criteria for a diagnosis of hysteria, and anxiety neurosis and phobic neurosis. As shown in Tables 3 and 4, they also satisfied the criteria for several RDC and

Table 2

(1) Percentage of Patients Having a Definite or Probable Diagnosis of Hysteria

Perley and Guze criteria	Feighner et al. criteria for hysteria	
	Including age of onset before 30	Exluding age of onset before 30
92%	71%	90%

(2) Percentage of Patients Having a Definite or Probable Diagnosis of Anxiety Neurosis

Feighner et al. criteria for anxiety neurosis	
Including age of onset before 40	Excluding age of onset before 40
95%	98% (84% "definite"-14% "probable")

(3) Percentage of Patients Having a Definite or Probable Diagnosis of Phobic Neurosis

Feighner et al. criteria for phobic neurosis (excluding Criterion 3 of Table 6)	
Including age of onset before 40	Excluding age of onset before 40
95%	100%

Table 3

Research Diagnostic Criteria and Other Symptom Clusters Simultaneously Satisfied by Sample

Diagnostic Category	Percent of Patients Satisfying Criteria
Panic Disorder	100
Generalized Anxiety Disorder	100
Phobic Disorder	100
Symptom cluster	
Obsessive Compulsive Symptoms	81
Hypochondriasis (Physical)	68
Hypochondriasis (Mental)	83
Dysphobic Mood "Atypical Depression"	92
Agoraphobic Syndrome (Marks 1969)	100
Polyphobic (as measured by Wolpe Lange FSS)	100

pages tightly bound

Table 4

DSM-III Categories Simultaneously Satisfied By Sample

Diagnostic Category	Percent of Patients Satisfying Criteria Excluding "Exclusionary Criteria"
Panic Disorder	100
Generalized Anxiety Disorder	100
Agoraphobia	100
Social Phobia	71
Simple Phobia	100
Obsessive-Compulsive Disorder	81
Conversion Disorder	100
Atypical Somatoform Disorder	100
Depersonalization Disorder	47
Hypochondriasis-Physical Health	68
Dysthymic Disorder	92

DSM-III categories simultaneously (DSM-III, 1980; Spitzer et al. 1975). This same sample of patients was found elsewhere to have a homogenous age of onset distribution, and a significant majority subsequently had satisfactory therapeutic responses to tricyclics and monoamine oxidase inhibitors (1980).

As indicated in Table 4, these figures were obtained when "exclusionary criteria" in the DSM-III were eliminated from the testing set of criteria. An exclusionary criterion is one that states that if a patient is given diagnosis X, he cannot also get diagnosis Y. An example from DSM-III (1980) is the last (exlusionary) criterion for panic disorder which states that such patients cannot have agoraphobia. It is by such charades that the pretense of mutually exclusive categories is maintained. However, there is no evidence in nature that having panic disorder confers an immunity against the development of agoraphobia. Indeed, quite the opposite seems to be the case. From this test on a fresh population it appears that these classification systems fail to satisfy the first criterion of a good classification—that of having categories that are mutually exclusive. Clearly there is considerable category overlap in these systems. The fable of the 10 blind men and the elephant may be relevant here. Each blind man holds a different part of the elephant and, in describing the part he holds, claims that it is the elephant. What is called for is a comprehensive overview and integration. If a patient seeks a physician's help stating he is anxious or describes some anxiety symptoms, there are 21 to 25 diagnostic categories in the DSM-III to which he might reasonably be assigned (*see* Table 5) (Sheehan & Sheehan, in press-a). Depending on the interest, or orientation of the diagnostician, any one or more of the patient's symptoms in the large cluster he suffers might be chosen and a diagnosis given around that cluster. Those with a medical model would favor panic disorder, while those with a behavioral orientation might select agoraphobia and social phobia.

Table 5

DSM-III Diagnoses Relating to Anxiety

Anxiety Symptoms	1. Panic Disorder 2. Generalized Anxiety Disorder 3. Atypical Anxiety Disorder 4. Adjustment Disorder With Anxious Mood
Avoidance	5. Agoraphobia—With Panic Attacks 6. Agoraphobia—Without Panic Attacks 7. Social Phobia 8. Simple Phobia 9. Avoidant Personality Disorder
Physical Somatic Symptoms	10. Somatization Disorder 11. Conversion Disorder 12. Atypical Somatoform Disorder 13. Depersonalization Disorder 14. Hypochondriasis 15. Histrionic Personality Disorder
Miscellaneous	16. Post-Traumatic Stress Disorder 17. Obsessive-Compulsive Disorder 18. Atypical Dissociative Disorder
Childhood	19. Separation Anxiety Disorder 20. Avoidance Disorder of Childhood/Adolescence 21. Overanxious Disorder
Possible	22. Factitious Disorder With Psychological Symptoms 23. Factitious Disorder With Physical Symptoms 24. Atypical Factitious Disorder With Physical Symptoms 25. Malingering

Table 6

Possible Coexistence of DSM-III Anxiety-Related Diagnoses

− = Combination Not Allowed
+ = Combination Allowed
138 Combinations Permitted

1 Panic Disorder	1																				
2 Generalized Anxiety Disorder	−	2																			
3 Atypical Anxiety Disorder	−	−	3																		
4 Adjustment Dis. With Anxious Mood	−	−	−	4																	
5 Agoraphobia With Panic Attacks	−	−	−	−	5																
6 Agoraphobia Without Panic Attacks	−	+	−	−	−	6															
7 Social Phobia	+	+	−	−	+	+	7														
8 Simple Phobia	+	+	−	−	+	+	+	8													
9 Avoidant Personality Disorder	+	+	+	−	+	+	+	+	9												
10 Somatization Disorder	+	−	+	−	+	+	+	+	+	10											
11 Conversion Disorder	+	+	+	−	+	+	+	+	+	−	11										
12 Atypical Somatoform Disorder	+	+	+	−	+	+	+	+	+	−	−	12									
13 Depersonalization Disorder	−	−	−	−	−	−	−	−	+	+	+	+	13								
14 Hypochondriasis	−	−	+	−	+	+	+	+	+	−	+	−	+	14							
15 Histrionic Personality Disorder	+	+	+	−	+	+	+	+	+	+	+	+	+	+	15						
16 Post Traumatic Stress Disorder	+	+	−	−	+	+	+	+	+	+	+	+	−	−	+	16					
17 Obsessive-Compulsive Disorder	−	−	−	−	−	−	+	−	+	+	+	+	−	−	+	+	17				
18 Atypical Dissociative Disorder	+	+	+	−	−	+	+	+	+	+	+	+	−	+	+	+	+	18			
19 Separation Anxiety Disorder	+	+	−	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	19		
20 Avoidance Dis. Of Childhood/Adol.	+	+	−	−	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	20	
21 Overanxious Disorder	+	+	−	−	−	−	−	−	−	+	+	+	−	+	+	+	−	+	−	−	21

As if it were not confusing enough to remember those 21 categories, the DSM-III recognizes that some of these categories could coexist. It therefore allows for the possible coexistence of some categories (1980). Table 6 outlines the relevant diagnostic categories that are permitted to coexist (+) and those that are not (−). This figure reveals that there are approximately 138 possible combinations of such diagnoses allowed by the DSM-III (1980). When a patient presents with a complaint of anxiety, the clinician has 138 combinations of diagnoses to consider. There may be more diagnostic combinations permitted than the patient has symptoms, a lucid example of misplaced precision. This makes useful comparison of studies from one center to the next difficult.

Case Illustration: Limits of a Cross-Sectional Perspective

Consider the following case of a patient admitted to the inpatient service at Massachusetts General Hospital, a patient whose entire cluster of symptoms responded well to phenelzine and behavior therapy (*see* Table 7) (Periy & Guze 1962;Spitzer et al. 1975).

Two years before admission the patient had attacks of unreality. At that point she fulfilled the criteria for a DSM-III diagnosis of depersonalization disorder (1980). One year prior to admission she became hypochondriacal about a few fleeting symptoms and sought much medical attention. At that point she fulfilled the DSM-III criteria for a diagnosis of hypochondriasis (1980). Six months prior to admission, the hyperactive episodes of autonomic manifestations of anxiety permitted the DSM-III label generalized anxiety disorder (1980). Three months prior to admission she choked on food while anxious and subsequently feared eating solid foods. This was sufficient to justify the label simple phobia, since this was now

Table 7

DSM-III Case Illustration

Time Before Treatment	DSM-III Diagnosis at Time
2 years	Depersonalization Disorder
1 year	Hypochondriasis
6 months	Generalized Anxiety Disorder
3 months	Simple Phobia
1 month	Social Phobia
6 days	Agoraphobia Without Panic Attacks
Admission	Conversion Disorder
1 week post-admission	Panic Disorder
2 weeks post-admission	Agoraphobia With Panic Attacks

her central concern. Her fears generalized so that before long she feared eating with her friends, going to restaurants, socializing at parties, being the focus of attention, eating with her family and, finally, even being seen eating by anyone. She preferred to eat alone. She had a social phobia. One week prior to admission she had a devastating panic attack while out driving and subsequently feared leaving her home. This was agoraphobia without panic attacks (she had not had three panic attacks over a 3-week period). With considerable effort, her family desensitized her to go out again. Their concern led to her being evaluated and admitted. On admission, the consultant described her central concern as preoccupation with choking sensations and a lump in her throat. This he diagnosed a conversion disorder (DSM-III) or what in the past would have been labeled globus hystericus. One week after admission she had a series of spontaneous panic attacks and now satisfied panic disorder criteria. Two weeks after admission, she was fearful of going anywhere. She could not leave the ward and even feared leaving the security of her room. She had agoraphobia with panic attacks (DSM-III) (1980).

Are we now to presume that this young lady had nine different diseases in the space of 2 years? If she had been seen cross sectionally at time period 3, would the authors have concluded she had generalized anxiety disorder and recommended a benzodiazepine? Or at time period 4, would a simple phobia have been described and behavior therapy and *in vivo* exposure been suggested? Or at time period 7, with a diagnosis of conversion disorder, might psychotherapy or hypnosis have been considered? At time period 8, the authors could comfortably recommend imipramine.

Clearly, a cross-sectional view can mislead. A more logical approach would be to view the case longitudinally as a process passing through several stages.

Stages of the Disorder: A Longitudinal Perspective

The majority of patients with this disorder may pass through the following seven stages in the natural progression of their illness (Sheehan & Sheehan, in press-c).

Stage 1 Subpanic Symptoms
Stage 2 Panic
Stage 3 Hypochondriasis
Stage 4 Single Phobia
Stage 5 Social Phobias
Stage 6 Agoraphobic Polyphobic Behavior
Stage 7 Depression

First, they usually suffer sudden episodes of isolated symptoms short of panic with little or no immediate stress, such as tachycardia, lightheadedness, or shortness of breath. These episodes may be followed by full-blown panic attacks which are more intense, and complete clusterings of several of these symptoms in the same time frame. Because there is frequently no apparent immediate stimulus for their physiology racing out of control, patients become hypochondriacal and repetitiously seek medical assistance. Over time, spontaneous panic attacks occur in increasingly varied situations. These spontaneous panic attacks can classically condition these situations to later elicit phobic anticipatory anxiety to these situations (induce single phobias). Over time, as the patients accumulated more phobias, they become more socially phobic and finally polyphobic and agoraphobic. Finally, as they become progressively restricted, and attempts at treatment fail, and they feel depressed and discouraged by their restrictions. All of these stages might be collapsed telescope fashion, into a short period of time. On the other hand, the progression may be protracted over many years or arrested at any one stage. It is the relentless onslaught of frequent, intense spontaneous panic attacks that dictates the rapidity and completeness of progression through the stages. (Sheehan & Sheehan, in press-a,c). This longitudinal perspective helps resolve the diagnostic confusion of many labels generated by the cross-sectional perspective (Sheehan & Sheehan, in press-a).

Toward a More Heuristic Classification

As a step towards a simpler, more practical classification system to guide research efforts and clinical management, a decision tree to another classification system is offered in Table 8 (Sheehan et al. 1981, Sheehan & Sheehan, in press-b,c). This classification proposes two kinds of anxiety disorders. The presence or absence of spontaneous anxiety or symptom attacks that occur with little or no stress is the key differentiating point that triages a patient to one or other category (Sheehan et al. 1981; Sheehan & Sheehan, in press-b,c). The exogenous anxiety category is an anxiety that normal people can relate to. It occurs when someone is suitably traumatized or under stress or has a specific monophobia with anxiety that is exclusively bound to only one stimulus. The endogenous anxiety is associated with multiple symptoms, e.g., panic attacks, and eventually complicated by the acquisition of multiple phobias (Sheehan et al. 1981; Sheehan & Sheehan, in press-b,c). The exogenous category is stress-related, while the endogenous appears to be a genetically inherited metabolic disease (Sheehan et al. 1980, 1981). Both exogenous and endogenous anxiety can be subdivided into subtypes along acute to chronic and mild to severe/complicated continua (*see* Table 8) (Sheehan & Sheehan, in press-b,c). In the endogenous anxiety class, phobias usually occur. The presence of phobias in such patients appears to be a function of the intensity and frequency of the spontaneous panic attacks. The identity of the phobia appears to be a function of the situation in which intense panic attacks occurred. Subsequently, the phobias are reinforced both from within the individual by the spontaneous panic attacks and are triggered by a classically conditioned response to the environmental stimulus to which they have been conditioned (Sheehan & Sheehan, in press-c). Over time, the phobias are reinforced both from within and from outside the individual (Sheehan & Sheehan, in press-c).

Is there evidence to support such a clustering? There are data to suggest that the age of onset distribution, sex ratio, and treatment response are different in the two kinds of anxiety (Sheehan et al. 1980, 1981). In endogenous anxiety, the age of onset distribution is uniformly unimodal, consistent with a biological illness model. In exogenous anxiety, the age of onset is evenly distributed through all ages, consistent with a stress induction or conditioning model (Sheehan et al. 1981). Table 9 lists the diagnostic criteria for each major category, followed by the other suggested points of differentiation.

As long as classification systems depend exclusively on symptom clustering, it is unlikely that consensus will be reached among investigators. Consensus will probably await the development of laboratory techniques such as psychophysiological measures, blood or other laboratory tests, genetic marking, and pharmacological dissection. These will undoubtedly lend validity to some existing classification system and add refinements that will be clinically meaningful. In the meantime, the above analysis and classification system may offer investigators and clinicians a clearer starting point and easier guide to correct diagnosis and treatment.

References

DSM-II—Diagnostic and Statistical Manual of Mental Disorders, 2nd ed. American Psychiatric Association, 1952.

DSM-III—Diagnostic and Statistical Manual of Mental Disorders, 3rd ed. American Psychiatric Association, 1980.

Feighner, M.P., Robins, E., Guze, S.B., Woodruff, R.A., Winokur, G., and Munoz, R. Diagnostic criteria for use in psychiatric research. *Arch. Gen. Psychiatry*, 26:57-63, 1972.

Perley, M.H., and Guze, S.B. Hysteria—The stability and usefulness of clinical criteria: A quantitative study based on a followup period of 6-8 years in 39 patients. *N. Engl. J. Med.*, 266:421-426, 1962.

Reynolds, H.T. Analysis of nominal data. In: Sullivan, J. (ed.), *Quantative Applications in the Social Sciences.* Beverly Hills/London:Sage Publications, Inc., 1977, p. 7.

Sheehan, D.V. The efficient treatment of phobic disorders. In: Manschrechk, T. (ed.), *Psychiatric Medicine Update.* Amsterdam:Elsevier/North Holland Biomedical Press, 1979, pp. 189-204.

Sheehan, D.V., Ballenger, J., and Jacobson, G. The treatment of endogenous anxiety with phobic hysterical and hypochondriacal symptoms. *Arch. Gen. Psychiatry*, 37:51-59, 1980.

Sheehan, D.V., and Sheehan, K. The classification of anxiety and hysterical disorders. Part I: Historical review and empirical delineation. *J. Clin. Psychopharmacol.* (In press)

Sheehan, D.V., and Sheehan, K. The classification of anxiety and hysterical disorders. Part II: Towards a more heuristic classification. *J. Clin. Psychopharmacol.* (In press)

Sheehan, D.V., and Sheehan, K. The classification of phobic disorders. *Int. J. Psychiatry Med.* (In press)

Sheehan, D.V., Sheehan, K., and Minichiello, W.E. Age of onset of phobic disorders. A reevaluation. *Compr. Psychiatry*, 22:544-553, 1981.

Spitzer, R. L., Endicott, J., and Robins, E. Research diagnostic criteria (RDC) for a selected group of functional disorders. 2nd ed. Biometrics Research, New York State Psychiatric Institute, 1975.

Table 8

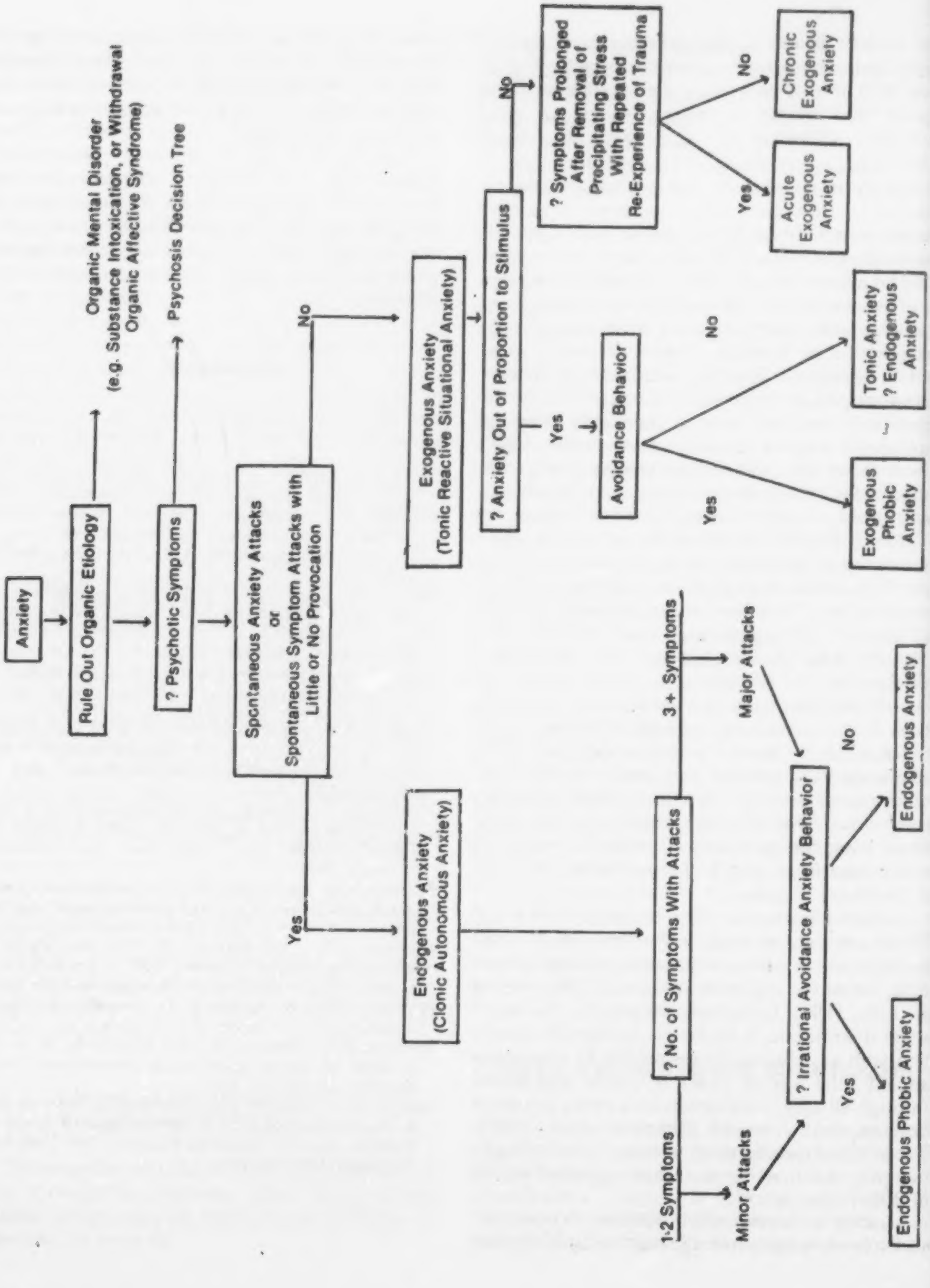

Anxiety
Rule Out Organic Etiology
Organic Mental Disorder
(e.g. Substance Intoxication, or Withdrawal Organic Affective Syndrome)
? Psychotic Symptoms
Psychosis Decision Tree
Spontaneous Anxiety Attacks
or
Spontaneous Symptom Attacks with Little or No Provocation
Yes
No
Endogenous Anxiety
(Clonic Autonomous Anxiety)
Exogenous Anxiety
(Tonic Reactive Situational Anxiety)
? No. of Symptoms With Attacks
1-2 Symptoms
3+ Symptoms
Minor Attacks
Major Attacks
? Irrational Avoidance Anxiety Behavior
Yes
No
Endogenous Phobic Anxiety
Endogenous Anxiety
? Anxiety Out of Proportion to Stimulus
Yes
No
Avoidance Behavior
Yes
No
Exogenous Phobic Anxiety
Tonic Anxiety
? Endogenous Anxiety
? Symptoms Prolonged After Removal of Precipitating Stress With Repeated Re-Experience of Trauma
Yes
No
Acute Exogenous Anxiety
Chronic Exogenous Anxiety

Table 9

Diagnostic Criteria

Endogenous Anxiety	Exogenous Anxiety
1. Spontaneous, autonomous, clonic, phasic, (subjectively reported) episodes of the following symptoms: (1-2 for a minor attack, 3 or more together for a major attack): (a) Skipping or racing of heart (b) Dizzy spells or faintness (c) Air hunger, difficulty getting breath, or hyperventilation (d) Smothering or choking sensation (e) Tingling or numbness (paresthesias) in hands, arms, feet, or face (f) Nausea or upset stomach or vomiting (g) sudden unexpected panic or anxiety feelings occurring with little or no provocation (h) Hot flushes or cold chills (i) Jelly legs or imbalance (j) Shaking or trembling (k) Derealization or depersonalization (l) Chest pain, pressure or discomfort (m) Hypochondriasis (n) Feeling will lose control, scream or "go insane" or die (o) Spontaneous clonic alteration in sensory perception e.g. increased or decreased clonic sensitivity to light, sound, touch, temperature taste, proprioception, muscle power (p) Diarrhea attacks (q) Sweating episodes	1. No spontaneous panic or anxiety attacks or history of the same
2. Such symptom attacks have persistently recured for at least one month. Within a 3 month period, at least 3 discrete major attacks must occur for a diagnosis of major endogenous anxiety, or at least 3 discrete minor attacks for a diagnosis of minor endogenous anxiety. Symptoms must occur in the absence of any psychotic disorder or medical illness that could explain the symptoms.	2. Tension and symptoms of anxiety occur *only* in response to immediate, clearcut, =identifiable environmental stimuli. Onset of each attack not very sudden or unexpected but related to immediacy of triggering stimulus. In the case of conditioned changes in motor, sensory symptoms or special senses the symptom may occur alone without any overt anxiety.
3. Phobic symptoms particularly fear of a spontaneous panic attack (phobophobia) and fear of crowded places. Phobias start only after onset of first spontaneous panic attack. Phobia may fluctuate in intensity over time.	3. Phobia restricted to one specific focus. Monophobic rather than polyphobic. Phobia rarely fluctuates in intensity over time.
4. Depression, neurasthenia (excessive tiredness and feeling everything is an effort), obsessive compulsive symptoms present to some degree in over 2/3 of cases.	4. Depression, neurasthenia, obsessive-compulsive symptoms-and other gross psychophathology absent.
5. Anxiety profile of spontaneous panic attack as in Figure 1 (although Figure 2 type may also occur)	5. Profile of anxiety attack as in Figure 2
6. Spontaneous fluctuations on GSR	6. No spontaneous fluctuations on GSR
7. Slow habituation rate on GSR	7. Normal or rapid habituation on GSR
8. Elevated resting pulse rate	8. Resting pulse within normal range

Table 9 (Continued)

9. Brisk reflexes	9. Reflexes not hypertonic
10. Family history of anxiety attacks and phobic symptoms especially among female relatives	10. Positive family history rare
11. Age of onset usually 12-40 years	11. May occur at any age
12. 80 percent of cases occur in women	12. ?Equal sex distribution
13. More likely to have visited medical doctor and emergency ward several times for treatment of symptoms. Spontaneous anxiety must occur: 1. In absence of medical illness that could cause such symptoms 2. In absence of life-threatening situations	13. Rarely seeks medical or emergency ward treatment
14. More likely to have seen several psychiatrists in treatment over many years.	14.
15. More likely to have had a hospital admission and surgical treatment for symptoms.	15.
16. Response to MAO inhibitors and imipramine good	16. Response to drugs poor.
17. Response to behavior therapy alone poor.	17. Response to behavior therapy good
18. Autonomy of clonic phasic course e.g. does not immediately improve when environmental circumstances seem favorable.	18. More clearly responsive to psychosocial stimulus
19. Anxiety attacks precipitated by sodium lactate I.V. and by marijuana administration	19. Anxiety attacks not precipitated by either lactate or marijuana

Vol. 18, No. 4, October 1982

New Antianxiety Agents

Jonathan O. Cole, M.D.[1]

As stated by Greenblatt in his paper in this publication (p. 58), there is no real reason to expect that newer benzodiazepines (e.g., prazepam, halazepam) which are converted by the body into desmethyldiazepam will have antianxiety effects different from chlorazepate. Indeed, it is very hard to find differences even between less closely related benzodiazepines (BDPs) with quite different pharmacokinetics (e.g., diazepam and lorazepam). The possibility that one of the new triazolo-benzodiazepines, alprazolam, may have atypical efficacy in the treatment of panic states, as described by Sheehan (personal communication) and in depression (Feighner, in press) does suggest that further molecular changes in the BDP molecule *might* yield different or superior clinical actions.

There has been continuing interest in the use of older, marketed non-BDP drugs in anxiety. Propranolol has been suggested as especially useful in somatic or cardiac anxiety symptoms or in anxiety-related tremor. The available evidence only suggests a weak antianxiety effect of propranolol in anxious outpatients (Altesman et al. 1980). There are, of course, a growing number of newer beta-blocking drugs which might be studied for antianxiety effects, but it is hard to tell whether such studies would be productive.

The recently completed National Institute of Mental Health collaborative study comparing imipramine, chlordiazepoxide, and placebo in nondepressed anxious outpatients (Kahn et al. 1981) is showing that imipramine has unsuspected efficacy in anxiety. This effect comes on slowly, and some patients drop out because of imipramine's side effects. Other antidepressants deserve similar study. At least one new potential antidepressant, synaptamine, a mianserin analog, is being studied both in anxious and in depressed patients.

Another approach to the uncovering of new antianxiety drugs is the study in man of non-BDP substances which bind to BDP receptors. At least one such compound, CL 230, 482, a pyrazolo pyrimidine, is currently in early clinical trial in the United States. It is too early to tell whether this rational approach will yield an unfortunately rational result—the drugs may turn out to be exactly like existing BDPs in everything except chemical structure, reminding one of the "nonbarbiturate" hypnotics developed 30 years ago; these turned out to be at least as bad as the barbiturates in all respects, although chemically different.

The author is acquainted with one new antianxiety drug, buspirone, developed by Mead Johnson. It has been studied in anxious patients (Goldberg & Finnerty 1979; Rickels, in press) and has been shown to be as effective as diazepam. Recently it has been studied against diazepam and placebo in a large multiclinic study in anxious outpatients. These studies indicate that the drug is equipotent to diazepam with less sedation, good effect on anxiety, and some superiority over diazepam in reducing irritability and hostility as measured by the Symptom Check List (Newton, in press). Studies on the drug's abuse liability done in recreational sedative abusers at McLean Hospital are showing that at a higher dose (40 mg), buspirone is dysphoric although sedating and therefore unlikely to be abused (Cole et al. 1982).

All this is of some extra interest because buspirone has no effect on BDP receptors and has an odd mixture of dopamine agonist and antagonist properties. It reverses neuroleptic-induced catalepsy in rodents both at low and at very high doses. It blocks the conditioned avoidance response without affecting escape, but also relieves conflict-induced behavioral suppression at doses similar to those at which diazepam has this "classic" antianxiety drug effect. Buspirone has neither neuroleptic nor BDP effects on social behavior in the rat, resembling low-dose piribedil, a presumed presynaptic dopamine agonist. It is much weaker at potentiating barbiturates than is diazepam. It is not anticonvulsant. In the cat, buspirone has effects on the quantitative electroencephalogram which resemble apomorphine. However, buspirone is an antiemetic. It does not produce physical dependence in rats (Riblet, in press).

---

[1] Psychopharmacology Services, McLean Hospital, Belmont, MA 02178.

Buspirone thus may be the first member of a quite different class of antianxiety drugs without the mild but bothersome abuse problems found with BDPs.

Hopefully, we are entering a new phase in the antianxiety area. For many years, the main and almost the only available drug group for treating depression was the tricyclic group, parallelling the BDPs in anxiety. Now a host of chemically and pharmacologically diverse antidepressants (e.g., trazodone, mianserin, zimelidine, nomifensine, buproprion) are available or in late clinical trial. Maybe buspirone will turn out to be effective and safe; maybe the new non-BDP drugs binding to BDP receptors will be usefully different; maybe some beta-blocker will be a first-class anxiolytic; maybe (quite likely) there are other new antianxiety drugs waiting in the wings unknown to us. One cannot be sure, but things seem to be looking up.

References

Altesman, R., Cole, J.O., and Weingarten, C. Beta-blocking drugs in psychiatry. In: Cole, J.O. (ed.), *Psychopharmacology Update*. Lexington, Ky. Collamore Press, 1980, pp. 43-68.

Cole, J.O., Orzack, M.H., Bird, M., Beake, B., and Bar-Tal, Y. Assessment of the abuse liability of buspirone in recreational sedative users. *J. Clin. Psychiatry*. (In press)

Feighner, J. Benzodiazepines as antidepressants: A triazolobenzodiazepine used to treat depression. In: Lehmann, H. (ed.), *Modern Problems in Pharmacopsychiatry*. (In press)

Goldberg, H., and Finnerty, R. The comparative efficacy of buspirone and diazepam in the treatment of anxiety. *Am. J. Psychiatry*, 136:1184-1187, 1979.

Kahn, R., McNair, D., Covi, L., Downing, R., Fisher, S. Lipman, R., Rickels, K., and Smith, V. Effects of psychotropic agents on high anxiety subjects. *Psychopharmacol. Bull.*, 17(3):97-100, 1981.

Newton, R. Controlled studies of buspirone in anxiety. *J. Clin. Psychiatry*. (In press)

Riblet, L. Buspirone: Pharmacology and neurochemistry. *J. Clin. Psychiatry*. (In press)

Rickels, K. Buspirone, diazepam, and placebo in anxiou outpatients: A controlled study. *J. Clin. Psychiatry*. (In press)

Vol. 18, No. 4, October 1982

Animal Models of Anxiety: Implications for Research in Humans

Thomas W. Uhde, M.D.,[1] Jean-Philippe Boulenger, M.D.,[1] Larry J. Siever, M.D.,[2] Robert L. DuPont, M.D.,[3] and Robert M. Post, M.D.[1]

In humans, behavioral and biological alterations may be associated with the subjective experience of anxiety (Krause 1961). However, no behavioral, biochemical, or neurophysiological correlates have been found to be specifically and consistently associated with the experience of anxiety. It is only by verbal report, therefore, that an observer can reliably detect the presence or absence of anxiety. In contrast, investigators using animal models must rely exclusively upon the behavioral and neurophysiological changes that develop in response to specific stimuli. Although it is impossible to develop specific criteria for anxiety in animals, there may be some useful parallels among the biological systems of nonhuman and human organisms.

Most animal models relevant to the topic of anxiety have been developed as systems for identifying drugs that may have anxiolytic properties in humans, rather than as attempts to induce a disorder in animals equivalent to the experience of anxiety in humans (Iversen 1979).

Models of Behavioral Inhibition

All of these models are based on the common principle that a number of different stimuli will induce a behavioral inhibition in animals (perhaps a consequence of fear) which can be antagonized by the administration of anxiolytic drugs (Gray 1981). The main purpose of these models is to differentiate the specific anxiolytic effect of the drug from sedation which would reinforce the behavioral inhibition (Simon & Soubrie 1979). The most commonly used of these models is the conflict test developed by Geller and Seifter (1960) in which the animals are conditioned to inhibit active food-seeking behavior in response to a signal of punishment. The barbiturates, meprobamate, and the benzodiazepines reinstate the suppressed behavior despite the occurrence of punishments, at doses which correlate well with their reported anxiolytic effects in humans (for review, *see* Sepinwall & Cook 1978). This so-called "anti-punishment" effect of anxiolytic drugs has been documented in several animal species (Dantzer 1977) as well as in humans (Carlton et al. 1981). However, no convincing results have been obtained on the conflict test with other substances such as morphine, ethanol, or beta-blockers, also known to have antianxiety effects (Sepinwall & Cook 1978).

These situations of conditioned fear, where a predictable and objectively unpleasant effect is expected, are different from those involving uncertainty, an emotion which may more closely approximate the human experience of generalized anxiety (File 1980). Uncertainty, triggered by a novel environment and/or different levels of illumination, has also been used in animal models to induce a decrease of exploratory behavior (Boissier et al. 1976; Crawley 1981) or social interactions (File 1980). Benzodiazepines also reverse the behavioral inhibition associated with these paradigms. It is interesting in this regard that agoraphobia may develop in some patients as a result of spontaneous panic attacks (Klein 1964, 1967) and that many patients restrict their life-

---

[1] Section on Psychobiology, Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205.
[2] Clinical Neuropharmacology Branch, National Institute of Mental Health, Bethesda, MD 20205.
[3] Phobia Program of Washington, Rockville, MD 20857.

Address reprint requests to: Dr. Thomas W. Uhde, Biological Psychiatry Branch, Room 3S-239, Building 10, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20205.

style and avoid social interactions, presumably in response to the unpredictability of these attacks.

Separation Behavior in the Monkey

The use of the monkey may help to avoid some of the drawbacks encountered with the use of rodents, especially problems related to the interpretation of fear-associated behaviors. In rhesus monkeys, a forcible separation from an attachment object during rearing has been shown to induce a propensity in later life to exhibit behavior patterns typically associated with fear reactions but occurring in the absence of any obvious and immediate fear stimulus (Suomi 1981). The manner and the relative frequency with which these animals display symptoms characteristic of fear (perhaps similar to some types of anxiety experienced in humans) depends on the amount and type of stress encountered and on constitutional factors such as autonomic responsivity to auditory stimuli (Suomi 1981). The effects of antianxiety agents (benzodiazepines) on this model have not been investigated, although preliminary results suggest that imipramine not only inhibits the depressive symptomatology induced by separation, but decreases the amount of protest behavior displayed by young monkeys during separation (Suomi 1981). These findings are interesting in relation to the beneficial effects of imipramine described in some categories of pathological anxiety in humans, e.g., panic attacks and agoraphobia (Klein 1964; Uhlenhuth 1981).

It is also noteworthy that separation in primates has been used as a model of depression, suggesting some further parallelism with the human situation where both anxiety and depressive syndromes often occur simultaneously and respond to common treatments such as the tricyclic and monoamine oxidase inhibitor (MAOI) antidepressants.

Lack of response to escapable shock following exposure to inescapable shock or "learned helplessness" has likewise been conceptualized as a model of both depression and "anxiety-related" behavior; learned helplessness also responds to treatment with antidepressants (Anisman 1982; Maier & Seligman 1976; Seligman 1975). An interesting aspect of this model is its sensitization and conditioning characteristics; behavioral impairment increases with increasing numbers of exposures. This and related sensitization models may be particularly useful in the conceptualization of mechanisms underlying the at times progressive development of psychopathology observed in some clinical anxiety syndromes (Post & Ballenger 1981). Panic attacks and generalized anxiety may, in some instances, increase in frequency and severity leading to progressive incapacity of the patient. Models which take into account the longitudinal course of symptoms may be of particular value in conceptualizing mechanisms and therapeutic interactions which may differ greatly depending on when in the acute or chronic time course they are considered.

Kindling is another model which helps to focus on the longitudinal and progressive development of symptoms in addition to possible limbic system substrates, and the relationship of antianxiety and anticonvulsant effects of drugs such as the barbiturates and benzodiazepines (Post & Ballenger 1981; Post & Kopanda 1976). In kindling, animals show increasing behavioral electrophysiological and convulsive responses to repeated, intermittent stimulation. Limbic areas such as the amygdala and hippocampus are most susceptible to kindling (Goddard et al. 1969). Anxiety is one of the common effects reported in patients following spontaneous or induced seizures of the limbic system. It is of interest that selected drugs are both anxiolytic and potent anticonvulsants.

The Locus Coeruleus as a Model of Anxiety

Recent advances in research techniques provide unique opportunities for studying the behavioral consequences of both "turning-on" and "turning-off" specific brain systems. Although several neurotransmitters have been implicated in the biological functions of fear and arousal, the noradrenergic system may be especially interesting in this regard (Boulenger & Uhde 1982; Redmond & Huang 1979; Uhde et al. in press). In studes in the rhesus monkey, Redmond (1977) and Redmond and Huang (1979) investigated the behavioral effects of both increasing and decreasing the activity of the locus coeruleus, the major brain noradrenergic nucleus located in the pons with projections to the cerebral cortex, cerebellum, limbic system, and spinal cord. Redmond (1977) and Redmond and Huang (1979) demonstrated that electrical and pharmacological activation of the locus coeruleus produced behaviors (e.g., eye scanning, head and body turning, scratching, biting fingers or nails, hand wringing, pulling hair) similar to those observed in monkeys exposed to natural threats in the wild. In contrast, electrical lesions and pharmacological inhibition of the locus coeruleus decreased these same fear-associated behaviors. For example, the microiontophoretic application of the alpha-2 adrenergic antagonists, yohimbine and piperoxane, simultaneously increased locus coeruleus firing and fear behaviors. Conversely, drugs which decrease locus coeruleus firing such as morphine, desmethylimipramine, MAOIs, and clonidine reduced fear-associated behaviors. These findings in the monkey may have interesting parallels in man. That is, drugs which increase locus coeruleus activity (piperoxane, yohimbine, methylxanthine) (Redmond 1977; Redmond & Huang 1979) or decrease it (morphine, desmethylimipramine, MAOIs, ethanol, diazepam) (Aghajanian 1978; Grant et al. 1980; Korf et al. 1974; Nyback et al. 1975; Redmond & Huang 1979; Strahlendorf & Strahlendorf 1981a,b) have been reported in humans to have anxiogenic and anxiolytic properties, respectively. Furthermore, propranolol, a beta-blocker with an anxiolytic profile in some humans also attenuates the postsynaptic effects of the norepinephrine released as a result of locus coeruleus activity (Redmond 1979). The relationship of locus coeruleus function to fear behaviors in the monkey, the potent inhibition of locus coeruleus activity by clonidine, and the fact that clonidine decreases both central and peripheral norepinephrine activity in man (Hanson & Hökfelt 1981; Leckman et al. 1980; Uhde, Siever, Post, and Jimerson, unpublished manuscript) led to the hypothesis that clonidine might have anxiolytic properties.

The Effects of Clonidine on Anxiety

Svensson et al. (1978) first reported in an open and uncontrolled study that clonidine had antianxiety properties in a group of patients with unspecified anxiety disorders. Uhde and coworkers (1980a) also found that clonidine dramatically decreased self- and nurse-rated items of anxiety in a group of nine opioid-addicted patients abruptly withdrawn from methadone. This antianxiety effect in addicted patients is noteworthy, since many symptoms of opiate withdrawal are similar to symptoms of severe anxiety. The authors' preliminary unpublished data also indicate that many panic-anxious patients obtain high ratings on the Addiction Research Center Inventory Subscale for Weak Opiate Withdrawal (ARCI) (Haertzen 1966), supporting the hypothesis that some aspects of opiate abstinence and panic anxiety may involve alterations of a common neurophysiological system.

As part of an ongoing anxiety research program at the National Institute of Mental Health (NIMH), intravenous clonidine (2μg/kg) and saline infusions were randomly administered under blind conditions to highly anxious depressed and agoraphobic patients (all had panic syndromes) and normal volunteers, in order to assess clonidine's effects on anxiety (Uhde et al. 1980, 1981, in press). As illustrated in Figure 1, the combined group of depressed and panic-phobic patients had significantly decreased ratings of anxiety following clonidine compared to baseline, but no change after placebo-saline infusions. The antianxiety and sedative effects were unrelated. Furthermore, neither clonidine nor placebo influenced baseline ratings of anxiety, as measured by the Spielberger State-Trait Anxiety Inventory in the normal volunteers. This lack of effect on anxiety in the authors' normal volunteers is consistent with the results of Leckman et al. (1980), although the normal subjects in both studies had low baseline ratings of anxiety before clonidine was administered. In another study, Liebowitz and colleagues (1981) administered open oral clonidine to 11 patients with panic disorder or agoraphobia with panic attacks. Four patients demonstrated a good antipanic response after a dose of 200–500 mcg daily. Four patients who initially improved with clonidine experienced a reduction in benefits with chronic administration, and three subjects (including one who reported less severe panic attacks) could not tolerate doses greater than 300 mcg daily. Hoehn-Saric et al. (1981) found clonidine superior to placebo in a double-blind treatment study of 23 patients with generalized anxiety or panic disorders. In the same study, clonidine was found to be as effective in the treatment of patients with generalized anxiety as those with panic attacks. These findings are noteworthy, since previous studies found that panic attacks are blocked by tricyclic antidepressants (Klein 1964) and MAOI (Sheehan et al. 1980) but not by benzodiazepines (McNair & Kahn 1981) or neuroleptics (Klein 1967). More recently, Ko and associates (in press) at Yale found clonidine comparable to imipramine in reducing panic attacks and blocking panic symptoms in patients who were exposed to phobic stimuli which previously elicited panic attacks.

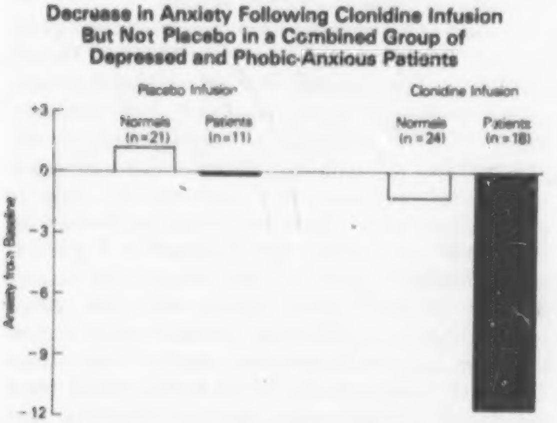


FIGURE 1. In a combined group of depressed ($N = 14$) and agoraphobic patients ($N = 4$), there was a significant decrease in ratings of subjective anxiety following clonidine compared to baseline. (Ten of fourteen depressed and four of four patients with agoraphobia experienced a reduction in anxiety as measured by the Spielberger State-Trait Inventory).

Preliminary data from the authors' double-blind crossover study at the NIMH (Uhde et al. in press) in five patients with panic disorder also suggest that ratings of generalized anxiety and panic attacks decreased after both the acute infusion and the first week of oral administration of clonidine. However, four of the five patients with panic disorder developed tolerance within 3 weeks of chronic clonidine administration (as illustrated in the single case in Figure 2). These findings are consistent with those reported by groups at Columbia (Liebowitz et al. 1981) and Johns Hopkins (Hoehn-Saric et al. 1981). Furthermore, the loss of anxiolytic effects with chronic treatment parallels the time course and development of tolerance to the inhibiting effects of clonidine on the firing rate of the locus coeruleus in animals (Engberg et al. 1982).

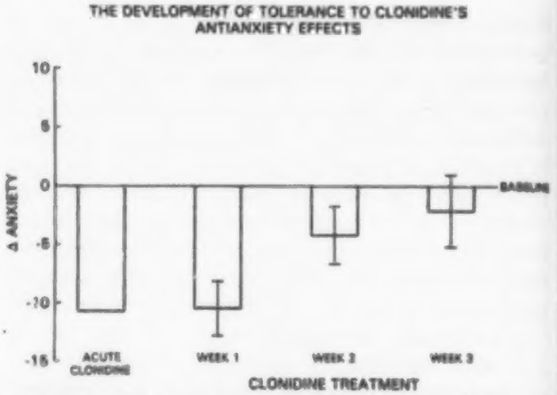


FIGURE 2. In a patient with panic disorder, clonidine treatment initially produced a decrease in self-rated items of anxiety comparable to that achieved by an acute intravenous challenge with clonidine. Ratings of state anxiety obtained during the third week of clonidine administration, however, are not significantly different from baseline-placebo scores, as measured by the Speilberger State-Trait Anxiety Inventory.

In addition to tolerance, clonidine treatment may be associated with a number of untoward side-effects such as drowsiness, sedation, and dry mouth (Hoehn-Saric et al. 1981; Liebowitz et al. 1981; Uhde et al. 1981). The role of the locus coeruleus in fear-related behaviors, arousal, and the sleep-waking cycle may explain the common association between anxiety reduction and sedation for most of the anxiolytic drugs, e.g., benzodiazepines, barbiturates, and meprobamate (Lader 1979).

The combined results of these studies suggest that clonidine may have noteworthy antianxiety effects in depressed, phobic, and panic-anxious patients, as well as patients undergoing opiate withdrawal. In addition, preliminary data suggest that independent measures of nonadrenergic activity may be related to clonidine's antianxiety properties (Ko et al. in press; Uhde et al. 1982, in press). Although clonidine may be less well tolerated by anxious patients than non-anxious hypertensive patients undergoing opiate withdrawal (Uhde et al. 1980a), double-blind comparisons of clonidine to standard drug treatments, e.g., imipramine, are indicated.

Discussion

Anxiety is a subjective experience unique to the human organism. It is impossible to induce in animals a state which, in all its aspects, is equivalent to human anxiety. Nonetheless, animal models may have both practical and heuristic value. For example, the Geller-Seifter test is useful for identifying drugs with antianxiety effects in humans. The disadvantage of this test and other paradigms of behavioral inhibition is that not all drugs with antianxiety (e.g., morphine) or anti-panic (e.g., imipramine) effects in man have anti-punishment effects in animals.

The fear behaviors associated with locus coeruleus function would appear to be a new model relevant for identifying drugs with not only anxiolytic (agents which decrease firing of the locus coeruleus) but also anxiogenic (agents which increase firing of the locus coeruleus) properties. On the basis of its inhibitory effects of the locus coeruleus, clonidine was predicted to have at least transient antianxiety effects in humans (Redmond 1979). Preliminary results would appear to support this hypothesis, since clonidine subsequently has been found to have anxiolytic properties in patients with endogenous anxiety disorders (Hoehn-Saric et al. 1982; Liebowitz et al. 1981; Uhde et al. 1982), depression (Siever et al. 1981; Uhde et al., 1981), and in patients undergoing opiate withdrawal (Uhde et al. 1980a). The noradrenergic locus coeruleus as a functional unit also may be useful as a model for conceptualizing how a single neurotransmitter system might influence opposite emotions on a continuum from "fearlessness" to "panic."

The most problematic aspect of any animal model of human psychopathology is that human emotion is influenced by an intricate and elaborate process of interpretation. That is, human emotion (anxiety) may depend, in part, on the "meaning" of a given stimulus or situation. On the basis of past experience and learning, the biological systems of animals may also be influenced by the "meaning" of a stimulus. The investigations of Segal and Bloom (1976a,b) involving the stimulation of the locus coeruleus during simultaneous recordings from hippocampal neurons may be relevant to this topic. The noradrenergic nucleus locus coeruleus may influence, among other systems, the function of the limbic system, a neuroanatomical substrate which also has been implicated in the modulation of anxiety, mood, and behavior. The locus coeruleus, therefore, may have some capacity for potentiating both inhibitory and excitatory responses which, in turn, may be differentially coded in the same neuron, depending on the relevance of that stimulation to the organism based on prior experience and learning.

Thus, despite the inadequacies of animal models, they may be of both practical clinical value in the development of new drugs and also of heuristic value in conceptualizing possible underlying mechanisms of human anxiety.

References

Aghajanian, G.K. Tolerance of locus coeruleus neurons to morphine and suppression of withdrawal response by clonidine. *Nature,* 276:186-187, 1978.

Anisman, H. Vulnerability to depression: contribution of stress. In: Post, R.M., and Ballenger, J.C. (eds.), *The Neurobiology of the Mood Disorders.* Baltimore:Williams & Wilkins. (In press)

Boissier, J., Simon, P., and Soubrie, P. New approaches to the study of anxiety and anxiolytic drugs in animals. In: Airaksinen, M. (ed.), *CNS and Behavioral Pharmacology.* Oxford:Pergamon Press, 1976, pp. 213-222.

Boulenger, J-P., and Uhde, T.W. Peripheral biological correlates of anxiety. *L'Encephale*, 8:119-130, 1982.

Carlton, P.L., Siegel, J.L., Murphree, H.B., and Cook, L. Effects of diazepam on operant behavior in man. *Psychopharmacology (Berlin),* 73:314-317, 1981.

Crawley, J.N. Neuropharmacologic specificity of a simple animal model for the behavioral actions of benzodiazepines. *Pharmacol. Biochem. Behav.*, 15:695-699, 1981.

Dantzer, R. Behavioral effects of benzodiazepines: A review. *Biobehav. Rev.*, 1:71-86, 1977.

Engberg, G., Elam, M., and Svensson, T.H. Clonidine withdrawal: Activation of brain noradrenergic neurons with specifically reduced alpha-2 receptor sensitivity. *Life Sci.*, 30:235-243, 1982.

File, S. The use of social interaction as a method for detecting anxiolytic activity of chlordiazepoxide-like drugs. *J. Neurosci. Methods,* 2:219-238, 1980.

Geller, I., and Seifter, J. The effects of meprobamate, barbiturates, *d*-amphetamine, and promazine on experimentally induced conflict in the rat. *Psychopharmacologia (Berlin),* 1:482-492, 1950.

Goddard, G.V., McIntyre, D.C., and Leech, C.K. A permanent change in brain function resulting from daily electrical stimulation. *Exp. Neurol.*, 25:295-330, 1969.

Grant, S.J., Huang, Y.H., and Redmond, D.E., Jr. Benzodiazepines attentuate single unit activity in the locus coeruleus. *Life Sci.*, 27:2231-2236, 1980.

Gray, J.A., Davis, N., Feldon, J., Nicholas, J., Rawlins, P., and Owen, S.R. Animal models of anxiety. *Prog. Neuropsychopharmacol.*, 5:143-157, 1981.

Haertzen, C.A. Development of scales based on patterns of drug effects using the Addiction Research Center Inventory (ARCI). *Psychol. Rep.*, 18:194, 1966.

Hansson, P.G., and Hökfelt, B. Changes in blood pressure, plasma catecholamines and plasma renin activity during and after treatment with tiamentidine and clonidine. *Br. J. Clin. Pharmacol.*, 11:73-77, 1981.

Hoehn-Saric, R., Merchant, A.F., Keyser, M.L., and Smith, V.K. Effects of clonidine on anxiety disorders. *Arch. Gen. Psychiatry*, 38:1278-1282, 1981.

Iversen, S. Animal models of relevance to biological psychiatry. In: Van Praag, H.M., Lader, M.H., Rafaelsen, O.J., and Sachar, E.J. (eds.), *Handbook of Biological Psychiatry, Part I.* New York:Marcel Dekker, 1979, pp. 303-335.

Klein, D.F. Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia (Berlin)*, 5:397-408, 1964.

Klein, D.F. The importance of psychiatric diagnosis in prediction of clinical drug effects. *Arch. Gen. Psychiatry*, 16:118-126, 1967.

Ko, G.N., Elsworth, J.D., Roth, R.H., Rifkin, B.G., Leigh, H., Hurzeler, M.A., and Redmond, D.E., Jr. Panic-induced elevation of plasma MHPG in phobic anxious patients: Effects of clonidine or imipramine. *Arch. Gen. Psychiatry*, (In press)

Korf, J., Bunney, B.S., and Aghajanian, G.K. Noradrenergic neurons: Morphine inhibition of spontaneous activity. *Eur. J. Pharmacol.*, 25:165-169, 1974.

Krause, M.S. The measurement of transitory anxiety. *Psychol. Rev.*, 68:178-189, 1961.

Lader, M.H. Anxiety reduction and sedation: Psychophysiological theory. *Br. J. Clin. Pharmacol.*, 7:99S-105S, 1979.

Leckman, J.F., Maas, J.W., Redmond, D.E., Jr., and Heninger, G.R. Effects of oral clonidine on plasma 3-methoxy-4-hydroxyphenylethylene-glycol (MHPG) in man: Preliminary report. *Life Sci.*, 26:2179-2185, 1980.

Liebowitz, M.R., Fyer, A.J., McGrath, P., and Klein, D.F. Clonidine treatment of panic disorder. *Psychopharmacol. Bull.*, 17:122-123, 1981.

McNair, D.M., and Kahn, E.J. Imipramine vs. a benzodiazepine for agoraphobia. In: Klein, D.F., and Rabkin, T. (eds.)., *Anxiety: New Research and Changing Concepts.* New York:Raven Press, 1981, pp. 69-80.

Maier, J.F., and Seligman, M.E.P. Learned helplessness: Theory and evidence. *J. Exp. Psychol. [Gen.]*, 105:3-46, 1976.

Nyback, H.V., Walters, J.R., Aghajanian, G.K., and Roth, R.H. Tricyclic antidepressants: Effects on firing rate of brain noradrenergic neurons. *Eur. J. Pharmacol.*, 32:302-312, 1975.

Post, R.M., and Ballenger, J.C. Kindling models for the progressive development of behavioral psychopathology: Sensitization to electrical, pharmacological, and psychological stimuli. In: van Praag, H.M., Lader, M.H, Rafaelsen, O.J., and Sachar, E.J. (eds.), *Handbook of Biological Psychiatry, Part IV.* New York:Marcel-Dekker Inc., 1981, pp. 609-651.

Post, R.M., and Kopanda, R.T. Cocaine, kindling, and psychosis. *Am. J. Psychiatry*, 133:627-634, 1976.

Redmond, D.E., Jr. Alterations in the function of the nucleus locus coeruleus: A possible model for studies of anxiety. In: Hanin, I., and Usdin, E. (eds.), *Animal Models in Psychiatry and Neurology.* Oxford/New York:Pergamon Press, 1977, pp. 293-305.

Redmond, D.E., Jr. New and old evidence for the involvement of a brain norepinephrine system in anxiety. In: Fann, W.E., Karachan, I., Porkorny, A.D., and Williams, R.L. (eds.), *Phenomenology and Treatment of Anxiety.* New York:Spectrum Publications, 1979, pp. 153-203.

Redmond, D.E., Jr., and Huang, Y.H. Current concepts. II. New evidence for a locus coeruleus-norepinephrine connection with anxiety. *Life Sci.*, 25:2149-2162, 1979.

Seligman, M.E.P. *Helplessness: On Depression, Development, and Death.* San Fransisco:W.H. Freeman & Co., 1975.

Sepinwall, J., and Cook, L. Behavioral pharmacology of antianxiety drugs. In: Iversen, L.L., Iversen, S.D., and Snyder, S.H. (eds.), *Handbook of Psychopharmacology.* Vol. 13. London:Plenum, 1978, pp. 345-393.

Sheehan, D.V., Ballenger, J., and Jacobsen, G. Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms. *Arch. Gen. Psychiatry*, 37:51-59, 1980.

Siever, L.J., Insel, T.R., and Uhde, T.W. Noradrenergic challenges in the affective disorders. *J. Clin. Psychopharmacol.*, 1:192-206, 1981.

Simon, P., and Soubrie, P. Behavioral studies to differentiate anxiolytic and sedative activity of the tranquilizing drugs. *Mod. Probl. Pharmacopsychiatry* 14:99-143, 1979.

Strahlendorf, H.K., and Strahlendorf, J.C. Iontophoretically applied benzodiazepines inhibit locus coeruleus unit activity. *Soc. Neurosci. Abstr.*, 7:793, 1981a.

Strahlendorf, J.C., and Strahlendorf, H.K. Response of locus coeruleus neurons to direct application of ethanol. *Soc. Neurosci. Abstr.*, 7:312, 1981b.

Suomi, S.J., Kraemer, G.W., Baysinger, C.M., and Delizio, R.D. Inherited and experiential factors associated with individual dfifferences in anxious behavior displayed by rhesus monkeys. In: Klein, DF., and Rabkin, T. (eds.), *Anxiety: New Research and Changing Concepts.* New York:Raven Press, 1981, pp. 179-199.

Svensson, T., Persson, R., Wallin, L., and Walinder, J. Anxiolytic action of clonidine. *Nordisk. Psykiatrisk. Tidsskrift*, 32:439-441, 1978.

Uhde, T.W., Redmond, D.E., Jr., and Kleber, H.D. Clonidine suppresses the opioid abstinence syndrome without clonidine-withdrawal symptoms: A blind inpatient study. *Psychiatry Res.*, 2:37-49, 1980a.

Uhde, T.W., Post, R.M., Siever, L.J., and Buchsbaum, M.S. Clonidine and psychophysical pain. *Lancet*, 2:1375, 1980b.

Uhde, T.W., Post, R.M., Siever, L., Buchsbaum, M.S., Jimerson, D.C., Silberman, E.K., Murphy, D.L. and Bunney, W.E., Jr. Clonidine: Effects on mood, anxiety, and pain. *Psychopharmacol. Bull.* 17:125-126, 1981.

Uhde, T.W., Siever, L.J., and Post, R.M. Clonidine: Acute challenge and clinical trial paradigms for the investigation and treatment of anxiety disorders, affective illness, and pain syndromes. In: Post, R.M., and Ballenger, J.C. (eds.). *The Neurobiology of the Mood Disorders.* Baltimore:Williams & Wilkins. (In press)

Uhde, T.W., Siever, L.J., Post, R.M., and Jimerson, D.C. Clonidine reduces state anxiety. *Sci. Proc. Am. Psychiatr. Assoc.*, 135:70, 1982.

Uhlenhuth, E.H. Specific anxiety syndromes: Current therapeutic options. *J. Clin. Psychiatry*, 42:27-33, 1981.

Caffeine Consumption and Anxiety: Preliminary Results of a Survey Comparing Patients with Anxiety Disorders and Normal Controls

Jean-Philippe Boulenger, M.D., and Thomas W. Uhde, M.D.[1]

Caffeine, a potent stimulant of the central nervous system (Rall 1980), is widely consumed in America where its estimated daily intake is approximately 200 mg per adult (Gilbert 1976). Symptoms of caffeinism, which are similar to those of anxiety, may develop in individuals who consume more than 500 mg of caffeine daily (Greden 1974). Furthermore, a significant association between caffeine consumption and self-ratings of trait-anxiety and depression has been demonstrated in a group of randomly selected students (Gilliland & Andress 1981). In psychiatric patients, similar results have been reported; i.e., high caffeine consumption was significantly associated with high scores of state-anxiety (Winstead 1976), depression, and both state- and trait-anxiety (Greden et al. 1978). In these studies, however, diagnostic subgroups were not taken into account, a factor which may influence caffeine-related symptomatology both qualitatively and quantitatively. Furthermore, the relationship between caffeine consumption and the incidence of psychopathological symptoms has never been studied in comparison with a control group, a methodological precaution that may be of importance since numerous factors, e.g., age and sex, may influence these two variable (Gilbert 1976; Sartorius 1980).

The authors therefore undertook a survey to study both caffeine consumption and the incidence of various symptoms in patients with anxiety disorders and major affective disorders that fulfilled the Research Diagnostic Criteria (RDC) (Spitzer et al. 1978). These data were compared with those obtained from a group of normal volunteers matched for age and sex. In this paper, as part of this ongoing research, preliminary results obtained in 16 anxious patients and 16 normal controls are presented.

Method

Sixteen anxious patients (15 females, 1 male) with a mean age of 41.2 ± 9.4 years (mean ± S.D.) and 16 age-matched (40.2 ± 10.2 years) and sex-matched controls without significant history of psychiatric illness, were invited to participate in this study. Fourteen patients had both panic and phobic disorders and two patients had both generalized anxiety and phobic disorders according to the RDC. Two patients with symptomatology consistent with a diagnosis of panic disorder were excluded because of concomitant medical illnesses. The 16 normal controls were recruited from the patients' relatives and friends in order to control for sociocultural variables.

Each subject completed a self-rating questionnaire (which may be obtained by writing to the authors), designed by the investigators to assess the consumption of various caffeinated beverages, foods, or drugs and the effects of caffeine on various somatic and psychological symptoms. The consumption of tobacco and medications (including over-the-counter medications) taken more often than twice-monthly was also recorded. The daily caffeine intake was calculated from this questionnaire according to the quantities of caffeine suggested by Gilbert (1976) for different

---

[1] Section on Psychobiology, Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205.

Address reprint requests to: Thomas W. Uhde, M.D., Biological Psychiatry Branch, Building 10, Room 3S-239, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20205.

beverages, i.e., dripped coffee: 110 mg/cup; percolated coffee: 75 mg/cup; instant coffee: 65 mg/cup; decaffeinated coffee: 2 mg/cup; tea: 30 mg/cup; cola drinks: 40 mg/12 oz.; cocoa: 20 mg/cup. The caffeine intake related to drugs or chocolate bars (20 mg/bar) was added to the previous total.

In addition, the Spielberger State-Trait Anxiety Inventory (STAI) (Spielberger et al. 1970) and the Hopkins Symptom Checklist (HSCL-90) (Derogatis et al. 1976) were administered. The following subscales were derived from the HSCL-90 items: General Symptomatic Index (GSI), Positive Symptom Distress Index (PSDI), anxiety and phobic factors (Derogatis et al. 1976), phobic-anxiety, agitated depression, retarded depression, interpersonal sensitivity, somatization, obsessive-compulsive, and anger-hostility factors (Lipman et al. 1979).

Results

Daily Caffeine Consumption

The anxious patients consumed 185.9 ± 157.9 mg/day (mean ± S.D.) of caffeine, whereas the normal controls consumed 216.2 ± 174.9 mg/day (*t*-test, N.S.). There was no relationship between daily caffeine consumption and age, smoking habits, drug, or psychiatric treatments. Of all the individuals who no longer drank coffee, a significantly greater number of anxious patients (7 of 9) reported doing so because of the induction of anxiety, tension, and/or nervousness compared to the normal controls (2 of 5) (chi-square, $p < 0.05$). With the exception of one patient with panic disorder, all subjects were still consuming significant amounts of other caffeinated beverages.

State- and Trait-Anxiety

As expected, the anxious patients had significantly higher ratings of state-anxiety (50.19 ± 10.26) and trait-anxiety (54.14 ± 10.85) compared to the normal controls (state = 32.09 ± 4.21, $p < 0.001$; trait = 33.36 ± 5.18, $p < 0.0001$). Furthermore, in the anxious patients there was a significant positive correlation between daily caffeine consumption and trait-anxiety ($r = 0.90$; $p = 0.0001$) but not state-anxiety ($r = 0.007$; N.S.) (*see* Figure 1)

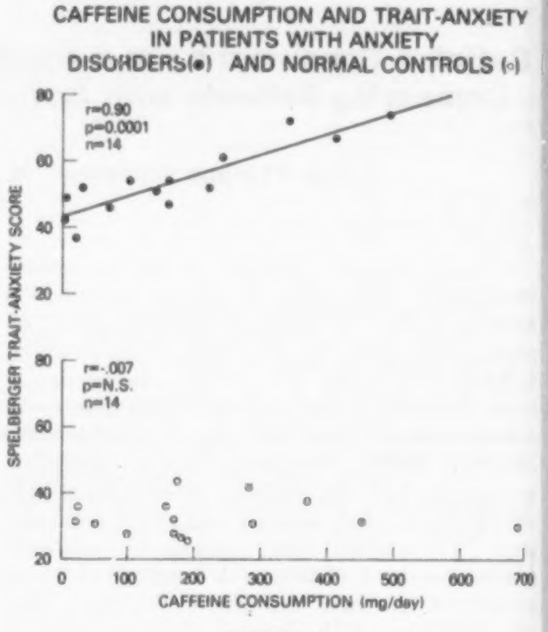
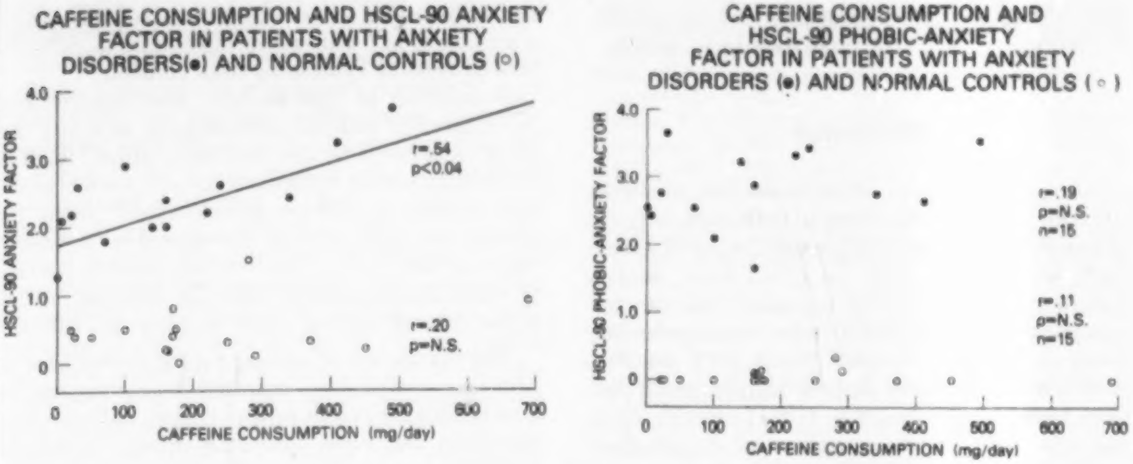


FIGURE 1

Subscales Derived From the HSCL-90

As expected, the anxious patients had significantly higher scores on the various subscales of the HSCL-90 compared to the normal controls, as indicated by the GSI (patients 1.55 ± 0.69; controls 0.38 ± 0.36; *t*-test $p < 0.0001$) and the PSDI (patients 2.31 ± 0.51; controls 1.43 ± 0.34; *t*-test $p = 0.0001$) indices. There was no relationship between caffeine consumption and the HSCL-90 subscales in the control group. However, in the anxious patients there was a significant positive relationship between caffeine consumption and the following subscales: retarded depression ($r = 0.80$; $p = 0.0003$; GSI ($r = 0.77$; $p = 0.0005$); obsessive-compulsive ($r = 0.74$; $p = 0.002$); hostility ($r = 0.72$; $p = 0.002$); somatization ($r = 0.68$; $p = 0.005$); PSDI ($r = 0.68$; $p = 0.006$); interpersonal sensitivity ($r = 0.61$; $p = 0.016$); agitated depression ($r = 0.53$; $p = 0.043$). Furthermore, it is noteworthy that in


CAFFEINE CONSUMPTION AND HSCL-90 ANXIETY FACTOR IN PATIENTS WITH ANXIETY DISORDERS(●) AND NORMAL CONTROLS (○)

CAFFEINE CONSUMPTION AND HSCL-90 PHOBIC-ANXIETY FACTOR IN PATIENTS WITH ANXIETY DISORDERS (●) AND NORMAL CONTROLS (○)

FIGURE 2

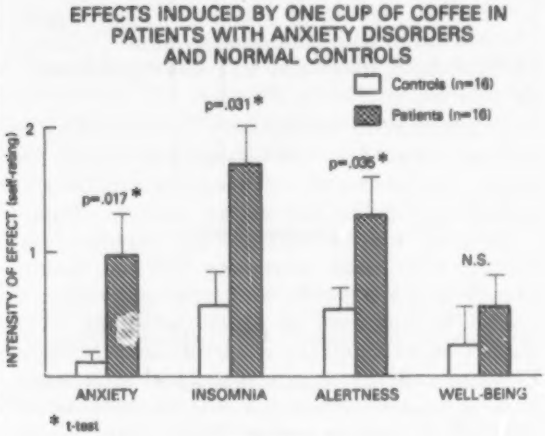

EFFECTS INDUCED BY ONE CUP OF COFFEE IN PATIENTS WITH ANXIETY DISORDERS AND NORMAL CONTROLS

FIGURE 3

the anxious patients there was a significant positive correlation between caffeine consumption and those factors which primarily reflect generalized anxiety (anxiety: $r = 0.54$; $p = 0.038$) but not those which primarily reflect agoraphobia (phobic-anxiety: $r = 0.19$; N.S.) (*see* Figures 2a and 2b).

Caffeine Effects on Various Psychological and Somatic Symptoms

All subjects were asked to rate changes, if there were any, in their anxiety, alertness, sleep, and mood induced by drinking one cup of coffee, on a 4-item scale. As illustrated in Figure 3, the consumption of even one cup of coffee was associated with more intense ratings of anxiety, insomnia, and alertness in the anxious patients compared to normal volunteers.

Because anxiety and insomnia may be present at baseline before any coffee consumption, subjects were asked to indicate whether coffee induced or increased symptoms already present. Among those for whom coffee induced symptoms, i.e., those having a baseline level equal to zero, the caffeine-induced effects were greater in the patients compared to the normal controls, although this effect was nonsignificant.

All subjects were also asked to check, on a list of 26 symptoms, those items they associated with the consumption of coffee and to rate their intensity on a 5-point scale (0-4). For the anxious patients the caffeine-induced symptoms reported to have a mean score > 1 were, by order of decreasing intensity (mean ± S.D.): tension, nervousness (1.87 ± 1.36); anxiety (1.69 ± 1.49); insomnia (1.69 ± 1.70); increased urination (1.27 ± 1.53); increased motor activity (1.12 ± 1.36); tremors (1.12 ± 1.59); diarrhea (1.00 ± 1.51). For the normal controls, these caffeine-induced symptoms were: insomnia (1.31 ± 1.30) and increased motor activity (1.19 ± 1.28). The intensity of the following caffeine-induced symptoms was significantly higher in the patient group (*t*-tests): anxiety ($p = 0.004$); tremors ($p = 0.016$); muscle tension ($p = 0.028$); panic attacks ($p = 0.041$); lightheadedness ($p = 0.044$); diarrhea ($p = 0.046$).

Discussion

The present investigation is the first to survey the consumption and effects of caffeine in a group of patients suffering from phobic disorders associated with either panic or generalized anxiety symptoms. In this group the daily caffeine consumption (185 mg/day) was nonsignificantly lower than in a control group (215 mg/day) matched for age and sex. A similar result had been found by Greden et al. (1981) when comparing the caffeine consumption of hospitalized psychiatric patients to that of hospitalized nonpsychiatric patients. In the present study the caffeine consumption found in both groups was similar to the average daily consumption in American adults reported by Gilbert (1976), i.e., 200 mg/day.

A major finding of this study was that a highly significant positive correlation ($r = 0.90$; $p < 0.0001$) existed between the daily caffeine consumption and the scores of trait-anxiety within the patient group but not in the control group (Figure 1). Such a correlation would not appear to be related to the consumption of benzodiazepines by the patients even though caffeine has been shown to antagonize the biochemical (Boulenger et al. 1982) and pharmacological (File et al. 1982) effects of benzodiazepines in humans. Only five patients who were caffeine users (10-240 mg/day) were also taking psychotropic drugs (all being minor tranquilizers). Thus, our preliminary results suggest that an increased sensitivity to the effects of caffeine may exist in anxious patients as composed to normal controls, a finding similar to that described for other compounds, e.g., lactate, epinephrine, or isoproterenol (for review, *see* Pitts & Allen 1979). This increased sensitivity would explain in part why significantly more anxious patients than controls have given up coffee because of its central nervous system stimulant properties, and why the caffeine-induced effects appear to be significantly more severe in the former than in the latter (Figure 3). It is also possible that the higher baseline levels of anxiety and/or insomnia of the anxious patients may have contributed to these results. Double-blind, caffeine-placebo challenges are indicated in order to determine whether anxious patients are truly more susceptible to caffeine-related anxiety symptoms than controls.

In contrast to trait-anxiety, state-anxiety was not related to caffeine consumption in either the anxious patients or the normal controls. Such a result may not be surprising since it is more likely that habits of caffeine consumption might be related to trait-anxiety (presumably a stable characteristic) rather than to state-anxiety (anxiety which fluctuates and reflects situational factors at the time of testing) (Spielberger et al. 1970).

Despite the use of similar rating scales (STAI), previous studies have reported conflicting results concerning the relationship between caffeine consumption and state- and trait-anxiety. While in normal students high caffeine consumption is asssociated with trait-anxiety but not state-anxiety (Gilliland & Allen 1981), studies of unspecified psychiatric inpatients have reported an association with state-anxiety alone (Winstead 1976) or both state- and trait-anxiety (Greden et al. 1978).

In addition to trait-anxiety, several HSCL-90 subscales were found to be significantly and positively correlated with caffeine consumption in the patient group but not in the controls. Such an association may be related to the increase of trait-anxiety found with increasing caffeine consumption or to a nonspecific and more generalized increase in the level of psychopathology. Other studies demonstrating a significant correlation between caffeine consumption and both anxiety and depression (Gilliland & Andress 1981; Greden et al. 1977) have also raised this problem. The extension of the present survey to include a group of patients with affective disorders should clarify the possible relationship between caffeine consumption and other types of psychiatric disorders.

Another interesting finding is the relationship between caffeine consumption and the scores of the HSCL-90 "anxiety" factor but not the "phobic-anxiety" factor (Figure 2). The "anxiety" factor, reflecting mainly generalized anxiety symptoms appears to be sensitive to caffeine effects in a dose-related manner while the "phobic-anxiety factor," reflecting mainly agoraphobic symptoms, is not significantly affected by caffeine consumption. These data are consistent with the description by Klein (1980) of agoraphobia as a distinct clinical entity with different clinical characteristics, symptoms, evolution, and pharmacologic response to antidepressant treatments.

In conclusion, the present study suggests that caffeine consumption is positively correlated with trait-anxiety in patients with phobic disorders associated with either panic or generalized anxiety disorders. Such a correlation may be related to an increased sensitivity of these patients to the effects of caffeine, particularly those symptoms related to generalized anxiety. In contrast, symptoms of agoraphobia do not appear to be influenced by caffeine consumption, a finding which supports its description as a distinct clinical entity. The correlation between the amount of caffeine consumed and other psychopathological factors such as depression raises the problem of the specificity of caffeine's effects on psychiatric disorders. Further surveys, including the use of caffeine challenge paradigms in various psychiatric patients, should help to clarify these relationships.

Acknowledgment. The authors gratefully acknowledge the scientific review by Robert M. Post, M.D., and the valuable technical assistance provided by Edward Wolff.

References

Boulenger, J-P., Patel, J., and Marangos, P.J. Effects of caffeine and theophylline on adenosine and benzodiazepine receptors in human brain. *Neurosci. Lett.*, 30:161-166, 1982.

Derogatis, L.R., Lipman, R.S., and Covi, L. SCL-90: An outpatient psychiatric rating scale: Preliminary report. In: Guy, W. (ed.), *ECDEU Assessment Manual for Psychopharmacology.* Washington, D.C.:DHEW Publications, 1976, pp. 320-327.

File, S.E., Bond, A.J., and Lister, R.G. Interaction between effects of caffeine and lorazepam in performance tests and self-ratings. *Clin. Psychopharmacol.*, 2:102-106, 1982.

Gilbert, A.M. Caffeine as a drug of abuse. In: Gibbins, A.J., Israel, Y., Kalant, H., Popham, R.E., Schmidt, W., and Smart, R.G. (eds.), *Research Advances in Alcohol and Drug Problems.* Vol. 3 New York:Wiley & Sons, 1976, pp. 49-176.

Gilliland, K., and Andress, D. Ad lib caffeine consumption, symptoms of caffeinism and academic performance. *Am. J. Psychiatry,* 138:512-514, 1981.

Greden, J.F. Anxiety or caffeinism: A diagnostic dilemma. *Am. J. Psychiatry,* 131:1089-1092, 1974.

Greden, J.F., Fontaine, P., Lubetsky, M., and Chamberlin, K. Anxiety and depression associated with caffeinism among psychiatric inpatients. *Am. J. Psychiatry,* 135:963-966, 1978.

Greden, J.F., Proctor, A., and Victor, B. Caffeinism associated with greater use of other psychotropic agents. *Compr. Psychiatry,* 22:565-571, 1981.

Klein, D.F. Anxiety reconceptualized. *Compr. Psychiatry,* 21:411-427, 1980.

Lipman, R.S., Covi, L., and Shapiro, A.F. The Hopkins symptom checklist (HSCL). Factors derived from the HSCL-90. *J. Affect. Disord.*, 1:9-24, 1979.

Pitts, F.N., and Allen, R.E. Biochemical induction of anxiety. In: Fann, W.E., Karacan, I., Porkorny, A.D., and Williams, R.L. (eds.), *Phenomenology and Treatment of Anxiety.* New York:Spectrum Publications, 1979, pp. 125-140.

Rall, T.W. Central nervous system stimulants. The xanthines. In: Goodman, G.A., Goodman, L.S., and Gilman, A. (eds.), *The Pharmacological Basis of Therapeutics,* 6th ed. New York:McMillan, 1980, pp. 592-607.

Sartorius, N. Epidemiology of anxiety. *Pharmakopsychiatrie,* 13:249-253, 1980.

Spielberger, C.D., Gorsuch, R.L., and Lushene, R.E. *State-Trait Anxiety Inventory (STAI) Manual.* Palo Alto: Consulting Psychologists Press, 1970.

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry,* 35:773-782, 1978.

Winstead, D.K. Coffee consumption among psychiatric inpatients. *Am. J. Psychiatry,* 133:1447-1450, 1976.

pages tightly bound

New Anxiolytics: Are They Really New?[1]

David J. Greenblatt, M.D.,[2] and Richard I. Shader, M.D.[2]

The pharmaceutical industry continues its search for more specific and more effective pharmacologic treatments of anxiety. With a few recent exceptions (Rickels 1981), the great majority of new anxiolytics are of the benzodiazepine category. Benzodiazepines as a class of compounds clearly have increased the overall efficacy of anxiolytic pharmacotherapy relative to drugs available prior to 1960, and also have greatly increased the safety of such treatment. However, numerous benzodiazepines are clinically available as anxiolytics, and although superior as a class of drugs, meaningful differences among various drugs within the class are at best subtle. It is of great importance to pharmacologists, practicing physicians, and members of institutional formulary committees that clinical and pharmacokinetic characteristics of new benzodiazepine anxiolytics be carefully and critically evaluated before promotional claims of newness or uniqueness are accepted as valid. This paper briefly considers the properties of several new benzodiazepine anxiolytics, together with an assessment of their potential role in the pharmacotherapy of anxiety.

Halazepam and the Parade of Desmethyldiazepam Precursors

Halazepam (Paxipam) was recently introduced as a benzodiazepine anxiolytic in the United States (Figure 1). Clinical trials hav demonstrated its comparability to other standar benzodiazepine antianxiety agents, both in term of efficacy and side effects (Rickels et al. 1977 Fann et al. 1982). The pharmacokinetic profile o halazepam, however, reveals interesting properties. Many benzodiazepines are precursors o desmethyldiazepam, being partly or completel transformed to this metabolic product (Figure 2) Two benzodiazepines already available in th United States—clorazepate and prazepam—are in fact, nearly completely transformed t desmethyldiazepam prior to reaching the systemi circulation (Allen et al. 1980; Shader et al. 1981 Greenblatt et al. 1981a). Current data o halazepam appears to put this drug in a simila category. After a single oral dose of halazepam the intact drug appears in systemic blood onl transiently and at relatively low levels, bein rapidly transformed to the principal metaboli desmethyldiazepam (Figure 3). Due to its ver long elimination half-life (Allen et al. 1980 Greenblatt et al. 1981a; Shader et al. 1981) desmethyldiazepam persists in blood much longe than halazepam. During multiple-dose therap with halazepam, the parent drug will accumula minimally, whereas the major metabolite will accumulate extensively, consistent with its very lon elimination half-life.

Since halazepam serves mainly as anothe precursor of desmethyldiazepam, it is difficult t conclude that this drug would add meaningfull to the already available armamentarium of lon half-life accumulating benzodiazepines such a diazepam, clorazepate, or flurazepam (Greenblatt et al. 1981a). Thus, halazepam serves as a example of a drug for which careful pharmacokinetic studies can readily establish its likel role in clinical practice.

---

[1] Supported in part by USPHS Grant MH-34223 from the National Institute of Mental Health.

[2] Division of Clinical Pharmacology, Department of Psychiatry, Tufts-New England Medical Center, Boston, MA 02111.

Address correspondence to: David J. Greenblatt, M.D., Division of Clinical Pharmacology, Box 1007, New England Medical Center Hospital, 171 Harrison Avenue, Boston, MA 02111.

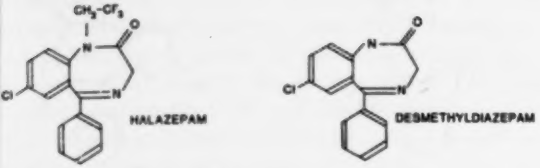

CH2-CF3
N
O
N
Cl
HALAZEPAM
N
O
N
Cl
DESMETHYLDIAZEPAM

FIGURE 1. Structural formula of halazepam and its major metabolite, desmethyldiazepam.

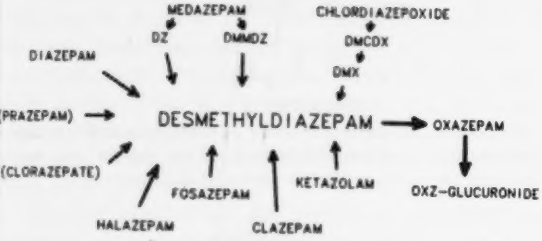
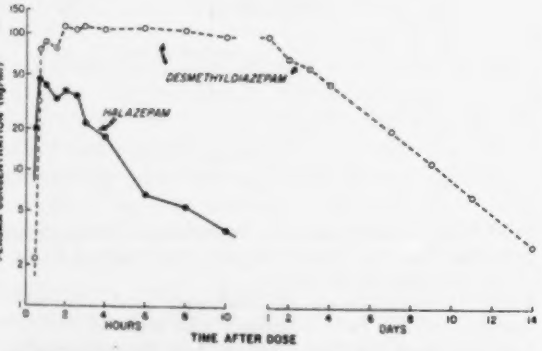

MEDAZEPAM
DZ
DMMDZ
CHLORDIAZEPOXIDE
DMCDX
DMX
DIAZEPAM
(PRAZEPAM)
DESMETHYLDIAZEPAM
OXAZEPAM
(CLORAZEPATE)
FOSAZEPAM
KETAZOLAM
OXZ-GLUCURONIDE
HALAZEPAM
CLAZEPAM

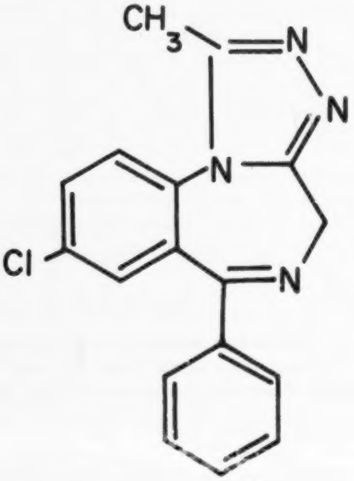
FIGURE 2. Schematic representation of the many benzodiazepines that are biotransformed to desmethyldiazepam.



IGURE 3. Plasma concentrations of halazepam and its ajor metabolite, desmethyldiazepam, in a volunteer ho ingested a single 40-mg oral dose of halazepam.

lprazolam: The Tirazolo Benzodiazepines

Another important research strategy for the levelopment and evaluation of new ben-odiazepines involves compounds whose structure leviates from the familiar 1,4-benzodiazepine onfiguration. The most important of these com-ounds is alprazolam, in which a triazolo ring is affixed to the positions previously designated as 1 and 2 (Figure 4). In clinical studies of anxiolytic efficacy in patients with neurotic anxiety, alprazolam performs similarly to other comparison benzodiazepines (Cohn 1981). An apparently unique property of this compound has been suggested by studies comparing its clinical efficacy to that of tricyclic antidepressants in patients with endogenous depression (Fabre & McLendon 1980). The results available to date suggest that alprazolam may have antidepressant as well as anxiolytic effects. If such findings are replicated in subsequent trials, this would be a unique and important property, since alprazolam has a relatively benign benzodiazepine-like profile of side effects as opposed to the more important and potentially serious side effect profile of the tricyclic antidepressants. Consistent with these reports are other preliminary findings suggesting that alprazolam may have efficacy in the treatment of panic attacks and related disorders.



ALPRAZOLAM

FIGURE 4. Structural formula of alprazolam.

None of these apparently unique clinical properties of alprazolam could have been predicted based on its pharmacokinetic profile (Greenblatt et al. 1982a). The metabolic disposition of alprazolam involves hepatic oxidation, yielding hydroxylated metabolites which reach the systemic circulation in negligible quantities. Therefore, essentially all of the clinical activity of alprazolam is attributable to the parent compound. The apparent elimination half-life of alprazolam in humans usually ranges from 8 to 16 hours (Figure 5). As in the case of other benzodiazepines transformed by oxidation (Greenblatt et al. 1982b), the half-life is prolonged in elderly as opposed to young males due to reduced oxidizing capacity in the elderly male population.

In mechanistic terms, it has not established why alprazolam should have antidepressant as well as anxiolytic properties. It may well be that other triazolo benzodiazepines such as triazolam or estazolam share similar properties.

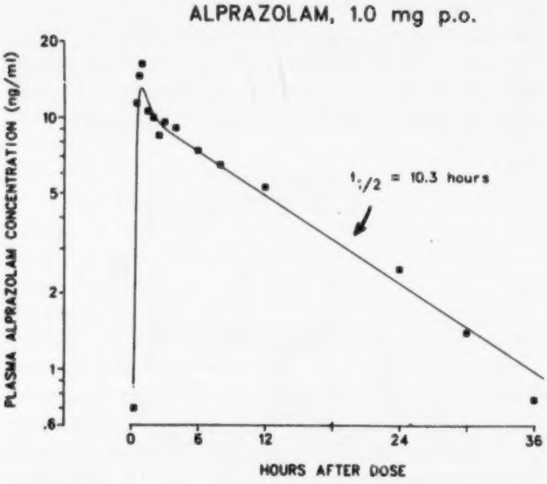


FIGURE 5. Plasma concentrations of alprazolam in a volunteer who ingested a single 1-mg oral dose. Solid line is the computer-determined pharmacokinetic function of best fit.

Clobazam: A Shift of the Nitrogen

Clobazam is a 1,5-benzodiazepine derivative, and thereby differs from other benzodiazepines in the position of the nitrogen substituents on the central nucleus (Figure 6). Its anxiolytic efficacy has been clearly established in many controlled trials, and the drug is extensively used as an antianxiety agent in Europe (Brogden et al. 1980).

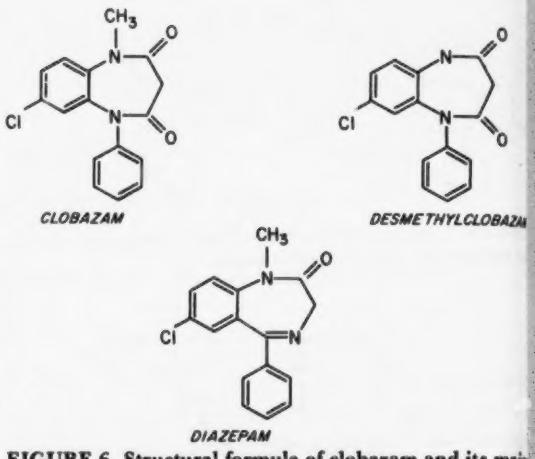


FIGURE 6. Structural formula of clobazam and its maj metabolite, desmethylclobazam. Also shown for com parison purposes is the structure of diazepam.

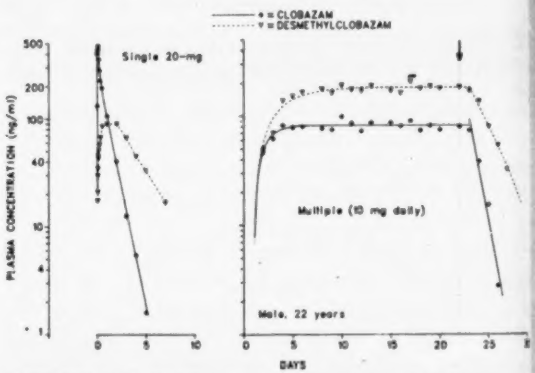


FIGURE 7. Left: Plasma concentrations of clobazam an desmethylclobazam in a volunteer who ingested a sing 20-mg oral dose of clobazam.
Right: Concentrations of clobazam and desmethyl diazepam in the same volunteer who ingested 10 mg o clobazam once daily for 22 days. Note the pattern of ac cumulation as well as washout for both compounds aft the last dose (arrow).

Despite the different positioning of the nitrog atoms, the metabolic profile of clobazam i humans closely resembles that of diazepam. Biotransformation of clobazam proceeds b hepatic N-demethylation, yielding the phar macologically active metabolite, desmethyl clobazam (Greenblatt et al. 1981b; Tedeschi et al 1981). This is entirely analogous to the situatio with diazepam, which is transformed to the activ substance desmethyldiazepam. For bot clobazam and diazepam, the elimination half-life of the metabolite is greater than that of the parent drug, and the clearance of the metabolic product is lower than that of the parent drug. For this reason, concentrations of desmethylclobazam after single oral doses of the parent drug persist in plasma considerably longer than those of clobazam (Figure 7). During multiple-dose therapy, accumulation of clobazam and desmethylclobazam is extensive, with levels of the metabolite generally exceeding those of the parent compound (Figure 7). After discontinuation of therapy, both compounds wash out from plasma at a slow rate, although desmethylclobazam persists longer than the parent drug. All of these characteristics are highly analogous to the situation seen during single and multiple dosing with diazepam.

Despite claims to the contrary, the kinetic similarity of clobazam and diazepam makes it unlikely that clobazam would provide meaningful advantages in clinical practice over what is already available from diazepam.

Conclusion

Evaluation of new anxiolytics in clinical practice—in particular, benzodiazepine anxiolytics—should involve careful metabolic as well as clinical testing. Clinical properties of specific compounds may emerge which are completely unrelated to or are not predicted by pharmacokinetic profiles, as is the case with alprazolam. In other cases, such as with halazepam and clobazam, pharmacokinetic similarities to already available benzodiazepines suggest that these drugs are unlikely to provide meaningful additional benefits. Multidisciplinary evaluation of new anxiolytics is essential to provide the most comprehensive picture of what can be expected from such agents.

Acknowledgment: We are grateful for the assistance of Marcia Divoll, Darrell R. Abernethy, Ann Locniskar, and Jerold S. Harmatz.

References

Allen, M.D., Greenblatt, D.J., Harmatz, J.S., and Shader, R.I. Desmethyldiazepam kinetics in the elderly after oral prazepam. *Clin. Pharmacol. Ther.*, 28:196-202, 1980.

Brogden, R.N., Heel, R.C., Speight, T.M., and Avery, G.S. Clobazam: A review of its pharmacological properties and therapeutic use in anxiety. *Drugs*, 20:161-178, 1980.

Cohn, J.B. Multicenter double-blind efficacy and safety study comparing alprazolam, diazepam, and placebo in clinically anxious patients. *J. Clin. Psychiatry*, 42:347-351, 1981.

Fabre, L.F., and McLendon, D.M. A double-blind study comparing the efficacy and safety of alprazolam with imipramine and placebo in primary depression. *Curr. Ther. Res.*, 27:474-482, 1980.

Fann, W.E., Pitts, W.M., and Wheless, J.C. Pharmacology, efficacy, and adverse effects of halazepam, a new benzodiazepine. *Pharmacotherapy*, 2:72-79, 1982.

Greenblatt, D.J., Divoll, M., Abernethy, D.R., Moschitto, L.J., Smith, R.B., and Shader, R.I. Alprazolam kinetics in the elderly: Relation to antipyrine disposition. *Arch. Gen. Psychiatry*. (In press)

Greenblatt, D.J., Divoll, M., Puri, S.K., Ho, I., Zinny, M.A., and Shader, R.I. Clobazam kinetics in the elderly. *Br. J. Clin. Pharmacol.*, 12:631-636, 1981b.

Greenblatt, D.J., Shader, R.I., Divoll, M., and Harmatz, J.S. Benzodiazepines: A summary of phamacokinetic properties. *Br. J. Clin. Pharmacol.*, 11:11s-16s, 1981a.

Greenblatt, D.J., Sellers, E.M., and Shader, R.I. Drug disposition in old age. *N. Engl. J. Med.*, 306:1081-1088, 1982b.

Rickels, K. Recent advances in anxiolytic therapy. *J. Clin. Psychiatry*, 42(11, Sect. 2); 40-44, 1981.

Rickels, K., Pereira-Ogan, J., Csanalosi, I., Morris, R.J., Rosenfeld, H., Sablosky, L., Schless, A., and Werblowsky, J.H. Halazepam and diazepam in neurotic anxiety: A double-blind study. *Psychopharmacology*, 52:129-136, 1977.

Shader, R.I., Greenblatt, D.J., Ciraulo, D.A., Divoll, M., Harmatz, J.S., and Georgotas, A. Effects of age and sex on disposition of desmethyldiazepam formed from its precursor clorazepate. *Psychopharmacology*, 75:193-197, 1981.

Tedeschi, G., Riva, R., and Baruzzi, A. Clobazam plasma concentrations: Pharmacokinetic study in healthy volunteers and data in epileptic patients. *Br. J. Clin. Pharmacol.*, 11:619-622, 1981.

Differentiating Depression and Anxiety: Is It Possible? Is It Useful?[1]

Edna B. Foa, Ph.D.,[2] and Uriel G. Foa, Ph.D.[3]

The terms "depression" and "anxiety" have been used to denote mood states as well as labels for diagnostic categories. As a mood state, depression is characterized by sadness, and anxiety by fear. When these mood states are of high intensity, long duration, and/or frequent, they are considered psychopathological signs or symptoms. When intense sadness appears in combination with other signs or symptoms such as sleep disturbance and loss of appetite, a diagnosis of depression is assigned. When a person with a fear mood state also exhibits autonomic arousal and/or avoidance behaviors, he or she will be diagnosed as "anxious." Thus, "depression" and "anxiety" have been used to denote two distinct syndromes or diagnostic entities.

The relationship between anxiety and depression as diagnostic categories has been the subject of controversy for many years. Some investigators believe that the two syndromes cannot or should not be distinguished, since they constitute manifestations of the same disturbance; others hold the contrary position. A recent comprehensive review of the relevant literature (Roth & Mountjoy 1982) essentially leaves the question open.

The purpose of this paper is twofold: To consider conceptual and methodological problems in the study of the relationships between anxiety an depression, and to present data bearing on thi relationship in obsessive compulsives who wer treated with behavior therapy.

Definition and Measurement

The symptoms and signs of the two psycho- pathological conditions can be divided into thre classes: 1) signs which are specific to anxiety; 2 those which are specific to depression, and 3 signs which are common to both syndromes. A present, the diagnostic criteria used to classify a patient as depressive also include signs of anxiety Thus, the definition of the two syndromes are no independent of one another. This is also true o the instruments which have been developed t measure depression and anxiety. Having been influenced by the traditional diagnostic criteria o the two syndromes, they reflect the overlap between them. The Hamilton Depression Scale, fo example, includes items on insomnia, agitation psychic anxiety, somatic anxiety, and somati symptoms, all contributing to the total score o depression. It is not surprising that this score wil correlate highly with measures of anxiety whic also include somatic complaint, agitation, and feelings of doom. The strong influence of the traditional overlay between the two syndromes on the measurement of depression is demonstrated in the argument by Snaith et al. (1971) that the Wakefield inventory constituted a better measurement of depression than the Beck and Zung inventories, since the latter failed to include items dealing specifically with anxiety. The remedy offered for this omission was an assessment tool of depression loaded with items pertaining to anxiety

---

[1] This study was supported in part by USPHS Grant MH-32634 from the National Institute of Mental Health awarded to Edna B. Foa, and by a study leave grant awarded to the first author by Temple University.

[2] Department of Psychiatry, Temple University Medical School, Philadelphia, PA 19129.

[3] Department of Psychology, Temple University, Philadelphia, PA 19122.

Reprint requests should be sent to: Edna B. Foa, Ph.D., Department of Psychiatry, Temple University Medical School at Eastern Pennsylvania Psychiatric Institute, Henry Avenue, Philadelphia, PA 19129.

Snaith et al.'s comments exemplify the absence of conceptual distinction between anxiety and depression which obscures the meaning of the high correlation between the two, often found when assessment by self-reports and by clinical observations was employed. What do these correlations represent? Do they reflect a high joint occurrence between anxiety and depression or are they merely an artifact of the overlap between the definitions and the measurements of the two syndromes?

Another conceptual and methodological problem is embedded in the fact that most instruments designed to measure anxiety or depression yield a single global score. Yet neither of the two is a unitary concept. Rather, each is composed of behavioral, psychophysiological, biochemical, and cognitive-emotional components which are imperfectly intercorrelated. The nature and the degree of the relationship between depression and anxiety may vary greatly, depending on the specific component under investigation. For example, Kelly and Walter (1969) found that the forearm blood flow of nonagitated depressives was less than that of normals, whereas agitated depressed and anxious patients showed increased blood flow. However, when self-reports of anxiety level were examined, the order among the groups changed. Agitated depressives evidenced the lowest level of anxiety, while nonagitated patients rated themselves to be as anxious as those in the anxious group. Thus, in investigating the relationships between anxiety and depression, it seems necessary to study multiple components with the aim of identifying *patterns* of relationships between the two concepts, rather than expecting unidimensional solutions.

The independent definitions of depression and anxiety should each include several component elements. Given the state of the art, however, it seems convenient to start by identifying criteria for classification of the cognitive and the behavioral components which are central to each of the two concepts, and to omit characteristics which are common to both. Measurements for depression and anxiety should be guided by these definitions. Having developed such measurements, we will be better equipped to investigate the relationships between anxiety and depression in various clinical populations, to observe possible changes in these relationships over time, or to examine the effects of anxiety and depression on treatment outcome. This line of investigation will provide an answer to the second question posed: Is the distinction between anxiety and depression useful? Such a distinction is of merit only if there is evidence for different aetiologies, treatments of choice, or treatment outcomes for the two categories.

Differences and Similarities

Notwithstanding the limitation discussed above, the data available point to some differences as well as to certain similarities between anxiety and depression. Not surprisingly, these findings have stoked the fires of proponents of separation (e.g., Roth et al. 1972) as well as of those arguing for unification of the two concepts (e.g., Lewis 1966). Let us consider this evidence briefly.

Psychophysiological Measures

A mixed picture of similarities and differences between depression and anxiety emerges from psychophysiological observations. Lader and his colleagues (Lader 1967, 1976; Lader et al. 1967; Lader & Wing 1964, 1966) demonstrated that patients with anxiety states showed high levels of electrodermal activity and slow habituation of skin conductance responses to repeated auditory stimuli. They also found that complex phobics (i.e., agoraphobics, social phobics, and anxiety states) evidenced more baseline arousal than monophobics with respect to both electrodermal activity and pulse rate; the monophobic group did not differ from normals.

When depressed patients were divided into subgroups of retarded and agitated depressives, differences in electrodermal activity also emerged (Lader & Wing 1969). The agitated depressed patients (who manifest intense anxiety) were more aroused than the retarded groups and, like anxious patients, they habituated more slowly to auditory stimuli than did normals. The retarded group showed almost no electrodermal activity. A similar picture emerged from observations of the cardiovascular responses. As mentioned earlier, Kelly and Walter (1969) found a lower level of forearm blood flow in nonagitated depressed patients than in the agitated depressives. Likewise, Lader and Wing (1969) reported an increase in pulse rate over normals in agitated but not in retarded depressives. Investigating evoked responses in depressed and anxious patients, Shagass (1955) applied photic stimulation at 10 and 15 Hz to normals, anxiety states, psychoneurotic depressive patients, and psychotic depressives. The ratio of responses at 15 Hz to those detected at 10 Hz was highest in the anxious state patients and lowest for both depressive groups with normals occupying an in between position. The difference among the groups was attributed to differences in the amount of harmonic activity induced by the photic stimulation; again, depressives showed less activity and anxious patients evidenced more activity than normals. It seems, then, that depression suppresses psychophysiological activity whereas anxiety increases it. As stated by Lader (1975), the psychophysiological literature favors a distinction between anxiety and depression "but only if particular care with subgrouping of patients is exercised" (p. 129).

Joint Occurrence

The view that depression and anxiety should be considered a unitary syndrome has been bolstered by the finding that a high proportion of neurotic patients, especially those who are not severely impaired, show both anxiety and depression. So much so that the term anxiety-depression has been proposed by several authors to denote a distinct diagnostic class (e.g., Cooper & Sylph 1973; Snaith 1981). Support for the unitary view is provided by the fact that a relatively high percentage (24 percent) of those who had been diagnosed as being in an anxiety state were rediagnosed several years later as depressives (Kandell 1974). This finding points to the existence of a relationship between anxiety states and depression. However, the fact that only 2 percent of those who were first diagnosed as depressed became anxious at a later time indicates that the two syndromes are distinct. This latter view is further supported by other investigations.

In a series of studies, Roth and his colleagues (Gurney et al. 1972; Roth et al. 1972) examined differences and similarities between patients diagnosed as anxious and those labeled depressed. A first bipolar component of anxiety vs. depression emerged when a principal component analysis was performed on the data. Moreover, the presence of an anxiety syndrome decreased the likelihood that a depressive syndrome would be detected in the same patient and vice versa. These results offer strong support for the separatist camp; they should, however, be considered with caution since the studies suffer from several methodological flaws.

Fleiss et al. (1971), in studying 500 admissions to New York and London mental hospitals, found depression and phobic anxiety to be distinct factors. In the total sample 14 subjects were classified as suffering from anxiety neurosis and 63 were neurotic depressives. When the scores of these patients on depression and on anxiety were examined, the authors found that both groups were equally depressed; but anxiety scores differentiated the two, being higher in the anxiety group. Further support for the separatist view was provided by Prusoff and Klerman (1974) as well as by Downing and Rickels (1974) who were able to separate anxiety from depression on the Hopkins Symptom Checklist. However, a relatively large overlap betwen the two groups existed (25 to 40 percent) and high correlations between anxiety and depression were consistently found. Interestingly enough, Klerman (1980) quoted the above studies in support of the distinction between depression and anxiety syndromes whereas Marks (in press) referred to these same studies when questioning the usefulness of such a separation.

A distinction between anxiety and depression has also emerged from a study on the effects of behavioral treatment of obsessive-compulsives conducted by the first author, (e.g., Foa & Goldstein 1978; Foa et al. 1980; Steketee et al., in press). In the course of evaluating the effectiveness of behavioral treatment, both the patients and an independent assessor rated depression and anxiety *mood states* on 9-point scales which were developed at the Maudsley Hospital in London (Watson et al. 1971). Depression was defined as loss of interest, crying, pessimistic outlook, sadness, and suicidal thoughts. Anxiety was defined as subjective tensions, autonomic arousal, and motor restlessness. There was almost no overlap between the guidelines given to the raters about the type of emotions and behavior they were to consider for determining the scores of the two variables. Data on levels of depression and anxiety in 71 obsessive-compulsives were thus obtained.

To investigate the joint occurrence of the two variables, patients were divided into three groups with respect to their level of depression. Those whose level of depression was greater than one standard deviation (SD) above the mean were considered "highly" depressed, those whose level was one SD below the mean were labeled "mildly" depressed, and the remainder were classified as "moderately" depressed. The same was done with regard to anxiety. The results were then cross-tabulated. They are given in Table 1.

A strong relationship emerged ($X^2(4) = 16.94$, $p < .01$). However, inspection of the joint occurrence of these variables revealed an interesting pattern. Only 50 percent of the sample fell on the diagonal where the degree of depression and of anxiety were equal. Those who were highly depressed were almost always highly anxious. On the other hand, most highly anxious patients were only moderately depressed. Further, mild depression was associated with *either* moderate or low anxiety. The moderately depressed patients were *either* very anxious or moderately anxious. This asymmetry in the relationships between levels of depression and levels of anxiety suggests that the authors tapped two distinct phenomena and that the relationship found does not merely represent a reliability score for two measures of the same variable.

Table 1

Joint Distribution of Anxiety and Depression Levels in Obsessive-Compulsives Before Treatment

Anxiety	Depression			
	High	Moderate	Mild	Total
High	8	20	2	30
Moderate	1	19	6	26
Mild	0	8	7	15
Total	9	47	15	71

Differences in Responsiveness to Behavioral Treatment

An important criterion favoring a distinction between two conditions is whether they respond differently to treatment. The literature on the effects of psychopharmacological agents on depressed and anxious patients has yielded a mixed picture in this regard and will not be discussed here. Instead, the authors shall consider the differential effects of pretreatment depression and anxiety mood states on effectiveness of behavioral techniques (i.e., exposure and response prevention) with obsessive-compulsive ritualizers. These techniques have been considered the treatment of choice for this disorder (cf. Foa & Steketee 1979). However, several authors suggested that obsessive-compulsives with marked depression do not benefit from treatment by exposure and response prevention as much as those with moderate or mild depression. Indeed, Foa et al. (1982) found that marked depression impeded the immediate effectiveness of behavioral treatment and resulted in a significantly higher rate of relapse.

In a subsequent analysis with a larger sample of 71 patients, the relationship of anxiety as well as of depression to treatment outcome were examined immediately following treatment and at 11 months followup (on the average). The scores for obsessions and compulsions as rated by an independent assessor were combined to yield one score of obsessive-compulsive symptomatology. This score was then converted into a percentage score of change from pretreatment baseline. On the basis of this score, the patients were divided into three groups: those who improved 70 percent or above were labeled "much improved"; those with improvement of 30 to 69 percent were labeled "moderately improved"; patients who failed to show improvement of more than 29 percent were considered "failures". This analysis was performed separately for outcome at posttreatment and at followup.

Prediction from Depression

The relationship between initial depression and treatment outcome was examined with a one-way analysis of variance (ANOVA). Significant differences were detected at posttreatment [$F(2,68) = 6.77$, $p < .002$]. The mean depression scores for those who succeeded, improved, or failed to benefit from behavioral treatment were 3.15, 4.64, and 5.19, respectively. Posthoc pairwise comparisons using the Bonferoni *t*-method revealed that the much improved group was significantly less depressed than the moderately improved group ($t = 3.14$, *d.f.* 68, $p < .01$) than those who failed ($t = 2.88$, *d.f.* 68, $p < .05$). At followup those who were treated successfully were significantly less depressed than the failures ($t = 2.92$, *d.f.* 51, $p < .05$), but did not differ from the moderately depressed patients.

The relationship between depression and treatment outcome was further explored by cross-tabulating the data at posttreatment and at followup. These results are given in Tables 2 and 3.

Table 2

Comparison of Initial Depressed Mood with Outcome at Posttreatment

Outcome	Depression High	Moderate	Mild	Total
Much Improved	1	17	12	30
Moderately Improved	7	23	2	32
Failure	2	7	0	9
Total	10	47	14	71

Table 3

Comparison of Initial Depressed Mood with Treatment Outcome at Followup

Outcome	Depression High	Moderate	Mild	Total
Much Improved	1	17	11	29
Moderately Improved	2	5	2	9
Failure	5	14	0	19
Total	8	36	13	57[a]

[a] At the time this analysis was performed, 14 of the 71 patients had not yet been followed up.

A chi-square performed on these data indicated significant differences at both posttreatment ($X^2(4) = 15.99$, $p = .003$) and at followup ($X^2 = 12.54$, $p = .01$). Inspection of these tables indicates that immediately after 2-3 weeks of daily 2-hour sessions by exposure and response prevention, 12 of the 14 patients who were mildly depressed were much improved, and none failed. The highly depressed groups had one success and two failures; the majority of the patients in this group were moderately improved (*see* Table 2). This pattern became more clear at followup (*see* Table 3). Of the eight patients with marked depression five were failures; none of the mildly depressed patients was a failure and 87 percent were highly improved. Thus, the level of depression at the extremes predicted response to treatment. Patients with marked depression were likely to fail to benefit from behavioral treatment; those with mild or no depression were highly likely to benefit from this treatment.

Table 4

Comparison of Initial Anxious Mood with Outcome at Posttreatment

Outcome	Anxiety High	Moderate	Mild	Total
Much Improved	10	9	12	31
Moderately Improved	16	13	2	31
Failure	5	3	1	9
Total	31	25	15	71

Table 5

Comparison of Initial Anxious Mood with Outcome at Followup

Outcome	Anxiety High	Moderate	Mild	Total
Much Improved	11	7	11	29
Moderately Improved	3	3	3	9
Failure	11	8	0	19
Total	25	18	14	57[a]

[a] At the time this analysis was performed, 14 of the 71 patients had not yet be followed up.

Prediction from Anxiety

A different picture emerged for the investigation of the relationship between anxiety and treatment outcome, although anxiety was also found related to responsiveness to behavioral treatment. (At posttreatment $F[2,68] = 4.99$, $p < .01$; a followup $F[2,51] = 3.24$, $p < .05$.) When degree o anxiety was cross-tabulated with degree of success in behavioral treatment, a significant relationship was again detected. (At posttreatment

$X^2(4) = 10.53$, $p < .03$; at followup $X^2(4) = 9.56$, $p = < .05$.)

However, the pattern for anxiety as a predictor of treatment outcome differed from that for depression. At posttreatment (*see* Table 4) one third of the highly anxious patients were much improved, although their chances were not as good as those who were initially mildly anxious. Among the latter, most were much improved and only one failed. A similar pattern emerged at followup (*see* Table 5).

In summary, mild depression predicted success and high depression predicted failure of behavioral treatment with obsessive-compulsives. By contrast, even a high level of anxiety was associated with good response to treatment. This pattern became more pronounced at followup (*see* Tables 3 and 5). Marked depression predicted failure, whereas high anxiety was equally associated with success and with failure.

Conclusion

The mood states of anxiety and depression have yielded a somewhat different prognosis in the study reported here, despite the crude measurements which have been employed. The existence of such a difference indicates that a distinction between depression and anxiety might be useful for predicting the outcome of behavioral treatment. Paradoxically, such a distinction is also a *sine qua non* for the investigation of the empirical joint occurrence of anxiety and depression, an issue that has gained much attention in the psychiatric literature. Only definitions which are independent of one another will lead to the construction of instruments of depression and anxiety which will not overlap each other. Only such instruments may yield valid data for the understanding of the relationship between two concepts.

Each instrument should include items from several components (at least from the cognitive and behavioral domains) and each should exclude items which are common to the two syndromes. In essence, then, the investigation of the relationship between depression and anxiety will involve comparisons of several clusters of observations rather than of two single indices composed of a variety of symptoms which has been forcibly combined. The results so obtained will hopefully contribute to a more lucid conceptualization of the two syndromes. As the relationship between concepts and data is a reciprocal one, more precise concepts lead to better measurements which, in turn, yield information that further clarifies theoretical issues.

References

Cooper, B., and Sylph, J. Life events in the onset of neurotic illness: An investigation in general practice. *Psychol Med.*, 3:421-435, 1973.

Downing, R.W., and Rickels, K. Mixed anxiety-depression: Fact or myth? *Arch. Gen. Psychiatry,* 30:312-317, 1974.

Foa, E.B., and Goldstein, A. Continuous exposure and complete response preventions in the treatment of obsessive-compulsive neurosis. *Behav. Ther.*, 9:821-829, 1978.

Foa, E.B., Grayson, J.B., and Steketee, G. Depression, habituation, and treatment outcome in obsessive compulsives. In: Boulougousis, J.C., (ed.), *Practical Applications of Learning Theories in Psychiatry,* New York:John Wiley & Sons, 1982.

Foa, E.B., and Steketee, G. Obsessive compulsives: Conceptual issues and treatment interventions. In: Herson, M., Eislers, R.M., and Miller, P.M. (eds.), *Progress in Behavor Modification,* Vol. 8. New York:Academic Press, 1979.

Foa, E.B., Steketee, G., and Milby, J.B. Differential effects of exposure and response prevention in obsessive-compulsive washers. *J. Consult. Clin. Psychol.*, 48:71-79, 1980.

Fleiss, J.L., Gurland, B.G., and Cooper, J.E. Some contributions to the measurement of psychopathology. *Br. J. Psychiatry,* 119:647-656, 1971.

Gurney, C., Roth, M., Garside, R.F., Kerr, T.A., and Schapira, K. Studies in the classification of affective disorders. The relationships between anxiety states and depressive illness. II. *Br. J. Psychiatry,* 121:162-166, 1972.

Kandell, R.E. The stability of psychiatric diagnosis. *Br. J. Psychiatry,* 124:352-356, 1974.

Kelly, D.H.W., and Walter, C.J.S. The relationships between clinical diagnosis and anxiety assessed by forearm blood flow and other measurements. *Br. J. Psychiatry,* 114:611-626, 1969.

Klerman, G.L. Anxiety and depression. In: Burrows, G.D., and Davies, B. (eds.), *Handbook of Studies on Anxiety.* Amsterdam:Elsevier/North Holland Biomedical Press, 1980.

Lader, M.H. Palmer skin conductance measures in anxiety and phobic states. *J. Psychosom. Res.*, 11:271-281, 1967.

Lader, M.H. *The Psychophysiology of Mental Illness.* London: Routledge & Kegan Paul, 1975.

Lader, M.H. Physiological research in anxiety. In: van Praag, H.M. (ed.), *Research in Neurosis.* Utrecht:Bohn, Scheltema, & Holkema, 1976.

Lader, M.H., Gelder, M.G., and Mark, I.M. Palmer skin conductance measures as predictors of response to desensitization. *J. Psychosom. Res.*, 11:283-289, 1967.

Lader, M.H., and Wing, L. Habituation of the psychogalvanic reflex in patients with anxiety states and in normal subjects. *J. Neurol. Neurosurg. Psychiatry,* 27:210-218, 1964.

Lader, M.H., and Wing, L. *Physiological Measures, Sedative Drugs, and Morbid Anxiety.* London:Oxford University Press, 1966.

Lader, M.H., and Wing, L.P. Physiological measures in agitated and retarded depressed patients. *J. Psychiatr. Res.,* 7:89-100, 1969.

Lewis, A.J. Psychological medicine. In: Bodley Scott, R. (ed.), *Practice of Medicine,* 10th ed. London:Oxford University Press, 1966.

Marks, I.M. Stress and other risk factors in anxiety disorders. In: Goldstone, S., and Goldman, H. (eds.), *Stress and Psychiatric Disorders.* NIMH Publication. (In press)

Prusoff, B, and Klerman, G.L. Differentiating depressed from anxious neurotic outpatients. *Arch. Gen. Psychiatry,* 30:302-309, 1974.

Roth, M., Gurney, C., Garside, R.F., and Kerr, T.A. Studies in the classification of affective disorders. The relationships between anxiety states and depressive illness. *Br. J. Psychiatry,* 121:147-161, 1972.

Roth, M., and Mountjoy, C.Q. The distinction between anxiety states and depressive disorders. In: Paykel, E.S. (ed.), *Handbook of Affective Disorders.* Edinburgh:Churchill Livingstone, 1982.

Shagass, C. Differentiation between anxiety and depression by the photically activated electroencephalogram. *Am. J. Psychiatry,* 112:41-46, 1955.

Snaith, R.P. *Clinical Neurosis.* New York:Oxford University Press, 1981.

Snaith, R.P., Ahmed, S.N., Mehta, S., and Hamilton, M. Assessment of the severity of primary depressive illness: Wakefield Self-Assessment Depression Inventory. *Psychol. Med.,* 1:143-149, 1971.

Steketee, G., Foa, E.B., and Grayson, J.B. Recent advances in the behavioural treatment of obsessive-compulsives. *Arch. Gen. Psychiatry.* (In press)

Watson, J.P., and Marks, I.M. Relevant and irrelevant fear in flooding: A crossover study of phobic patients. *Behav. Ther.,* 2:235-245, 1971.

Differentiating Anxiety and Depression in Anxiety Disorders: Use of Rating Scales

Ronald S. Lipman, Ph.D.[1]

Both anxiety and depression have been conceptualized as normal affects or moods, as symptoms (when their intensity or duration persists beyond "normal" limits), as syndromes (when a cluster of co-occurring symptoms are identified), and as diagnostic entities (when notions of differential etiology, prognosis, and/or treatment response as well as boundaries between mental disorders are employed) (Diagnostic and Statistical Manual-III 1980; Lehmann 1966).

This paper will focus on differentiating anxiety and depression at the level of syndromes and diagnoses. It should be made clear that while some writers consider anxiety and depression as phenomenally indistinguishable (e.g., Lewis 1966), the overwhelming consensus in the field is that these two affective disorders are separable and, indeed, that neither anxiety nor depressive disorders are themselves single mental disorders. This area has recently been reviewed by McNair and Fisher (1978) and, indeed, the reader is probably familiar with both statistical typologies such as Overall et al. (1966) (based on Brief Psychiatric Rating Scale scores on Anxious, Hostile, Agitated, and Retarded Depression), and clinical typologies such as Klein's (1974) concept of reactive, endogenomorphic, and neurotic depression. Since the Diagnostic and Statistical Manual-III (DSM-III) (1980) differentiates among and between anxiety disorders and affective disorders, which subsume depresssion, it is probably worthwhile to examine the DSM-III classification of primary anxiety disorders. In this regard, DSM-III, as a result of the research of Klein (1978), differentiates between Panic Disorder and Generalized Anxiety Disorder, both characterized by free or manifest anxiety, and Phobic and Obsessive-Compulsive Disorders, where the patient goes to extremes to avoid experiencing the anxiety of either the dreaded object or situation or of the resisted obsession or compulsion. A good description of Phobic and Anxiety States, based on DSM-III, has been developed by Davis et al. (1981) and is presented in Table 1.

Table 1

Diagnostic Description of Phobic Disorders and Anxiety State

Sudden spontaneous unexplained panic attack characterized by feeling of terror, autonomic symptoms of anxiety, and flight response

Symptoms during an attack may include:

- Anxiety, terror, helplessness, impending doom
- Smothering or choking feeling, difficulty getting breath
- Dizziness or faintness
- Trembling
- Tingling, hot or cold spells
- Chest pain or discomfort
- Nausea
- Palpitation and rapid heart beat
- Sudden empty feeling in pit of stomach

Fear of places where attack occurs

- Public places (restaurants, stores, buses)
- Fear that one cannot reach secure place such as home

---

[1] The Johns Hopkins University School of Medicine, The Henry Phipps Psychiatric Clinic, Baltimore, MD 21205.

Table 2

RDC Inclusion Criteria for Major Depressive Disorders: The Presence of a-d Are Required

YES	NO	(a)	Dysphoric mood or pervasive loss of interest or pleasure. The period(s) of dysphoric mood is/are characterized by such symptoms as "depressed, sad, blue, hopeless, down in the dumps, don't care anymore or irritable."
YES	NO	(b)	At least *five* of the following symptoms are necessary to have occurred as part of the episode for "definite" depression and *four* for "probably" depression.
YES	NO		(1) Poor appetite or weight loss or increased appetite or weight gain (change of 1 pound a week of 10 pounds a year with no dieting).
YES	NO		(2) Sleep difficulty or sleeping too much.
YES	NO		(3) Loss of energy, fatigability, or tiredness.
YES	NO		(4) Psychomotor agitation or retardation (but not mere subjective feeling of restlessness or being slowed down
YES	NO		(5) Loss of interest or pleasure in usual activities, including social contact or sex (not included or limited to a period when delusional or hallucinating). (The loss may or may not be pervasive).
YES	NO		(6) Feelings of self-reproach or inappropriate guilt (either may be delusional).
YES	NO		(7) Complaints or evidence of diminished ability to think or concentrate, such as slowed thinking, or indecisiveness (do not include if associated with marked formal thought disorder).
YES	NO		(8) Recurrent thoughts of death or suicide, or any suicidal behavior.
YES	NO	(c)	Duration of dysphoric features at least 1 week beginning with the first noticeable change in the subject's usual condition ("definite" means lasted more than 2 weeks, "probably" if 1 to 2 weeks).
YES	NO	·(d)	Sought or was referred for help from someone during the dysphoric period, took medication, or had impairment in functioning with the family, at home, at school, or socially.

The Phobic Disorders are subdivided into agoraphobia (with or without panic attacks), Simple Phobia, and Social Phobia.

DSM-III also recognizes and defines a number of depressive disorders based on such considerations as severity, and whether or not there has been a history of manic or hypomanic features (see DSM-III, pp. 220-224). Since a number of large-scale collaborative studies are employing the Research Diagnostic Criteria (RDC) for Major Depressive Disorder (Feighner et al. 1972), these inclusion criteria are summarized in Table 2.

In practice, many research studies focused on the evaluation of pharmacotherapy and/or psychotherapy for the treatment of nonpsychotic, nonbipolar, depressed outpatients, as well as studies on nonpsychotic outpatients. These studies have employed rating scales and checklists to help define their anxious and depressed cohorts (e.g., Lipman et al. 1981). In this regard, two relatively simple physician rating scales have been developed by Raskin and by Covi (Lipman et al. 1981). Each scale employs three subscales which tap the dimensions of verbal report, behavior, and somatic symptoms. Typically, a minimal severity sum of 7, 8, or 9 has been employed on thes scales (range from 0 to 15) to select patients with sufficient severity of anxiety and/or depresssion to qualify the patient for inclusion in treatment outcome studies with antidepressant and/or antianxiety medications. The Covi Anxiety Scale is presented in Table 3 and the Raskin Depresssion Scale is shown in Table 4.

Table 3

not at all	somewhat	moderately	considerably	very much	Anxiety Scale (Covi)
1	2	3	4	5	**Verbal Report:** Feels nervous, shaky, jittery, jumpy, suddenly scared for no reason; fearful, apprehensive, tense or keyed up; has to avoid certain things, places, activities because of getting frightened; finds it hard to keep mind on task.
1	2	3	4	5	**Behavior:** Appears frightened, shaking, restless, apprehensive, jumpy, jittery.
1	2	3	4	5	**Somatic Symptoms of Anxiety:** Unjustified sweating, trembling; heart pounding or racing; trouble getting breath; hot or cold spells; restless sleep; going unjustifiably more frequently to bathroom; discomfort at pit of stomach; lump in throat.

Table 4

not at all	somewhat	moderately	considerably	very much	Depression Scale (Raskin)
1	2	3	4	5	**Verbal Report:** Feels blue; talks of feeling helpless, or worthless; complains of loss of interest; may wish to be dead; reports of crying spells.
1	2	3	4	5	**Behavior:** Looks sad, cries easily, speaks in a sad voice; appears slowed down; lacking energy.
1	2	3	4	5	**Secondary Symptoms of Depression:** Insomnia or hypersomnia; G.I. complaints; dry mouth; history of recent suicide attempt; lack of appetite; difficulty in concentrating or remembering.

In addition to these very simple scales, the study utilized other physician (therapist) rating scales, namely, the American College of Neuropsychopharmacology (ACNP) Checklist for Anxiety and Depression (Wittenborn 1977); and the Hamilton Anxiety and the Hamilton Depression Scales (ECDEU Assessment Manual 1976). Since the ACNP Anxiety and Depression checklists are not generally available, and since these scales were specifically developed as guidelines for the Food and Drug Administration (FDA) in evaluating the adequacy of subject selection for trials of antianxiety and antidepressant medications, respectively, they are presented here in Tables 5 and 6.

Table 5

ACNP Depression Checklist

YES	NO	Main Symptoms
____	____	Dysphoric Mood (depressed, sad, despondent, hopeless, down in the dumps, discouraged).
		Associated Symptoms
____	____	Poor appetite and weight loss (2 lbs per week or 10 lbs per year, if not dieting).
____	____	Sleep difficulty (insomnia or hypersomnia)
____	____	Loss of energy (fatigability, tiredness)
____	____	Agitation or retardation
____	____	Recent loss of interest in usual activities and decreased libido
____	____	Self-reproach or guilt feelings
____	____	Complaints of (or actually diminished) thinking and concentration (slow thinking, mixed-up thoughts)
____	____	Recurrent thoughts of death or suicide, wish to be dead
____	____	Anhedonia (inability to experience pleasure)
____	____	Bodily complaints.

It should be noted that the ACNP Anxiety guidelines require "moderate" levels, or higher, on the first two manifestations (feeling nervous, jittery, jumpy; feeling fearful, apprehensive, anxious, panicky) and at least three other symptoms and signs of anxiety. The syndrome definition of depression requires depressed mood (characterized by "sad, low, blue, despondent, hopeless, gloomy") plus four or five of the associated symptoms. It is interesting to note that anxiety and tension (Item 14) and agitation (Item 6) which are included as symptoms of the depressive syndrome are also contained as part of the symptomatology of the anxiety syndrome. Similar overlaps of symptomatology, i.e., sleep disturbance, are also present on the Hamilton Anxiety and Hamilton Depression Scales. The members of the ACNP task force that drafted these guidelines were aware of the issues around the separation and overlap among patients with anxiety and/or depression.

In this regard, they indicate "the coexistence of anxiety and depression...also presents a special problem. Although the two states frequently occur together in varying degrees, most patients can be classified as primarily anxious or primarily depressed." (p. 220)

Table 6

ACNP Anxiety Checklist

YES	NO	Main Symptoms
____	____	Feeling nervous, jittery, jumpy
____	____	Feeling fearful, apprehensive, anxious, panicky
		Associated Symptoms
____	____	Fears of fainting, screaming, losing control, crowds, places, disaster, death
____	____	Avoiding certain places, things or activities because of fear
____	____	Feeling tense or keyed up
		Muscular or Motor Phenomena
____	____	Tense Muscles, aches
____	____	Trembling, shaking
____	____	Restlessness, fidgeting
		Autonomic Phenomena
____	____	Heart beating fast or pounding; chest pain
____	____	Trouble catching breath, air hunger, smothering, lump in throat, choking
____	____	Sweating, especially armpits, palms, soles of feet
____	____	Cold clammy hands
____	____	Dry mouth
____	____	Dizziness, faintness, lightheadedness, weakness
____	____	Tingling feelings in hands or feet
____	____	Stomach "gas," nausea, upset stomach

Table 7

HSCL Anxiety Cluster

Items	R11
Nervousness or shakiness inside	
Heart pounding or racing	
Sweating	
Suddenly scared for no reason	
Trouble getting your breath	
Trembling	
Hot or cold spells	
Feeling tense or keyed up	
Faintness or dizziness	
Feeling fearful	
A lump in your throat	0.80

Table 8

HSCL Depression Cluster

Items	R11
Feeling low in energy or slowed down	
Thoughts of ending your life	
Poor appetite	
Feeling blue	
Feeling no interest in things	
Feeling hopeless about the future	
Blaming yourself for things	
Loss of sexual interest or pleasure	
Crying easily	
Feeling lonely	
Constipation	0.81

In addition to the use of therapist rating scal to help select anxious or depressed patients, man research teams also make use of patient sel ratings. Among the most frequently used of th patient self-rating scales is the Hopkins Sympto Checklist (Lipman et al. 1979). Normative dat are available for the 58-item version of this Scal (Derogatis et al. 1974) and many investigato have required that patients rate themselves at level of distress on the Anxiety and/or Depressio Clusters at least two standard deviations highe than the means of the normative sample, i.e., score of 1.65 on the Anxiety Cluster and a score o 1.70 on the Depression Cluster. The items tha define these clusters are presented in Tables 7 an 8.

The clusters themselves reflect the consens among experienced clinicians that the items subsumed in each cluster reflect either anxiety o depression (Lipman et al. 1968). In this regard there was at least 75 percent agreement amon each of 20 experienced clinicians that the item given in Tables 7 and 8 reflected either anxiety o depression. The Hopkins Symptom Checkli (HSCL) was employed by Prusoff and Klerma (1974) in a study of anxious and depressed outpatients who participated in trials of antianxiety an antidepressant medications, respectively. Th depressed sample consisted of patients who wer treated in either New Haven or Baltimore; th anxious patients all had participated in controlle psychotropic drug trials at the Johns Hopkin University and were selected from a much large data file to match the depressed sample on age, sex, and social class. A discriminant functio analysis was employed to determine whether o not the five factors of the HSCL would reliably differentiate the anxious and depressed samples. While the 66 percent discrimination of diagnostic groups was reliably better than would by expected by chance, these data suggest considerable overlap among diagnostic groups. The main discrimination in this study was derived from the Somatization factor of the HSCL which was higher in the anxious sample despite the generally higher level of distress in the depressed group. The use of the individual items of the HSCL did not add much to the separation of diagnostic groups. In an earlier less systematic study by Kellner et al. (1972), somatic symptoms were also found to occur more with anxiety than with depression.

In a very large sample collaborative study supported by the Pharmacologic and Somatic Treatments Research Branch of the National Institute of Mental Health, Johns Hopkins University (L. Covi, Principal Investigator), Boston University (D. McNair, Principal Investigator), and the University of Pennsylvania (K. Rickels, Principal Investigator), the issue of the distinctiveness between anxiety states and depressed disorders was addressed within the context of a placebo-controlled drug trial which employed tranquilizers and tricyclic antidepressants. The preliminary results of this study were reported at the December 1980 meeting of the ACNP, and four papers were subsequently published in the July 1981 issue of the *Psychopharmacology Bulletin* (Covi et al. 1981; Downing et al. 1981; Kahn et al. 1981; Lipman et al. 1981).

In order for outpatients to be selected for this study, they must have self-rated themselves as significantly anxious and/or depressed on the corresponding HSCL clusters of Anxiety (1.65 or higher) or Depression (1.70 or higher) and must also have been rated at least "moderately" anxious and/or depressed by the intake psychiatrist on the Raskin and/or Covi screens (8 or higher). Additionally, the patient must have been anxious and/or depressed for at least 2-3 weeks prior to intake and must not have ever been schizophrenic, alcoholic- or drug-addicted, mentally retarded, organically impaired, sociopathic, or bipolar.

In addition to these main inclusion and exclusion criteria, patients were also classified by DSM-II criteria and according to categories of anxiety and/or depression as proposed by such investigators as Klein and Davis (1969) and Overall et al. (1966). Since the primary purpose of the study was to assess the clinical response of anxious and depressed outpatients to commonly employed anxiolytics and antidepressants, the reliability with which these groups can be identified and the distinctiveness of the groups in terms of diagnosis and presenting symptomatology is critical. In order to address these issues, each patient was classified as primarily anxious or primarily depressed on three separate occasions: 1) by an intake psychiatrist; 2) 1 week later by the psychiatrist who treated the patient; and 3) by this same treating psychiatrist after the patient had completed a 2-week placebo washout period. The agreement in diagnostic assignments was reflected by Kappas of .62 between the intake and treating psychiatrists and .73 between the same psychiatrists before and after the 2-week placebo period. Eighty-seven percent of the patients classified as depressed at intake and 75 percent of those classified as anxious at intake were again so classified by an independent psychiatrist 1 week later. These respective proportions were 90 and 83 percent in the ratings of the same psychiatrists which were made 2 weeks apart. Clearly, then, the assignment of anxious and depressed patients to diagnostic groups has been made with reasonable reliability.

In addition to the scales already mentioned, the study also employed the Hamilton Anxiety and Hamilton Depression Scales and the ACNP Checklist for Anxiety and for Depression. A typical psychiatric and family history was also collected on each patient, and DSM-II diagnoses were made. Not surprisingly, 93 percent of the patients judged to be primarily anxious received the diagnosis of Anxiety Neurosis, whereas about 88 percent of those patients classified as primarily depressed were given the diagnosis of Depressive Neurosis. Other diagnostic details are given in Downing et al. (1981).

Although there was considerable overlap in levels of anxiety and depression between the 424 patients classified as primarily depressed and the 240 patients classified as primarily anxious, each scale reliably differentiated between the diagnostic groups in the expected direction. On the Covi Anxiety Scale the mean for the anxious group (10.4) was significantly higher ($p < .001$) than the mean (8.31) for the depressed group. On the Raskin Depression Scale the mean for the depressed (10.4) sample was reliably higher

($p<.001$) than the mean for the anxious (7.65) sample. Statistically significant differences of roughly comparable magnitude were also found when the mean scores of the anxious and depressed groups were contrasted on the ACNP checklists of Anxiety and Depression. Similar results were also observed for the Hamilton Anxiety and the Hamilton Depression Scales. The results for the ACNP Anxiety and Depression Checklist are shown in Figure 1.

ANXIETY AND DEPRESSION — FDA GUIDELINE CHECKLIST
(Anxiety: N=226; Depression: N=404)

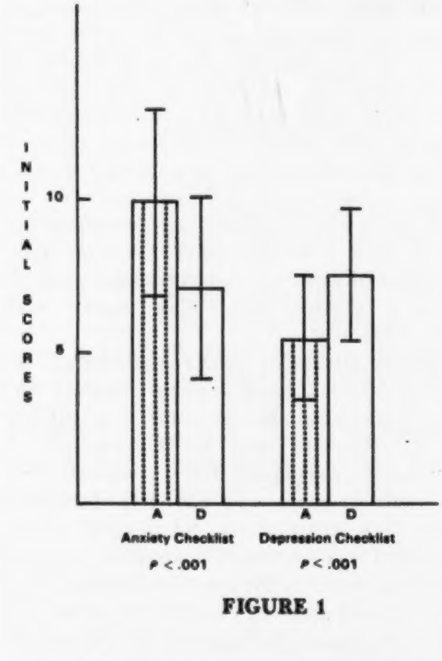


FIGURE 1

The results obtained on the HSCL agree with the prior findings of Downing and Rickels (1974), "...anxiety and depression dominated the symptom profiles of all patients, but in anxiety study patients, anxiety was the more severe...while in depression study patients, depression was the more severe." In the present study, mean cluster scores for the anxious group were significantly higher for Anxiety ($p<.025$) and Somatization ($p<.025$) whereas in the depressed group, mean scores were higher on the Depression ($p<.001$), Obsessive-Compulsive ($p<.001$), and Anger-Hostility ($p<.025$) clusters. In the depressed group, the ranking of symptom distress from hi to low was Depression, Obsessive-Compulsiv Anxiety, Somatization, and Anger-Hostility. T corresponding ranking in the anxious group wa Anxiety, Depression, Obsessive-Compulsiv Somatization, and Anger-Hostility. A somewh more fine-grained breakdown of symptom profil for the nine apriori factor scores postulated to b contained in the 90-item version of the HSCL i presented in Figure 2.

As expected, the anxious group self-ra themselves higher than the depressed group o items contained in the Phobic-Anxiety clust ($p<.001$). When the relative rankings of the ni clusters of the HSCL are compared in the anxio and depressed groups, it is of interest that th rank-order correlation (RHO) of .87 ($p<.01$) i quite high. This indicates that, despite th statistically significant differences in level o distress on these dimensions of symptomatolog the pattern or profile of distress is quite similar i primarily anxious and primarily depressed pa tients. Indeed, were it not for the differences be tween groups in the relative rank ordering of anx iety (1.5 in the anxious group vs. 6 in the depres ed group) and depression (4 in the anxious vs. 1 i the depressed), the correlation in ranks would b almost perfect.

To further pursue the question of qualitativ differences in symptomatology between th primarily anxious and primarily depresse groups, the RHO among the 17 items comprisin the depression cluster and the RHO among the 1 items comprising the anxiety cluster wa calculated. For the depressed vs. anxious grou on the Depression cluster the rho was .95 ($p<.0$ while the RHO was .88 ($p<.05$) between group on the Anxiety cluster. In fact, the RHO of .7 was significant across groups on the 6-ite Phobic-Anxiety cluster. Clearly, then, there i both a remarkable similarity of symptom profile across the various domains of outpatient distres as well as within the more specific areas o depressive and anxious symptomatology. I should also be made clear to the reader that th symptom levels of nonpatient groups ar remarkably low and very significantly differen statistically than the observed levels in our anx ious and depressed groups (Derogatis et al. 1974)

In a further step to explore differences in symp tomatology between anxious and depresse samples, the specific symptoms which were rate

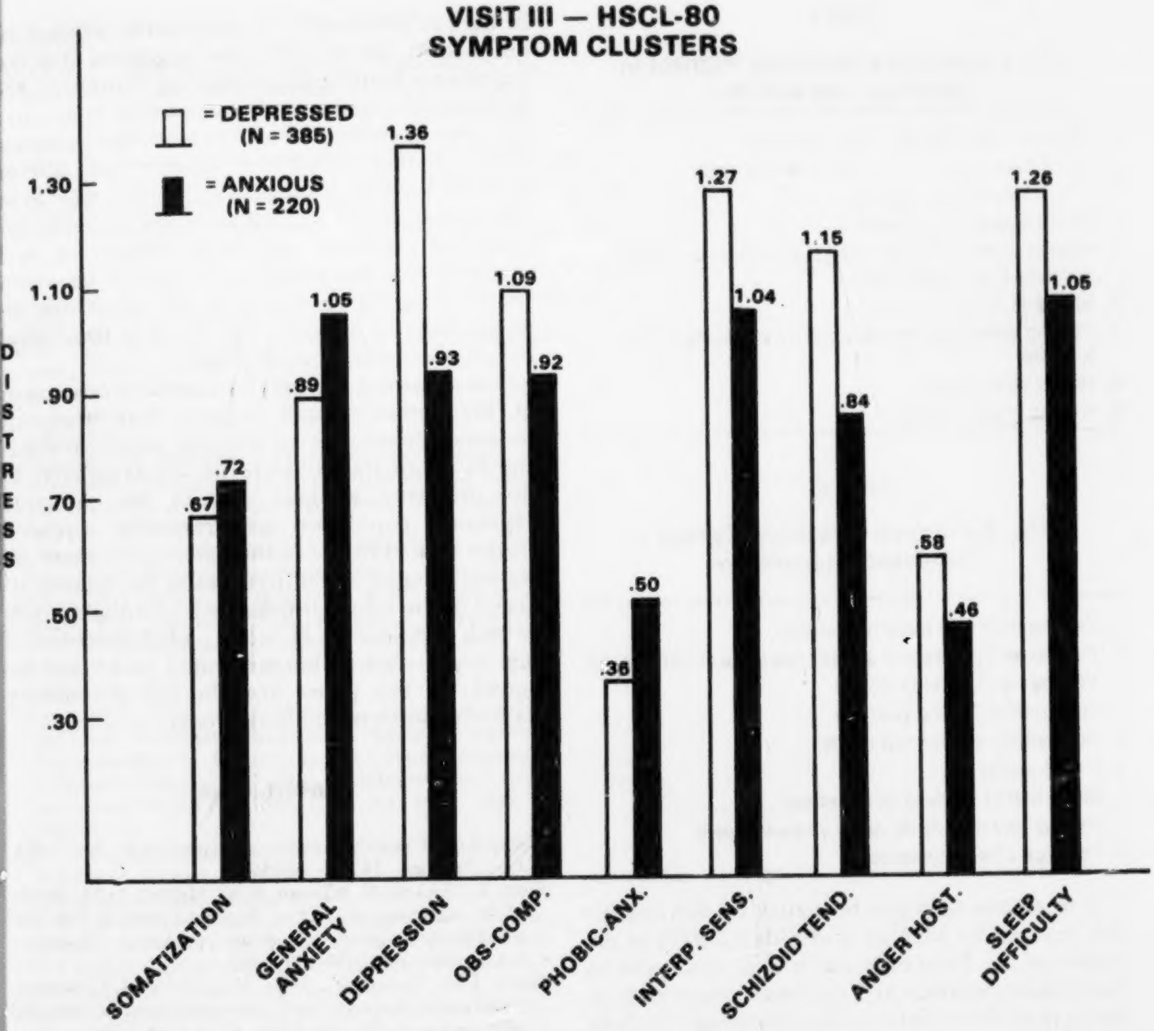


FIGURE 2

higher by anxious than depressed patients are presented in Table 9. The items comprising this table are clinically very meaningful and, in DSM-III terminology, they are associated with the diagnosis of Agoraphobia with Panic Attacks.

A similar analysis of items rated higher by depressed than anxious patients was cut off after nine items, since the depressed sample was relatively more distressed on all the items of the HSCL-80 with the exception of those items listed in Table 9. The nine items rated highest by the depressed group are presented in Table 10. First, it is clear that all the items in Table 10 are reflective of depression and, second, that the depression has an endogenous quality. Again, these are a very meaningful cluster of symptoms.

Table 9

HSCL Symptoms Relatively Highest in Anxious Outpatients

1. Feeling afraid you will faint in public
2. Numbness or tingling in parts of your body
3. Heart pounding or racing
4. Trouble getting your breath
5. Having to avoid certain things, places, or activities because they frighten you
6. Spells of terror or panic
7. Feeling uneasy in crowds such as shopping or at a movie
8. Hot or cold spells
9. A lump in your throat

Table 10

HSCL Symptoms Relatively Highest in Depressed Outpatients

1. Feeling hopeless about the future
2. Feeling all the pleasure and joy has gone out of your life
3. Feeling no interest in things
4. Thoughts of ending your life
5. Not getting any fun out of life
6. Crying easily
7. Sleep that is restless or disturbed
8. Feeling you may never enjoy yourself again
9. Feelings of worthlessness

One cannot help but be struck by the conclusion reached by McNair and Fisher (1978) in the review of the Newcastle study that attempted to discriminate anxious and depressed inpatients on the basis of their initial symptomatology. McNair and Fisher indicated: "several single symptoms correctly classified the sample...a little reflection on these symptoms suggests that panic anxiety versus endogenous depression or agoraphobia versus endogenous depression might more precisely name the factor."

As was pointed out early in this paper, neither anxiety disorders nor depressive disorders are unitary illnesses, and it would seem easier to differentiate certain types of anxiety disorders from certain types of depressive disorders. Again, these distinctions seem to be quantitative, rather than qualitative.

It should be noted that other domains than symptomatology as assessed by rating scales can be used to differentiate anxiety and depression. I this regard, Beck (1971) has suggested that th cognitive schemata characterizing depression di fer from the cognitive schemata found in anxiet He stresses themes of loss as underlying depre sion, whereas themes of danger are said underlie anxiety. Biological differences such as i blood flow and in cortisol secretion probably di ferentiate between primarily depressed an primarily anxious patients. Psychiatric history i terms of age of onset and family psychiatric il nesses are also relevant. Finally, it is also critic to consider treatment response.

The results of the collaborative study discusse in the present paper suggest that treatme response differences to tricyclic antidepressan and to minor tranquilizers are not as different i the primarily anxious and in the primaril depressed population as previously suppose (Kahn et al. 1981). On the other hand, there ar clinically important differences in the relative ef ficacy of the minor tranquilizer chlordiazepoxid in both populations. However, a full discussion o this more subtle difference would go beyond th bounds of this paper and the still preliminar nature of some of the data analytic results.

References

Beck, A.T. Cognition, affect, and psychopathology. *Ar Gen. Psychiatry*, 24:495-500, 1971.

Covi, L., Rickels, K. Lipman, R.S., McNair, D.M., Smith V.K., Downing, R., Kahn, R., and Fisher, S. Effects o psychotropic agents on primary depression. *Psychopha macol. Bull.*, 17(3):100-103, 1981.

Davis, J.M., Suhayl, N., Spira, N., and Vogel, C. Anxiety Differential diagnosis and treatment from a biologic perspective. *J. Clin. Psychiatry*, 42:11:4-41, 1981.

Derogatis, L.R., Lipman, R.S., Rickels, K., Uhlenhuth E.H., and Covi, L. The Hopkins Symptom Checklis (HSCL): A self-report symptom inventory. *Behav. Sci.* 19(1):1-15, 1974.

Diagnostic and Statistical Manual, 3rd ed. Washington, DC American Psychiatric Association, 1980.

Downing, R.W., and Rickels, K. Mixed anxiety-depression Fact or myth? *Arch. Gen. Psychiatry*, 30:312-317, 1974.

Downing, R.W., Rickels, K., McNair, D.M., Lipman R.S., Kahn, R.J., Fisher, S., Covi, L., and Smith, V.K Description of sample, comparison of anxious and depres ed groups, and attrition rates. *Psychopharmacol. Bull.* 17(3):94-96, 1981.

ECDEU Assessment Manual for Psychopharmacology, (Revised 1976). Rockville, MD: DHEW Publication No. (ADM 76-338), 1976.

Feighner, M.P., Robins, E., Guze, S.B., Woodruff, R.A. Winokur, G., and Munoz, R. Diagnostic criteria for us in psychiatric research. *Arch. Gen. Psychiatry,* 26:57-63, 1972.

Kahn, R.J., McNair, D.M., Covi, L., Downing, R.W., Fisher, S., Lipman, R.S., Rickels, K., and Smith, V.K. Effects of psychotropic agents on high anxiety subjects. *Psychopharmacol. Bull.,* 17(3):97-99, 1981.

Kellner, R., Simpson, G.M., and Winslow, W.W. The relationship of depressive neurosis to anxiety and somatic symptoms. *Psychosomatics,* 13:358-362, 1972.

Klein, D. Endogenous depression. *Arch. Gen. Psychiatry,* 31:447-454, 1974.

Klein, D., and Davis, J. *Diagnosis and Drug Treatment of Psychiatric Disorders.* Baltimore: Williams and Wilkins, 1969.

Klein, D.F., Zitrin, C.M., and Woerner, M. Antidepressants, anxiety, panic, and phobia. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress.* New York:Raven Press, 1978, pp. 1401-1410.

Lehmann, H.E. Depression: Categories, mechanisms, and phenomena. In: Cole, J.O., and Wittenborn, J.R. (eds.), *Pharmacotherapy of Depression.* Springfield, Ill.: Charles C Thomas, 1966, pp. 161-189.

Lewis, Sir A.J. *Price's Textbook of the Practice of Medicine.* London:Oxford University Press, 1966.

Lipman, R.S., Covi, L., Downing, R.W., Fisher, W., Kahn, R.J., McNair, D.M., Rickels, K., and Smith, V.K. Pharmacotherapy of anxiety and depression: Rationale and study design. *Psychopharmacol. Bull.,* 17(3):91-95, 1981.

Lipman, R.S., Covi, L., Rickels, K., Uhlenhuth, E.H., and Lazar, R. Selected measures of change in outpatient drug evaluation. In: Efron, D.H. (ed.), *Psychopharmacology: A Review of Progress, 1957-1967.* Washington, D.C.:U.S. Government Printing Office, Publ. No. 1836, 1968, p. 249-254.

Lipman, R.S., Covi, L., and Shapiro, A.K. The Hopkins Symptom Checklist (HSCL): Factors derived from the HSCL-90. *J. Affect. Disord.,* 1:9-24, 1979.

McNair, D.M., and Fisher, S. Separating anxiety from depression. In: Lipton, M.A., DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress.* New York:Raven Press, 1978, pp. 1411-1418.

Overall, J.R., Hollister, L.E., Johnson, M., and Pennington, V. Nosology of depression and differential response to drugs, *JAMA,* 195:946-948, 1966.

Prusoff, B., and Klerman, G.L. Differentiating depressed from anxious neurotic outpatients: Use of discriminant function analysis for separation of neurotic affective states. *Arch. Gen. Psychiatry,* 30:302-309, 1974.

Wittenborn, J.R. Guidelines for clinical trials of psychotropic drugs. *Pharmakopsychiatr. Neuropsychopharmakol.,* 10:205-231, 1977.

Are There Anticompulsive or Antiphobic Drugs? Review of the Evidence

Isaac Marks, M.D.[1]

This paper summarizes a more detailed review of controlled studies of antidepressants for phobic and obsesssive-compulsive disorders (Marks et al. in press). Despite their impressive differences in phenomenology, obsessive-compulsive and phobic disorders are dealt with together because they share common features of avoidance and accompanying discomfort as well as frequently coexisting dysphoria* (anxious-depressed mood), and both respond similarly to antidepressants and to behavioral treatments.

A literature search found 12 controlled studies of antidepressants for predominantly phobic and 4 for predominantly obsessive-compulsive problems which satisfied the criterion of a minimum of 8 patients who completed drug treatment (Ananth 1980; Gittelman-Klein & Klein 1971; Insel et al. 1982; Lipsedge et al. 1973; Marks et al. 1980, in press; Mavissakalian & Michelson 1982; McNair & Kahn 1981; Mountjoy et al. 1977; Pecknold et al.,1980; Sheehan et al. 1980; Solyom et al. 1981; Thorén et al. 1980; Tyrer et al. 1973; Zitrin et al. 1978, 1982). All reported drug dosages in the moderate-high range usually considered adequate for depressive illnesses. All concerned mainly female, adult populations aged 20-60 with problems which have usually been there from 1-10 years or more. Most concerned outpatients, though three involved inpatients who were obsessive-compulsive (Insel et al., 1982; Marks et al. 1980; Thorén et al. 1980). The phobics were largely agora- and social with panic attacks and anxiety-depression (dysphoria). The latter concerns symptoms, not diagnosis, as most studies excluded patients who had either severe depression as a symptom or depresssive illness as a diagnosis. One study concerned school phobics (Gittelman-Klein & Klein 1971) and another included a group of simple phobics (Zitrin et al. 1978).

Anxiety-Depression and Outcome

One predictor of drug effect seems to be the *starting level of dysphoria,* drug effects generally being absent where this is low. Lack of common measures across studies complicates the task, but five paired comparisons were possible of studies with common measures (Insel et al. 1982; Marks et al. 1981, in press; Mavissakalian & Michelson 1982; Sheehan et al. 1980; Solyom et al. 1981; Zitrin et al. 1980). In four of the five comparisons, the studies reporting drug effects had significantly higher starting levels of dysphoria than those finding no drug effects. The exception is Zitrin et al.(1980), whose patients had as low a rating as those of Marks et al. (1982) on the single depressive item on which they could be compared (Klein, personal communication).

Table 1 shows a detailed comparison between Sheehan et al. (1980) and Marks et al. (1982)—the latter's London sample tended to be *more* agoraphobic as well as *less* dysphoric than the former's Boston sample. This indicates that London and Boston patients did not differentially respond high or low to questions as a whole (no difference in response set), but rather to certain types of symptoms (they differed in the kinds of symptoms they emphasized. These comparisons highlight the difficulty in obtaining closely comparable populations across centers merely by utilizing diagnostic categories alone, and illustrate the additional need to report initial phenomenological features on standard measures.

---

[1] Institute of Psychiatry, London SE5 8AF, England. (This study was done while Dr. Marks was at the Center for Advanced Study in the Behavioral Sciences, Stanford, California.)

*"Dysphoria" here denotes symptoms of anxiety-depression, not the diagnosis of the syndromes of generalized anxiety state, dysthymia, or depressive illness. Anxiety and depression overlap so much both as symptoms and as syndromes that they are often indistinguishable (reviewed by Marks 1981b).

Table 1

Comparison of Initial Scores of Agoraphobics of Marks et al.*1982 (M) and Sheehan et al. 1980 (S)

		a None or Mild (Percent)	b Moderate (Percent)	c Extreme (Percent)
Depression				
(S) Feeling blue	$N = 57$	28	40	32[b]
(M) Feeling miserable or depressed	$N = 45$	55	32	13[b]
Agoraphobia				
(S) Phobia: Going out of house alone	$N = 57$	25	19	56[c]
(M) Phobia: Going out alone far from home	$N = 45$	16	11	73[c]

[a] none or mild = score 0, 1, or 2; moderate = score 3, 4, 5; extreme = score 6, 7, or 8.
[b] X^2 $p < .01$ (a vs. b vs. c)
[c] X^2 $p < .07$ (a + b vs. c)

A coarser way of judging the effect of dysphoria is by grouping the studies according to initial levels of dysphoria, regardless of the particular measure used (Table 2). Levels are based on scores reported elsewhere (Marks, in press-b). The lower right sector of Table 2 shows that in those four studies where a drug effect was absent the starting level of dysphoria was especially low. The placing of the study of Zitrin et al. (1980) is unclear, because on the Brief Psychiatric Rating Scale (BPRS) the sample would be rated as mild-moderately dysphoric, yet on another item (Table 1, and Klein, personal communication) it would be mild-absent.

Table 2

Outcome Versus Initial Depression Score (Controlled Studies of Phobics and Obsessive-Compulsives)

	Initial Mean Depression Score		
Drug Effect	Moderate	Moderate-Mild	Mild-Absent
Present	Sheehan et al. (1980)	Tyrer et al. (1973)	?Zitrin et al. (1980)
	McNair & Kahn (1981)	Zitrin et al. (1980)	
	Pecknold et al. (1980)	Mavissakalian & Michelson (1982)	
	Ananth et al. (1980)	Gittelman-Klein & Klein (1971)	
	Marks et al. (1980)	Insel et al. (1982)	
	Thoren et al. (1980)		
Absent			Marks et al. (1982)
			Solyom et al. (1981)
			Marks et al. (1980)
			Thoren et al.[a] (1980)

[a] See analysis of subsamples by Marks (1981, p. 176) and Table 1 of Thoren et al. (1980).

Initial depression scores not reported:
Drug effect present: Lipsedge et al. (1973)
Zitrin et al. (1978)
Drug effect absent: Mountjoy & Roth (1974)

Within three of the studies on obsessive-compulsives, direct comparison was possible between patients with the highest and the lowest levels of initial dysphoria. Two of these comparisons showed that the effect of clomipramine was exclusively attributable to those patients with the highest levels of dysphoria at the start, and was absent in those with initially low levels. Table 3 displays the data for clomipramine patients taken from Table 1 of Thorén et al. (1980).** Three of the eight clomipramine patients had secondary depression and these three responded in the open part of the study, while only one of the five without secondary depression was a drug responder (these were also the five patients with the highest plasma levels of clomipramine—Åsberg, personal communication). During the 5-week controlled phase of the study, pa-

---

**The Childrens' Psychiatric Rating Scale depression improvement scores were kindly supplied by Dr. Marie Åsberg.

Table 3

Effect of Depression on Outcome of Obsessive-Compulsive Disorders (From Table 1, Thorén et al. 1980)

Patient's Sex/Age	Secondary Depression?	Responder in Open Study After 5 Weeks?	Improvement At 5 Weeks Obsessional Symptoms	OCD Scale	Depression
M44	yes	yes	2.5	9.0	8.0
F50	"	"	2.0	7.5	9.0
F28	"	"	3.0	7.5	9.5
			$\bar{x}\,\boxed{2.5}$	$\bar{x}\,\boxed{8.0}$	$\bar{x}\,\boxed{8.8}$
F36	no	no	1.5	.0	5.5
F32	"	"	1.0	5.0	2.0
F35	"	"	1.5	2.5	2.0
F20	"	"	.0	1.0	2.5
F55	"	yes	.0	4.0	4.5
			$\bar{x}\,\boxed{0.8}$	$\bar{x}\,\boxed{2.5}$	$\bar{x}\,\boxed{2.9}$

tients with initial depression subsequently improved significantly less than those without depression (analysis of variance).

The Figure shows a similar analysis for th ritualizers of Marks et al. (1980); here the tw samples represented the highest and lowest qua tiles for depression on the Hamilton an Wakefield scales. Again, the clomipramine eff occurred exclusively in those with the highest star ting levels of depression. Further analysis cf the patients (Mawson et al. 1982) found that a singl 0-8 scale for initial free-floating *anxiety* was almo as good a predictor of clomipramine effect as wa depression, which is not surprising given their in tercorrelation of .70, but suggests that we shoul speak of dysphoria rather than depression.

A third comparison had discordant finding Insel et al. (1982, personal communication) com pared outcomes of his obsessive-compulsives wit the highest and lowest initial depression scale and found that both subsamples retained th superiority of clomipramine over clorgyline.

Among phobics, McNair and Kahn (198 found that imipramine had no significant drug ef fect on agoraphobia overall; a significan agoraphobia × depression interaction indicate

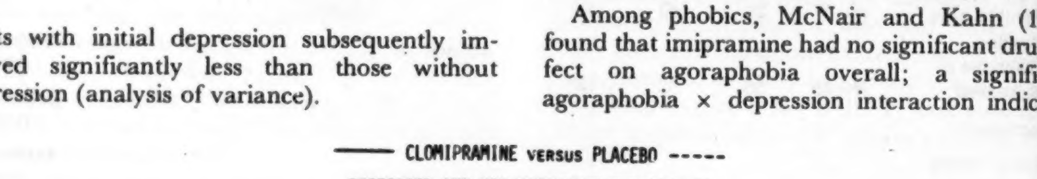


FIGURE. Outcome of ritualizers with clomipramine: Initially high vs. initially low depression (from Marks et al. 1980).

that imipramine reduced agoraphobia only when it was accompanied by depression. Imipramine did produce a significant reduction in depression and also in panics independently of depression.

Zitrin et al. (1980) found a negative correlation between starting level of depression and several measures of outcome, but did not compare outcomes of those with the highest and lowest starting levels, which might have detected effects obscured by their many patients in the middle starting level. The potential importance of this point is testified by the obvious relationship between initial depression and outcome in the ritualizers of Marks et al. (1980) when the top and bottom quartiles were compared, but the virtual disappearance of this relationship when it was sought for in the entire sample (Raskin, personal communication). Sheehan et al. (1980) found no relationship between five vegetative signs of endogenous depressive illness and outcome. Working with their data, this author could also find no relationship between outcomes contrasted in patients with the highest and the lowest levels of initial depression. However, even those with the lowest levels had fairly high starting levels (only two had Zung scores below 55). Table 2 suggests that there may be a threshold of moderate dysphoria below which a drug effect is unlikely, and the Boston sample had too few cases without dysphoria to test this hypothesis

Of the twelve studies in adult phobics (Lipsedge et al. 1973; Marks et al., 1980, in press; Mavissakalian & Michelson 1982; McNair & Kahn 1981; Mountjoy et al. 1977; Pecknold et al. 1980; Sheehan et al. 1980; Solyom et al. 1981; Tyrer et al. 1973; Zitrin et al. 1978, 1980), five found no drug effect on phobias (Lipsedge et al. 1973; Marks et al., in press; McNair & Kahn 1981; Mountjoy et al. 1977; Solyom et al. 1981). Of these five, two had patients with low initial levels of dysphoria (Marks et al. in press; Solyom et al. 1981), one found an antidepressant and antipanic but no antiphobia effect (McNair & Kahn 1981), and two did not report initial depression levels (Lipsedge et al. 1973; Mountjoy et al. 1977). The predominantly agoraphobic sample of Mountjoy et al. (1977) did not improve significantly on agoraphobia or on depression, only on a social phobia scale; all these patients had, in addition to phenelzine, a daily dose of 15 mg diapezam and 10 mg nitrazepam, which confounds interpretation. In the agoraphobics of Lipsedge et al. (1973), iproniazid had a significant effect on phobic anxiety but not on phobic avoidance.

A report which has been omitted because it dealt with patients who had a diagnosis of primary depression of at least 4 weeks' duration, often with additional phobic symptoms, is that of Nies and Robinson (1981). These phobias accompanying depression responded to either phenelzine, 60 mg/day (but not 30 mg), or to amitriptyline, 150 mg/day.

Antidepressants are Broadly Patholytic, While Exposure is More Specifically Antiphobic and Anticompulsive

The patterns of antidepressant drug effects among different outcome measures are of considerable interest. In general, studies which found a significant drug effect for phobias or obsessive-compulsive phenomena also found a significant effect for depression (Ananth 1980; Insel et al. 1982; Marks et al. 1980; Mavissakalian & Michelson 1982; Pecknold et al. 1980; Sheehan et al. 1980). Exceptions are Zitrin et al. (1980) and Tyrer et al. (1973), where drug effect was present for phobias but not for depression and, in the case of Tyrer et al., not for panic either. It is relevant here that in anxiety disorders, too, imipramine was more effective than chlordiazepoxide or placebo in reducing depression as well as anxiety (Kahn et al. 1981).

When present in these syndromes, the drug-effect is not restricted to phobias, rituals, and anxiety-depression, but seems more general. In the few studies which report measures across a broad spectrum of different symptoms, antidepressant drugs seem to improve most measures in a pattern of *general patholysis*. As an example, Sheehan et al. (1980) found that imipramine and phenelzine patients improved significantly on every measure, regardless of whether it concerned phobias, anxiety, depression, hostility, interpersonal sensitivity, somatic, obsessive-compulsive or other scores. Marks et al. (1980) found the same general patholysis for rituals, depression, anxiety, and social adjustment (*see* their Table 3 and their Figures 2A and 2B). Similarly, McNair and Kahn (1981) found an imipramine effect across a variety of problems such as panic, depression, and anger, though not for phobias (Table 4, modified from their Table 5). We do not yet know whether initial dysphoria is a better predictor of drug effect than is initial panic, anger, or hostility. Level of initial rituals or phobias has not been a good predictor where it has been examined.

Table 4

General Patholytic Effect of Imipramine in Agoraphobics Efficacy Summary for Completers at Week 8 (from McNair & Kahn 1981)

Criterion	Imipramine Effect	Imipramine X Depression	Imipramine X Phobic Severity
Agoraphobia-	.05	.05	
Phobic anxiety (SCL)	–	.05	.05
Panic	.05	–	–
Tension-anxiety (POMS)	.1	–	.05
Depression (SCL-self)	.05	–	–
" (SCL-Dr.)	.05	–	.01
" (POMS)	.1	–	–
" (Beck)	–	?	.05
Anger (SCL-self)	.001	.05	.001
" (SCL-Dr.)	.05	–	–
" (POMS)	.001	–	.01
Somatic (SCL-self)	.1	.1	.05
Global improvement	–	–	.05

.05, .01, etc. = Significant on ANCOVA
– = Not significant

Given the general patholytic effect of antidepressant drugs on several aspects of distress like panic, free-floating anxiety, and depression, among others, all of which intercorrelate highly to the order of 0.60 or more, it might be misleading to concentrate on panic attacks as the focus of action, as some authors do (Sheehan et al. 1980; Zitrin et al. 1978, 1980). Undoubtedly imipramine can block panic attacks, but it also blocks a lot of other cohering pathological features simultaneously. It is illogical to accept any one of those features as primary unless and until detailed analysis has shown that change in that feature precedes change in the other aspects. This has not yet been done. Tyrer et al. (1973) found no improvement in panics despite improvement in phobias; ratings concerned symptoms over the previous 3 days. Zitrin et al. (1980) are the only ones to actually report measures of panic which improved along with phobias, and did not demonstrate that panic improves before phobias, which sequence needs to be demonstrated if panic is to be regarded as the critical issue.

There is no reason to assume primacy of panic in agoraphobia. Panics are one of several manifestations of disturbed *mood*, others being free-floating background anxiety and depression, all of which tend to occur together. It is wise to heed the caution of McNair and Kahn (1981, pp. 77-78) that their "findings are not entirely congruent with Klein's views that relief of the agoraphobic component by imipramine is also independent of depression or that imipramine is ineffective for anticipatory anxiety. All of this underlines the need for greater knowledge of the role of depression, both secondary and primary, in the development and treatment of the panic-phobic syndrome."

It is of great interest to know why panics are so frequent in agoraphobia and in generalized anxiety disorder and unusual in obsessive-compulsive neurosis. A further issue is what differentiates anxiety disorders without agoraphobia from agoraphobic anxiety disorders. The question also arises why mood disturbance is so commonly associated with agoraphobia and obsessive-compulsive disorder.

The Diagnostic and Statistical Manual-III (DSM-III) subdivisions of dysthymic disorder, panic disorder, generalized anxiety disorder, and agoraphobia with and without panic attacks are not yet firmly based on hard scientific data showing that they have therapeutic or prognostic import. Symptoms of anxiety-depression (dysphoria) are a frequent feature not only in all these and in obsessive-compulsive disorder but also in many physical disorders, and are also the most common complaint in primary care populations across the globe. In one community survey "psychic distress," i.e., dysphoria, was present in 67 percent of agoraphobics (Balter, personal communication). The level of dysphoria may vary considerably among samples and partly accounts for differences in drug effects. Dysphoria from varied causes may be as responsive to antidepressants as is inflammation of diverse origins to aspirin, in both instances as long as the drug is given. We need to distinguish between drug effects on less specific features associated with a syndrome-like inflammation or dysphoria from effects on more central features like bacteria in the tissues, or ritualistic or phobic behavior.

In contrast to the general patholytic action of antidepressants which tends to cease when the drug is stopped, the action of exposure treatment is both more specific and more lasting. Exposure therapy is only indicated where there is *persistent avoidance* of some discomforting situation or feeling. Exposure mainly improves rituals and phobias and, after a delay, work and social adjustment which had formerly been crippled by the rituals and phobias. This improvement continues over 2-7 years' followup (Marks, in press-a).

Despite its efficacy for phobias and rituals, exposure leads to a less impressive gain in mood, though this can become significant some time after phobias and rituals improve. Unlike drugs, behavioral treatment dissects apart the dual pathology in obsessive-compulsive and phobic patients. On the one hand, all of them have persistent rituals of phobias which can be specifically helped by exposure *in vivo*, and lastingly so, even though this has limited action on any coexisting dysphoria. On the other hand, in patients who have coexisting fluctuating dysphoria this is temporarily suppressed by antidepressants; as dysphoria improves do so coexisting rituals and phobias. While exposure treatment does not greatly modify disturbed mood, it protects against the reemergence of rituals and phobias in full strength when mood disturbance recurs; it uncouples the two pathologies (Marks 1981).

Are Any Antidepressants Especially Valuable?

Few comparisons are available. For ritualizers, clomipramine was effective in all four studies which used it (Ananth 1980; Insel et al. 1982; Marks et al. 1980; Thorén et al. 1980), but was not significantly superior to nortriptyline or amitriptyline. (Nortriptyline, amitriptyline, and clorgyline were each ineffective in one study (Ananth et al. 1980; Insel et al. 1982; Thorén et al. 1980). Antiphobic effects were found for imipramine in five (Mavissakalian & Michelson 1982; Sheehan et al. 1980; Tyrer et al. 1973; Zitrin et al. 1978, 1980) of seven studies (ineffective in Marks et al., in press; McNair & Kahn 1981), for phenelzine in two (Sheehan et al. 1980; Tyrer et al. 1973) of three studies (ineffective in Solyom et al. 1981), and for iproniazid (Lipsedge et al. 1973) and clomipramine (Pecknold et al. 1980) in one study each. For phobics between-drug comparisons are only available in one study, for phenelzine vs. imipramine (Sheehan et al. 1980); there was little to choose between them.

Problems of Drug Treatment

Relapse after drug withdrawal: In most of the phobic and obsessive-compulsive populations reviewed in this paper the disorder had been present for many years, often for more than a decade, by the time treatment began. In such chronic populations treatments are more valuable if their benefits last for years after the treatment ceases. This is true for exposure therapy but not, unfortunately, for antidepressants. Where a drug effect has been found, there is a uniformly high relapse rate on stopping the drug, even after it has been taken for 6-8 months. This is a drawback to drugs whose side effects over long periods are unclear. It indicates that the pathology is being suppressed rather than cured by such drugs, and there is a tendency for the mood disturbance to persist in a fluctuating manner for years. This finding contrasts sharply with the lasting improvement attributed to exposure treatments, which improved phobias and rituals up to the 2-9 years (reviewed by Marks, in press-a). The pattern of relapse following drug withdrawal, even after prolonged drug administration, is similar to that found with antidepressants in depressive illness, phenothiazines in schizophrenia, and cimetidine in duodenal ulcer.

High dropout rate with drugs in phobics: Another drawback to antidepressants is the high dropout rate found by almost all authors in phobics, these mostly from a quarter to a third (Lipsedge et al. 1973; Marks et al., in press; Mavissakalian & Michelson 1982; McNair & Kahn 1981; Sheehan et al. 1980; Tyrer et al. 1973; Zitrin et al. 1978, 1980). Interestingly, dropouts are common with placebo as well, suggesting that phobics are poor pilltakers. Often they interpret preexisting somatic complaints as drug side effects as soon as they start the drug. These misattributions are an interesting feature of the syndrome which deserve further study.

In contrast, the only three studies to report dropout rates with obsessive-compulsives found these to be 4-14 percent (Insel et al. 1982; Marks et al. 1980; Thorén et al. 1980), comparing well with the 16 percent dropout rate for behavioral treatment as a whole in several hundred neurotic patients treated in the author's unit.

Implications for Research and for Clinical Practice

Future research studies could be better compared if they were to adopt a minimum number of standard measures. These might include a short Beck Depression Inventory and the Hamilton Depression Scale, target ritual or target phobia measures like those of Marks et al. (1980, 1982) and, for phobics only, the Fear Questionnaire of Marks and Mathews (1979) and panic scale of Zitrin et al. (1980).

Plasma monitoring of drug levels is desirable, and a followup for a minimum of a year after cessation of the drugs is essential to check on relapse. Also necessary is report of absolute mean scores, standard deviations, and cell size of each measure at each rating point from pretreatment to end of followup. Such data can be reported in one table taking up merely one journal page, and would greatly facilitate the task of comparing populations and effects across research centers.

References

Ananth, J. Systematic studies with clomipramine in obsessive neurosis. *Pharmaceut. Med.*, 2:138-151, 1980.

Gittelman-Klein, R, and Klein, D.F. Controlled imipramine treatment of school phobia. *Arch. Gen. Psychiatry*, 25:204-207, 1971.

Insel, T.R., Alterman, I., and Murphy, D.L. Antiobsessional and antidepressant effects of clomipramine in the treatment of obsessive-compulsive disorders. *Psychopharmacol. Bull.*, 18(4):115-117, 1982.

Kahn, R.J., McNair, D.M., Covi, L., Downing, R.W., Fisher, S., Lipman, R.S., Rickels, K., and Smith, V.K. Effects of psychotropic agents in high anxiety subjects. *Psychopharmacol. Bull.*, 17(3):97-100, 1981.

Lipsedge, M., Hajioff, J., Huggins, P., Napier, L., Pearce, J., Pike, D.J., and Rich, M. The management of severe agoraphobia: A comparison of iproniazid and systematic desensitization. *Psychopharmacologia (Berlin)*, 32:67-80, 1973.

Marks, I.M. *Cure and Care of Neuroses.* New York:Wiley & Sons, 1981.

Marks, I.M. Toward an empirical science. *Behav. Ther.* (In press-a)

Marks, I.M. Stress and other risk factors in anxiety dis- orders. In: Goldman, H., and Goldstone, S. (eds.), *Stre in Psychiatric Disorders.* NIMH Publication. (In press-b)

Marks, I.M. Are there anticonvulsive or antiphobic drugs? Review of the evidence. (Submitted for publication

Marks, I.M., and Mathews, A.M. Brief standard self-rating for phobic patients. *Behav. Res. Ther.*, 17:263-267, 1979.

Marks, I.M., Stern, R.S., Mawson, D., Cobb, J., and McDonald, R. Clomipramine and exposure for compulsive rituals. *Br. J. Psychiatry*, 136:1-25, 1980.

Marks, I.M., et al. Imipramine and exposure for agoraphobics. *Arch. Gen. Psychiatry.* (In press)

Mavissakalian, M., and Michelson, L. Agoraphobia Behavioral and pharmacological treatments, preliminary outcome, and process findings. *Psychopharmacol. Bull* 18(4):91-103, 1982.

Mawson, D., Marks, I.M., and Ramm, L. Clomipramine and exposure for compulsive rivals. III. Two-year followup and further findings. *Br. J. Psychiatry*, 140:11-18 1982.

McNair, D.M., and Kahn, R.J. Imipramine compared with a benzodiazepine for agoraphobia. In: Klein, D.F., and Rabkin, J. (eds.), *Anxiety: New Research and Changing Concepts.* New York: Raven Press, 1981, pp. 69-80.

Mountjoy, C.Q., Roth, M., Garside, R.F., and Leitch, I.M. A clinical trial of phenelzine in anxiety, depression, and phobic neuroses. *Br. J. Psychiatry*, 131:486-492, 1977.

Nies, A., and Robinson, D.S. Comparison of clinical effects of amitriptyline and phenelzine. In: Youdim, M.P.H., and Paykel, E.S. (eds.), *Monoamine Oxidase Inhibitors—Sta of the Art.* New York: Wiley & Sons, 1981, pp. 161-168.

Pecknold, J.C., McClure, D.J., Appeltauer, L., Allan, T., and Wrzesinski, L. Potentiation of clomipramine by tryptophan in the treatment of agoraphobic and social phobic patients. (Unpublished manuscript, 1980.)

Sheehan, D., Ballenger, J., and Jacobsen, G. Rx of endogenous anxiety and phobic, hysterical, and hypochondrial symptoms. *Arch. Gen. Psychiatry*, 37:51-59, 1980.

Solyom, C.L., Lapierre, Y., Pecknold, J., and Morton, L. Phenelzine and exposure in the Rx of phobias. *Biol Psychiatry*, 16:239-247, 1981.

Thorén, P., Åsberg, M., Cronholm, B., Jörnestedt, L., and Träskman, L. Clomipramine Rx of obs-comp disorder. I. A controlled clinical trial. *Arch. Gen. Psychiatry*, 37:1281-1285, 1980.

Tyrer, P., Candy, J., and Kelly, D. Clinical effects of phenelzine and placebo in the treatment of phobic anxiety. *Psychopharmacologia (Berlin)*, 32:237-254, 1973.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Behavior therapy, supportive psychiatric treatment, imipramine, and phobias. *Arch. Gen. Psychiatry*, 35:307-316, 1978.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Treatment of agoraphobia, with group exposure *in vivo* and imipramine. *Arch. Gen. Psychiatry*, 37:63-72, 1980.

Medication in the Treatment of Panic Attacks and Phobic States

Donald F. Klein, M.D.[1]

Diagnostic Issues

In the now superseded Diagnostic and Statistical Manual-II (DSM-II) an anxiety neurosis was characterized by "anxious over-concern extending to panic and frequently associated with somatic symptoms. Unlike Phobic Neurosis, anxiety may occur under any circumstances." A patient with a phobic neurosis might show similar symptoms, but only when exposed to specific situations or objects, though these were consciously recognized as presenting no real danger.

Clinical research findings of the past two decades permit us to more precisely discriminate among anxiety and phobic conditions.

The crucial distinction is that the core event is the spontaneous panic attack, which may lead to the secondary development of anticipatory anxiety and tertiary phobic avoidances. That the panic attack is qualitatively distinct from, and not just an intensification of anticipatory anxiety, is supported by both the course of the disorders and differential pharmacological responses. Spontaneous panic attacks antecede the development of generalized anxiety rather than vice versa. Further, Klein (1964) demonstrated that the spontaneous panic attacks could be blocked by the tricyclic antidepressant imipramine which, however, did not affect anticipatory anxiety. Benzodiazepines and other minor tranquilizers, on the other hand, ameliorate anticipatory anxiety but have no marked effect on the panic attacks themselves. Thus, panic attacks appear to represent a form of anxiety biologically distinct from anticipatory (or "free-floating") anxiety.

This distinction leads to a more useful classification of anxiety and phobic disorders, separating those involving spontaneous panic attacks from those that do not. In DSM-III, the former are classified as Panic Disorder or Agoraphobia with Panic Attacks, depending on whether an individual with spontaneous panic attacks also develops a widespread inability to travel outside the home based in turn on fear of spontaneous panics. The attacks themselves are often episodic, and may clear for no apparent reason after 6-12 months. However, they tend to recur in volleys and occasionally become chronic. In addition, the agoraphobic avoidant and dependent behavior often becomes chronic because after a time the patient may give up trying to enter feared situations.

Other phobias that do not involve spontaneous panics are included in DSM-III as: Agoraphobia without Panic Attacks, Social Phobia, and Simple Phobia. Agoraphobia without Panic Attacks is, in the author's experience, regularly associated with episodic dysautonomic experiences; primarily light-headedness and gastrointestinal distress. Social Phobia is defined in DSM-III as a persistent, irrational fear of, and compelling desire to avoid, a situation in which the individual is exposed to possible scrutiny by others and fears that he or she may act in a way that will be humiliating or embarrassing. Examples of Social Phobia are fears of public speaking or performing in public, using public lavatories, eating in public, and writing in the presence of others. Simple Phobia involves an irrational fear of, and desire to avoid, specific, well-delineated, objects or situations not included in the definitions of Agoraphobia and Social Phobia. These often involve animals, particularly dogs, snakes, insects, and mice, or situations such as closed spaces (claustrophobia) or heights (acrophobia). A trial of imipramine in Simple Phobia showed no specific benefit (Klein et al. 1980), as would be expected if the medication only affected spontaneous panics.

---

[1] New York State Psychiatric Institute, New York, NY 10032.

Physical disorders such as hypoglycemia, pheochromocytoma, hypercaffeinism, hyperthyroidism, and withdrawal from sedatives may cause symptoms similar to a panic attack and must be ruled out when making the diagnosis of Panic Disorder or Agoraphobia with Panic Attacks. These diagnoses are not made in DSM-III if the panic attacks are symptomatic of another mental disorder, such as Schizophrenia, Major Depressive Disorder, or Somatization Disorder.

It may be a mistake not to diagnose Panic Disorder in the presence of major depressive disorder, since recent findings indicate that concurrent depression and Panic Disorder may have a higher degree of familial loading than depression alone (J. Leckman and M. Weissman, personal communication).

A number of features complicate the clinical picture and serve to obscure the diagnosis of Panic Disorder. Some patients manifest symptoms of depersonalization or derealization during a panic, which may also occur at times other than the panic attack. There may also be a relationship between separation anxiety in childhood and panic attacks, since between 20 percent (outpatients) and 50 percent (inpatients) of agoraphobic adults who come for treatment have a history of separation anxiety in childhood, often manifested as difficulty attending school (Klein 1964). It is noteworthy that imipramine has benefited school phobics refractory to psychotherapy in a controlled clinical trial (Klein et al. 1980).

Adult patients with Agoraphobia with Panic Attacks, who may present as housebound, desperately clinging, and fearful of being alone, have often been regarded as infantile personalities with severe, unmet dependency needs. The tendency has been to regard their symptoms as evidence of a failure to master the early stages of psychological development involving object constancy and separation-individuation. Long courses of psychoanalytic treatment were often prescribed which, in the light of recent findings, are not likely to be the treatment of choice.

Other complications of panic attacks are alcohol or sedative abuse. These may involve attempts at self-medication, which diminish anticipatory anxiety but have no effect on blocking panic attacks. Hence the dosages are often increased until physical or psychological dependence supervenes. An inquiry about antecedent panic attacks should always be included in the evaluation of alcohol- or sedative-abusing patients.

Panic attacks may also occur in conjunction with depressive illness (Pariser et al. 1979). At times the panic attacks may be the original symptom, with depressive complaints supervening. Most often this involves demoralization in response to the travel restrictions and attendant loss of self-esteem, and lacks many of the vegetative and autonomous mood disturbance features of a full-blown depressive syndrome. On the other hand, the illness may start with a major depression and be complicated by the subsequent development of panic attacks.

Several recent reports have also linked anxiety-panic syndromes to cardiovascular disorders such as hyperdynamic beta-adrenergic state (Easton & Sherman 1976; Frolich et al. 1969) and mitral valve prolapse syndrome (MVPS) (Pariser et al. 1979). While hyperdynamic beta-adrenergic circulatory state was originally described in patients who had attacks of palpitations, chest discomfort, or tachycardia after exercise or stress (Frolich et al. 1976), it has more recently been reported as brief episodes of nervousness or anxiety, often occurring without physical or emotional precipitants, that can be reproduced by isoproterenol infusions and blocked by maintenance propranolol (Easton et al. 1976). These findings suggest that some panic-attack patients may have increased beta-adrenergic receptor site reactivity.

Lactate Infusions and Panic Attacks

Patients with spontaneous panic attacks may have a pathophysiological aberration, since intravenous lactate infusions precipitate panic attacks in such individuals but not in normal controls (Pitts & McClure 1967).

This finding, established under double-blind circumstances, has been amply replicated by numerous investigators (Appleby et al. 1981;

Bonn et al. 1971; Fink et al. 1970; Kelly et al. 1971). It must be considered one of the better demonstrated facts in the experimental precipitation of psychopathological states. The meaning of this finding, however, still remains obscure. For instance, Pitts and McClure (1967) believe that the panicogenic effect was due to the chelation of calcium; they demonstrated that adding calcium to the sodium lactate mitigated the occurrence of panic attacks. Fink et al. (1970) replicated this finding.

Ackerman & Sachar (1974) raised the question whether there was truly a specific panicogenic effect from lactate. Perhaps some sort of conditioned response was responsible. During the lactate infusion autonomic symptomatology slightly reminiscent of the onset of the panic attack may occur which might engender a panic attack in patients, but not in normals who had not learned such a sequence.

Although possible, this hypothesis seems contradicted by several bodies of fact. First, EDTA infusions administered by Pitts (1967) produced profound hypocalcemic symptoms but no anxiety attacks in either anxiety neurotics or controls. Such infusions should certainly produce sufficient autonomic disturbance to throw patients into a panic attack if all that was required was a nonspecific trigger. Second, lactate-induced panic attacks resemble spontaneous panic attacks with regard to the blocking effects of antidepressants. Kelly's group (1971) induced panic attacks in eight agoraphobic patients and then treated them with phenelzine. Five of the eight patients responded well to the medication and did not have panic attacks upon reinfusion with lactate; the remaining three patients did not respond well to phenelzine and did reexperience panic attacks upon reinfusion with lactate.

More recently the author's research group has administered lactate infusions to 62 patients with Panic Disorder; 43 experienced panic attacks. After clinical recovery with imipramine, and while still on the drug, 28 were reinfused; only four showed evidence of a panic attack.

Even more telling, in a double-blind procedure 16 patients in remission from Panic Disorder were randomized to either continue on tricyclic antidepressants or to be withdrawn onto the peripherally acting anticholinergic drug, methscopolamine. After a month, they were reinfused with lactate. None of these patients panicked.

Pharmacotherapy

Tricyclic Antidepressants

That imipramine would block panic attacks (Klein 1964, 1967; Klein & Fink 1962; Zitrin et al. 1978) is of heuristic and practical importance. Agoraphobic patients with panic attacks had often been thought of as having a fear of open spaces or other specific situations, with long outpatient psychotherapies devoted to an exploration of unconscious sexual and aggressive impulses; the phobically barred areas were seen as symbols of forbidden temptations. Patients given imipramine report a dramatic decrease or cessation of panic attacks, however, many are still reluctant to change their phobic behavior patterns. Thus, persuasion, direction, support, or minor tranquilizers are often required, once the panic attacks had been blocked, to help patients extinguish their anticipatory anxiety which is not ameloriated directly by the tricyclic antidepressants, and to reenter the phobically avoided situations.

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors are also effective in blocking panic attacks. Sheehan et al. (1980) recently reported a study in which phenelzine (45 mg/day) was at least as effective, if not more so, than imipramine (150 mg/day) in treating agoraphobics with panic attacks. That both major classes of antidepressants are effective in treating panic attacks should prove of marked heuristic importance.

Other Agents

In a detailed, thoughtful review of 16 controlled or partially controlled studies of beta-adrenergic blockers in anxiety disorders, Cole et al. (1979) concluded that this class of drugs may have a weak antianxiety effect. Specifically, the drugs often appear more helpful with somatic than with psychic aspects of anxiety. This conclusion was also reached in a recent study by Noyes et al. (1980), who did a propranolol-placebo crossover study in patients with panic disorder. As such, it is useful for treating the anxiety symptoms that accompany the fear of public speaking and other social phobias. However, no controlled study has systematically examined the specific efficacy of propranolol in blocking panic attacks.

As mentioned before, minor tranquilizers are helpful in treating the anticipatory anxiety of Panic Disorder patients, but do not block the panic attacks. Preliminary findings of a controlled study by McNair and Kahn (1980) support this clinical impression. Panic attacks are also refractory to all classes of antipsychotic drugs, which may even exacerbate the condition. Because these patients are often considered borderline, and seen as decompensating when in acute panic, antipsychotics are often administered with a worsening of symptoms, use of more drug, further worsening, etc. leading to a vicious cycle (Klein 1962, 1964).

Hoehn-Saric et al. (1981) recently reported a double-blind, crossover placebo control study of clonidine in 23 patients. Nine patients were diagnosed as General Anxiety Disorder, and 14 as Panic Disorder. The period of active drug treatment was 2 weeks. The effect of clonidine was comparable in both anxiety disorders, and superior to placebo in patients who tolerated the drug. The main effect of clonidine was a decrease of anxiety attacks and psychic symptoms. No difference was found in the effectiveness of either drug for the two anxiety disorders. Hoehn-Saric (personal communication) reports a waning of clonidine beneficial effects with time.

An open pilot study of clonidine was conducted (Liebowitz et al., in press) in 12 patients with Panic Disorder. Only a third of the patients showed sustained improvement over a 6-week period. One third showed a transient improvement, which would have been registered as a positive course in Hoehn-Saric's (1981) 2-week trial, and a third was unable to tolerate the drug. Since clonidine also shows a waning of its inhibitory effect upon the locus coeruleus. this disappointing clinical finding may still be of marked theoretical importance.

A new drug, alprazolam (Xanax), a triazolobenzodiazepine with supposed antidepressant effects, may also be an antipanic drug. (Sheehan, personal communication).

Is the Antipanic Activity of Antidepressant Medication a Reflection of Antidepressant Effects?

Marks has recently completed a study of the imipramine treatment of agoraphobic patients, and found no benefit from imipramine (Marks et al. in press). There are several problems with this study, including the dosage level attained and the statistical analysis. It is also not unusual for a Type II statistical error to occur in the study of active compounds; that is, not finding statistically significant effects when they, in fact, exist.

Marks, however, has suggested the alternative hypothesis that imipramine is only beneficial in the treatment of depressed agoraphobic patients and that the antipanic effect is actually part of a general patholytic effect. This line of thinking is supported by his findings in the chlorimipramine treatment of obsessive-compulsive disorder, where concurrent depression seemed necessary for beneficial drug effect. Marks also interprets a study by Thorén et al. as supportive of this viewpoint.

This is a controversial area. Marie Åsberg (personal communication) has disagreed with Marks' interpretation of this data. However, this discussion will be restricted to Marks' agoraphobia data, since there is no necessary parallel between drug effects on obsessive-compulsive disorder and agoraphobia.

Marks' handling of the term "depression" does not deal with the real difficulties in understanding just what different authors are referring to when they use this ambiguous word. In particular, the distinction of depression from demoralization seems crucial, since demoralization is a nonspecific response to many life defeats that manifests itself in depressive complaints. However, it is not generally considered to be a drug responsive depressive condition.

Marks has tabulated a number of studies where there are measures available that indicate that his sample, and the sample of Solyom et al. (1981) were relatively low in depression, and that this is consonant with his views concerning the essential role of depression in allowing therapeutic benefit. Unfortunately, the Solyom study is not good evidence, since the sample contains an unstated proportion of social phobics, who are not generally considered drug sensitive. Therefore, Marks' study remains entirely alone in finding a lack of antidepressant benefit in agoraphobic patients.

When Zitrin and colleagues' study (1978) was compared to Marks' in terms of baseline depression measures, on the one measure where comparability was possible, there was no difference between samples. Further, in Zitrin's study there was no antidepressant effect of imipramine. This is not surprising, since in this study patients with more than moderate levels of depression, or with diagnosable major depressive disorder, were specifically excluded. Since there was no specific antidepressant effect, it is hard to see how an antidepressant effect could be a precondition for a therapeutic effect of imipramine in agoraphobic patients.

Marks points to the study of McNair and Kahn (1980) and of Sheehan (1980) where antidepressant effects were found as contradicting Zitrin's findings. However, in neither of these publications is there any indication that depressed patients were excluded from these studies. Further, in an analysis by Sheehan, no relationship was found between his measures of depression and antiphobic drug effect.

In the McNair and Kahn study (1981) there was a more complicated finding. Their results were analyzed for the 26 completers who were randomized to imipramine or chlordiazepoxide. They found that the imipramine effect on panic attacks was independent of degree of depression present in the sample. With regard to agoraphobia, that is avoidant behavior as a target, the best imipramine responders were the more depressed who were also more phobic. Because of the high correlation between degree of depression and phobia, these effects could not be statistically disentangled.

McNair and Kahn (1981) did not find a main imipramine effect on agoraphobia (avoidance behavior) but agreed that there was a definite effect on panic attacks. This finding is quite consistent with Klein's hypothesis that the initial antidepressant effect is blockading the panic attacks, and that the decrease in avoidant behavior is secondary. McNair's study lasted for only 8 weeks. This is a period that would allow for the development of antipanic effects, but would probably not have increased substantial secondary decreases in avoidance as indicated in the study of Zitrin et al. (1978).

Marks also discusses the possibility that antidepressants are broadly patholytic, while exposure is more specifically antiphobic. He asserts that drug effects are not restricted to phobias, rituals, and anxiety-depression, but seem more general. He supports this by referring to a group of univariate analyses which show many improvements with medication.

There are real methological problems with such an interpretation of multiple univariate contrasts. One does not know whether there is a general patholytic effect or whether there are a host of independent effects, or there is a central effect with a number of secondary beneficial reverberations. Finally, there may be a marked halo effect so that improvement in one area erroneously induces a perception of improvement in other areas. These methodological complexities are not alluded to. Further, other authors have shown a distinctly more spotty pattern of drug effects.

One problem is that it is not clear whether Marks is raising a strong hypothesis of general patholysis. If he is insisting that drugs always affect all symptoms, he is clearly wrong. If he is simply stating that drugs have effects on areas over and above phobias, anxiety, and depression, he is clearly right but the meaning of this remains to be elucidated.

Marks also states that it is misleading to focus on panic attacks since imipramine has effects on many other pathological features *simultaneously*. However, his data base does not allow this assertion of simultaneity.

Unfortunately the data regarding the effects of imipramine over an extended period of time are not definitive. The author's hypothesis that the effect is first upon panic attacks, and then secondarily upon anticipatory anxiety and avoidance has not been demonstrated in a longitudinal controlled way. It is quite consonant, however, with very extensive clinical therapeutic experience. It is also consonant with followup findings that relapse is initiated by the recurrence of spontaneous panic attacks. Finally, the blockade of lactate-induced panic attacks by antidepressants argues against considering the panic attack as just one more symptom.

Summary

The general question of the utility of medication in the treatment of Panic Disorder and Agoraphobia with Panic Disorder is reviewed. The utility of antidepressants is particularly striking. The claim that these beneficial effects depend upon the presence of concurrent depression with panic attacks, and that antidepressants have a general patholytic effect is critically examined.

Studies of the blockading effects of imipramine upon lactate-induced panic attacks also indicate a specific antidepressant-panic disorder interaction that is not related to depression.

References

Ackerman, S.M., and Sachar, E.J. The lactate theory of anxiety: A review and reevaluation. *Psychosom. Med.*, 36(1):69-81, 1974.

Appleby, I.L., Klein, D.F., Sachar, E.J., and Levitt, M. Biochemical indices of lactate-induced panic: A preliminary report. In:Klein, D.F., and Rabkin, J.G. (eds.), *Anxiety: New Research and Changing Concepts.* New York:Raven Press, 1981.

Bonn, J.A., Harrison, J., and Rees, W.L. Lactate-induced anxiety: Therapeutic applications. *Br. J. Psychiatry,* 119: 468-471, 1971.

Cole, J.O., Altesman, R.I., and Weingarten, C.H. Beta-blocking drugs in psychiatry: Psychopharmacological update. *McLean Hosp., J.,* 40-68, 1979.

Easton, J.D., and Sherman, D.G. Somatic anxiety attacks and propranolol. *Arch. Neurol.,* 33:689-691, 1976.

Fink, M., Taylor, M.A., and Volavka, J. Anxiety precipitated by lactate. *N. Engl. J. Med.,* 281:1129, 1970.

Frolich, E.D., Tarazi, R.C., and Dustan, H.P. Hyperdynamic beta-adrenergic circulatory state. *Arch. Intern. Med.,* 123:1-7, 1969.

Hoehn-Saric, R., Merchant, A.F., Keyser, M.L., and Smith, V.K. Effects of clonidine on anxiety disorders. *Arch. Gen. Psychiatry,* 38(11):1278-1282, 1981.

Kelly, D., Guirguis, W., Frommer, E., Hegga, N.M., and Sargant, W. Treatment of phobic states with antidepressants. *Br. J. Psychiatry,* 116:387-398, 1970.

Kelly, D., Mitchell-Heggs, N., and Sherman, D. Anxiety and the effects of sodium lactate assessed clinically and physiologically. *Br. J. Psychiatry,* 119:129-141, 1971.

Klein, D.F. Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia (Berlin),* 5:397-408, 1964.

Klein, D.F. The importance of psychiatric diagnosis in prediction of clinical drug effects. *Arch. Gen. Psychiatry,* 16:118-126, 1967.

Klein, D.F., Gittelman, R., Quitkin, F.M., and Rifkin, A. Diagnosis of anxiety, personality, somatoform, and fectitious disorders. In: *Diagnosis and Drug Treatment of Psychiatric Disorders: Adults and Children.* Baltimore, Md.: Williams & Wilkins, 1980, pp. 493-521.

Klein, D.F., and Fink, M. Psychiatric reaction patterns to imipramine. *Am. J. Psychiatry,* 119:432-438, 1962.

Liebowitz, M.R., Fyer, A.H., McGrath, P., and Klein, D.F. Clonidine treatment of panic disorder. *Psychopharmacol. Bull.* (In press)

Marks, I.M. Imipramine and exposure for agoraphobics. *Arch. Gen. Psychiatry.* (In press)

McNair, D.M., and Kahn, E.J. Imipramine vs. a benzodiazepine for agoraphobia. In: Klein, D.F., and Rabkin, J.G. (eds.), *Anxiety: New Research and Changing Concepts.* New York: Raven Press, 1981, pp. 69-80.

Noyes, R., Kathol, R., Clancy, J., and Crowe, R. Beta-blocking drugs: Clinical evidence for site of antianxiety activity. In: Klein, D.F., and Rabkin, J.G. (eds.), *Anxiety: New Research and Changing Concepts.* New York: Raven Press, 1981.

Pitts, F.N., Jr., and McClure, J.M., Jr. Lactate metabolism in anxiety neuroses. *N. Engl. J. Med.,* 277:1328-1336, 1967.

Pariser, S.F., Jones, B.A., Pinta, E.R., Young, E.A., and Fontana, M.E. Panic attacks: Diagnostic evaluations of 17 patients. *Am. J. Psychiatry,* 136:105-106, 1979.

Redmond, D.E. New and old evidence for the involvement of a brain norepinephrine system in anxiety. In: Fann, W.E., Karacan, I., Pokorny, A.D., and Williams, R.L. (eds.), *Phenomenology and Treatment of Anxiety.* New York: Spectrum Publications, 1979, pp. 153-203.

Sheehan, D.V., Ballenger, J., and Jacobsen, G. Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms. *Arch. Gen. Psychiatry,* 37:51-57, 1980.

Solyom, L., Heseltine, G.F.D., McClure, D.J., Solyom, C., Ledgewidge, B., and Steinburg, G. Behavior therapy versus drug therapy in the treatment of phobic neurosis. *Can. Psychiatr. Assoc. J.,* 18:51-59, 1973.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Behavior therapy, supportive psychotherapy, imipramine, and phobias. *Arch. Gen. Psychiatry,* 35:307-316, 1978.

Agoraphobia: Behavioral and Pharmacological Treatments, Preliminary Outcome, and Process Findings[1]

Matig Mavissakalian, M.D.,[2] and Larry Michelson, Ph.D.[2]

Introduction

Within the last two decades agoraphobia has become well delineated as a syndrome in its own right (Hallam & Hafner 1978; Marks 1969; Snaith 1968), and this recognition has been coupled with the development of effective behavioral and pharmacological treatments (Mavissakalian & Barlow 1981a). The behavioral treatments which aim primarily to reduce phobic anxiety and avoidance share a common denominator, namely exposure to feared stimuli (Mavissakalian & Barlow 1981b). A number of analogues as well as clinical studies have demonstrated the superiority of *in vivo* exposure to imaginal exposure (Barlow et al. 1969a, 1970; Crow et al. 1972; Emmelkamp & Wessels 1975; Stern & Marks 1973). However, variations in the practice of *in vivo* exposure (e.g., prolonged exposure, successive approximations, therapist-assisted, home-based individual or group treatments), seem to be equally effective (Emmelkamp 1974; Emmelkamp & Ultee 1974; Everaerd et al. 1973; Hafner & Marks 1976; Hand et al. 1974; Mathews et al. 1977; Teasdale et al. 1977). New developments in the pharmacological treatment of agoraphobia have drawn attention to the antidepressant group of drugs, and numerous clinical studies have shown that both the monoamine oxidase (MAO) inhibitors (Kelly et al. 1970; King 1962; Mountjoy et al. 1977; Tyrer et al. 1973a, 1973b; Tyrer & Steinberg 1975) and the tricyclics (Colgan 1975; Klein 1964, 1967; Klein & Fink 1962; Marshall & Micev 1975; Sheehan et al. 1980; Waxman 1975; Zitrin et al. 1978, 1980) can be very effective.

To date, the literature does not permit definitive conclusions regarding the relative effectiveness of exposure and antidepressant treatments of agoraphobia, as controlled studies directly comparing these two treatments have not been reported. However, despite the existing methodological and assessment differences between studies cited above, certain overall similarities and differences emerge. First, it appears that dropout rates are comparable in behavioral and pharmacological studies and that they hover around 25 percent. Second, improvement rates are also comparable and center around 70 percent of treated patients. However, a major difference between these two treatments occurs in regard to relapse rate: Whereas improvement with exposure treatments is known to be maintained over long followup periods (Emmelkamp & Kuipers 1979; Marks 1971; McPherson et al. 1980), nearly 30 percent of patients experience relapse following cessation of antidepressants (Klein 1964; Klein & Fink 1962; Sheehan et al. 1980; Tyrer & Steinberg 1975; Zitrin et al. 1978, 1980). One of the major aims of this study, therefore, was to directly compare the effectiveness of *in vivo* exposure (flooding) and imipramine in the treatment of agoraphobia.

The literature suggests that antidepressants act by controlling or suppressing panic attacks (King 1962; King & Fink 1962; Klein 1964; Sheehan 1980; Zitrin 1978, 1980) and that exposure *in vivo*

---

[1] This research was supported in part by USPHS Grant MH-34177 from the National Institute of Mental Health.

[2] Department of Psychiatry, University of Pittsburgh, Western Psychiatric Institute and Clinic, Pittsburgh, PA 15213.

Reprint requests should be sent to Matig Mavissakalian, M.D., Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213.

may be the final common pathway leading to habituation or extinction of phobic anxiety and avoidance behavior (Mavissakalian & Barlow 1981b). It would follow that a combination of these two effective treatments with different mechanisms of action might prove maximally beneficial to the patient. Previous investigations of the combined behavioral-antidepressant treatment of phobias are rare, and until recently none had studied a homogeneous group of agoraphobics, nor had any study utilized exposure *in vivo,* the behavioral treatment of choice (Lipsedge et al. 1973; Solyom et al. 1973; Zitrin et al. 1978. The only exception is a study by Zitrin et al. (1980) comparing combined exposure-imipramine and exposure alone in 76 agoraphobic patients. They found that the majority of patients in both groups improved but that the combined treatment showed more improvement in panic and marked global improvement ratings. The second major aim of this study, therefore, was to directly compare the effectiveness of the combined flooding-imipramine treatment to that of flooding alone and imipramine alone.

Another major aim was the investigation of possible differential rates and patterns of change across the treatments. Because of the presumed differences in the mechanism of action underlying the effects of flooding and imipramine, and the possibility of an additive or synergistic effect in their combination, it was hypothesized that: 1) significantly greater change would be found earlier with the combined treatments than with the individual treatments, 2) mood, as measured by panic, anxiety, and depression, would improve earlier in treatment with imipramine than with flooding, 3) phobia and avoidance behavior would improve earlier in treatment with flooding as compared with imipramine and, 4) concordance between all measures of change would be greater in the later, rather than earlier phases of treatment due to desynchronous patterns of change, initially, across measures.

Finally, the question of nonspecific factors in psychiatric treatment is both a troublesome and a fascinating one. Troublesome, because if not properly isolated and controlled, far more credit will go to the presumed active therapeutic ingredients. Fascinating, because nonspecific factors could be looked upon as respectable treatments in their own right. In the special case of agoraphobia, practicing *in vivo* exposure between sessions seems to be the final common pathway for any successful treatment and it is possible, indeed likely, that a certain percentage of patients might improve with instructions, encouragement, and support by a therapist (Gelder et al. 1973; Jannoun et al. 1980; Mathews et al. 1976; McDonald et al. 1979). The third major aim of this study, therefore, was to assess the true effectiveness of the imipramine, flooding, and the combined imipramine-exposure treatments compared to a control group receiving nonspecific treatment.

In 1980 a clinical research program was established at Western Psychiatric Institute and Clinic at the University of Pittsburgh to investigate flooding and imipramine treatments in 80 agoraphobic patients. This paper reports the results of the first 32 subjects who entered the project.

Method

Subjects

The 32 subjects of this study were selected on the basis of the following inclusion criteria: 1) Diagnostic and Statistical Manual-III (DSM-III) diagnosis of Agoraphobia, 2) age of onset prior to age 40, 3) duration of present illness of at least 1 year, 4) a score of 4 or greater on the clinician rating of global assessment of severity, and 5) failure to complete either the standardized behavioral test or the idiosyncratic behavioral test or completing both behavioral tests while experiencing definitive anxiety (a rating of 4 or more on a 0-8 scale of anxiety). Exclusionary criteria were: 1) presence of features indicative of and/or previous diagnosis of Major Affective Disorder, Schizophrenia, Organic Brain Syndrome, and Obsessive-Compulsive Disorder, 2) social phobics and anxiety neurotics without the typical fears of going out alone to open spaces, streets, shops, crowds, cars, and means of public transport, and 3) presence of physical illness precluding the use of imipramine either because of the illness itself or because of treatment necessary for that illness. Additionally, patients selected for the study were withdrawn from psychotropic medications at least 2 weeks prior to initiation of treatment. This selection process eliminated 27 diagnosed agoraphobics. The main reasons for their rejection, in decreasing order, were mild condition, physical or medical problems, and refusal to take experimental medications.

The 32 patients had a mean age of 39 years. There were 5 males and 27 females: 2 were single, 3 divorced, and 27 married. The majority were white with only 2 blacks. The average duration of illness was 14 years. Ninety-one percent of the patients had received previous psychiatric treatment of an average duration of 22 months. Eighty-seven percent of the patients had received anxiolytic medication, 32 percent had received antidepressants, and none had been prescribed antipsychotics. Only 16 percent of the patients had been previously hospitalized.

Six patients did not complete the treatment phase. All of them were females. One patient withdrew after two sessions because she was hospitalized with gynecological problems for possible hysterectomy. Two patients attended two sessions each but quit because they preferred to return to conventional group therapy. One patient withdrew after one session because of difficulty in arranging transportation to the clinic. The last two patients missed several sessions in a row and were disqualified. Additionally, three patients discontinued drugs within the first 2 weeks of treatment but completed the entire treatment phase. For the purposes of data analysis, they were reassigned to the placebo (no medication) group. Thus, the final composition of the groups was as follows: Imipramine/Flooding—five patients, Imipramine—six patients, Flooding—six patients, and Nonspecific treatment—nine patients.

Treatment Conditions and Design

The experimental design of the study is a 2 × 2 factorial design with eight patients randomly assigned to each of the four following treatment conditions: Group IF (combined treatment group) consisted of patients receiving 1) imipramine; 2) 90-minute group flooding; and 3) individual 15-minute therapeutic instructions. Group I (imipramine treatment group) consisted of patients receiving 1) imipramine; 2) 90-minute group discussion; and 3) individual 15-minute therapeutic instructions. Group F (flooding treatment group) consisted of patients receiving 1) placebo; 2) 90-minute group flooding; and 3) individual 15-minute therapeutic instructions. Group NS (nonspecific treatment group) consisted of patients receiving 1) placebo; 2) 90-minute group discussion; and 3) 15-minute individual therapeutic instructions. The entire treatment phase consisted of 12 weekly sessions.

Drug Treatment

Patients were assigned to either imipramine or matched placebo according to a predetermined randomization order known only to the hospital pharmacist. Thus, drug treatment was double-blind. In the weekly individual sessions, one tablet of imipramine 25 mg or placebo was prescribed at bedtime and increased by 25 mg increments every second day until a tolerable maintenance dosage or a maximum of 200 mg (8 tablets) was reached. The average maintenance dosage of imipramine attained in the last month of treatment was 119 mg per day (range 25-200 mg) and that of placebo was 166 mg (range 50-200 mg).

Behavioral Treatment

In addition to the individual sessions, patients, in groups of eight, were assigned alternatingly to either flooding or discussion conditions. In the flooding condition, they were encouraged to enter their most phobic situations either alone or with the assistance of the therapist at first. This typically involved going to the center of town, visits to department stores and shopping malls, bus rides, and walking in congested areas alone uninterruptedly for longer and longer distances. The patients assigned to the group discussion met with the same therapist for general discussion of their phobias and their progress. Instructions and reinforcement for self-controlled *in vivo* practice were repeatedly given, and general practical suggestions such as engaging the help of a friend or spouse and/or selecting certain specific phobic situations for that particular week's practice were offered. However, specific cognitive strategies such as paradoxical intention or self-statement training were not given. The mean number of sessions attended by the patients was 11.

Therapeutic Instructions

All patients were given the same therapeutic rationale and instructions. Briefly, they were told that the reason why their fears had continued and even increased with time was due to their habitual avoidance behavior, and that in order to overcome their fears and anxieties they should stop avoiding and start entering their phobic situations. It was strongly suggested to them that once in a phobic situation, they should remain there and tolerate the anxiety-discomfort until it decreased to fairly comfortable levels and/or until their urge to escape abated (i.e., habituation took place). They were also told that it is a good principle to proceed with their self-controlled exposure practices along a hierarchy from the least to the most phobic situations. Their progress was reviewed weekly, reported gains in improvement were reinforced, and patients were encouraged to proceed with their self-controlled *in vivo* practices. Furthermore, it was emphasized to them that whatever additional treatment they received, such as the drugs and the group treatments, was designed to facilitate their carrying out self-controlled *in vivo* exposure practices.

Therapists

The same psychiatrist (MM) saw all the patients in the weekly 15-minute individual sessions, and the same clinical psychologist (LM) conducted the group sessions.

Assessment

A comprehensive assessment battery consisting of clinical ratings of severity of illness, general symptom checklist, clinical ratings of phobia, anxiety, panic, and depression as well as direct measures of agoraphobia in behavioral, subjective, and physiological response systems was administered at pretreatment, at 4, 8, and 12 weeks of treatment, and at 1 month posttreatment. The rationale for using these numerous measures was to enable subsequent and more detailed psychometric and clinical analyses of their inter- and intrarelationships. The authors are currently examining these widely used outcome measures in regard to both internal consistency (i.e., Kudar-Richardson 21 reliabilities, factor analysis, and item analyses), and external validity (i.e., discriminant, convergent, concurrent, and predictive).

Results

Repeated measures analysis of variance (ANOVAS) were performed across pre-4-8-12 weeks and 1 month posttreatment assessments and between the four experimental conditions, as presented in Table 1, and indicated significant main effects, repeated measures effects, and interaction effects on numerous dependent measures.

Table 1

Repeated Measures analysis of Variance on Measures Showing Significant Difference Among Imipramine-Flooding (IF), Imipramine (I), Flooding (F), and Nonspecific Treatment Groups (NS) Post-Hoc Comparisons Using Newman-Keuls Tests Between Treatment Groups

Measure	Group	Pre $\bar{X}$	4 $\bar{X}$	8 $\bar{X}$	12 $\bar{X}$	1 Month $\bar{X}$	Main Effects *F*-Ratio	Repeated Measures *F*-Ratio	Interaction Effects *F*-Ratio	4th Week	8th Week	12th Week	1 Month Post-treatment
SRS	IF	7.3	4.0	3.8	2.0	1.8	3.21^a	55.54^c	1.65	NS^a	NS	1234	2314
	I	6.2	3.6	3.0	2.2	0.8							
	F	6.8	4.0	3.6	2.4	1.4							
	NS	7.2	4.8	5.4	4.0	4.8							
HSCL	IF	101.6	(—)	(—)	63.8	61.4	5.49^b	31.73^c	0.86	(—)	(—)	2314	2314
	I	80.8			52.8	55.4							
	F	95.8			60.8	57.3							
	NS	107.0			79.4	91.4							

Table 1 (Continued)

MHC	IF	88.8	85.2	80.2	75.6	79.6	3.33^a	22.07^c	1.23	NS	NS	2134	NS
	I	88.5	78.0	72.8	70.6	78.6							
	F	87.8	81.2	78.7	76.5	73.0							
	NS	85.3	86.3	82.7	85.0	87.6							
FQ-T	IF	82.2	61.8	51.2	31.0	31.4	3.11^a	40.76^c	4.24^c	NS	3214	3214	1324
	I	67.0	39.6	34.4	39.6	28.0							
	F	57.3	33.8	31.2	26.2	18.8							
	NS	62.0	61.3	56.5	52.0	62.5							
PAA	IF	7.4	4.0	3.6	1.8	1.2	3.43^a	102.16^c	2.76^b	NS	NS	123 4	132 4
	I	7.8	4.6	3.4	2.3	1.6							
	F	7.3	4.8	3.6	2.5	1.4							
	NS	7.4	6.0	4.9	.3	4.9							
MAS	IF	21.0	12.6	16.6	14.8	15.2	4.78^b	15.83^c	1.91^a	231 4	231 4	2314	3214
	I	19.0	12.2	10.6	8.6	9.2							
	F	23.2	15.2	12.3	10.7	7.7							
	NS	21.0	21.0	20.2	18.0	19.2							
Panic	IF	5.6	3.0	2.4	2.5	2.0	3.37^a	11.77^c	0.91	NS	NS	NS	3214
	I	3.8	1.5	2.3	1.0	0.7							
	F	5.7	3.0	1.2	0.8	0.6							
	NS	6.3	4.6	5.7	2.7	4.3							
BDI	IF	18.0	12.0	7.0	7.2	5.4	3.27^a	24.97^c	0.90	231 4	NS	2314	2314
	I	15.0	5.8	2.4	1.4	1.8							
	F	12.2	7.5	6.8	4.3	4.8							
	NS	20.0	13.0	9.6	10.8	13.0							
SDS	IF	58.6	46.8	44.6	41.6	43.2	3.54^a	10.71^c	1.22	NS	3214	2134	2314
	I	50.6	39.8	43.2	32.3	32.2							
	F	56.2	46.7	39.8	41.7	40.0							
	NS	55.8	52.2	58.0	49.0	53.8							
S-SUDS	IF	3.1	1.6	2.1	0.3	0.4	3.15^a	9.73^c	1.01	NS	NS	1324	1324
	I	2.2	3.3	2.3	1.6	0.8							
	F	3.6	3.5	3.0	0.5	0.5							
	NS	4.8	4.0	3.1	2.8	3.2							

[a] $p<.05$ [b] $p<.01$ [c] $p<.001$ [d] (NS = Not significant)

NOTE: (—) = No data for that assessment phase.

Abbreviation used:
SRS = Self-Rating of Severity
HSCL = Hopkins Symptom Checklist
MHQ = Middlesex Hosp. Question.
FQ-T = Fear Questionnaire-Total
SDS = Zung Depression Scale
MAS = Taylor Manifest Anxiety Scale
PAA = Phobic Anxiety and Avoidance
Panic = Panic Scale
BDI = Beck Depression Inventory
S-SUDS = Mean Subjective Unit of Discomfort During Behavioral Course

Outcome Analyses

Two (medication vs. placebo) × two (flooding vs. discussion) analyses of covariance were performed on all major dependent measures at the 1 month posttreatment assessment. The results, as presented in Table 2, show significant main effects, medication effects, flooding effects, and interaction effects for the vast majority of the measures. Indeed, there were significant main effects across all domains of functioning including severity of illness, phobia, anxiety, depression, and behavioral measures of phobic anxiety and avoidance. In regard to medication effects significant findings were also obtained within each of these above domains. Similarly, flooding effects were pronounced across all domains, except for the two depression measures. As can be seen in Table 2, significant interaction effects were also obtained on all but two measures.

After obtaining statistically significant main effects, the four experimental groups were compared using Neuman-Keuls posthoc analyses (see Table 1). The results indicated that the nonspecific (NS) control group was significantly less effective than the other three treatments. Indeed, the NS group evidenced statistically significant weaker therapeutic effects on 10 major dependent measures across all domains of functioning. However, as can be seen in Table 1, there were no significant differences between the imipramine and the flooding groups. Furthermore, no significant differences were found between the combined treatment (IF) and its individual components. These results suggest equivalency across the flooding, imipramine, and combined treatments.

Next, a series of clinically oriented analyses were performed based on operationally defined measures of improvement and end-state functioning. Table 3 shows that at 1 month posttreatment assessment, 73 percent of the patients had improved highly and 58 percent were functioning at a high level.

Table 2

2 × 2 Analyses of Covariance Between Combined Imipramine-Flooding, Imipramine, Flooding, and Nonspecific Treatment Conditions

Major Dependent Measures at 1 Month Posttreatment	Main Effects F-Ratio	Medication Effects F-Ratio	Flooding Effects F-Ratio	Interaction Effects F-Ratio
Severity/General Symptomatology				
Global Assessment of Severity (GAS)	8.00^{b}	13.10^{b}	4.08^{a}	<1
Self-Rating of Severity (SRS)	7.50^{b}	9.09^{b}	5.91^{b}	13.46^{b}
Hopkins Symptom Checklist (HSCL)	5.61^{b}	4.37^{a}	7.12^{b}	8.39^{b}
Middlesex Hospital Questionnaire (MHQ)	2.67^{a}	<1	5.26^{b}	<1
Phobia				
Fear Survey Schedule (FSS)	<1	<1	<1	—
Fear Questionnaire—Total (FQ-T)	15.11^{c}	13.19^{c}	21.53^{c}	9.03^{b}
Fear Questionnaire—Agoraphobia (FQ-Ag)	13.43^{c}	11.48^{b}	15.15^{c}	3.32^{a}
Phobic Anxiety and Avoidance (PAA)	9.61^{c}	8.67^{b}	11.35^{b}	9.07^{b}
Anxiety				
Zung Self-Rating Anxiety Scale (SAS)	6.37^{b}	2.80^{a}	10.49^{b}	3.32^{a}
Taylor Manifest Anxiety Scale (MAS)	1.57	<1	3.08^{a}	20.13^{c}
Panic Scale	3.57^{a}	<1	6.67^{b}	12.39^{c}
Depression				
Beck Depression Inventory (BDI)	4.01^{a}	7.28^{a}	<1	6.41^{b}
Zung Self-Rating Depression Scale (SDS)	2.01	3.82^{a}	<1	7.86^{b}
Behavioral Measures				
Standard Course Battery (S-BAT)	<1	<1	<1	—
Subjective Unit of Discomfort S-SUDS	7.58^{b}	4.18^{a}	9.40^{b}	4.58^{a}
Idiosyncratic Behavioral Test (I-BAT)	1.72	3.44^{a}	<1	—
Subjective Unit of Discomfort I-SUDS	8.05^{c}	7.23^{b}	7.83^{b}	6.06^{b}

$^{a}p< .05$ $^{b}p< .01$ $^{c}p< .001$

Table 3

Improvement and End-State Functioning at the 1-Month Posttreatment Assessment

Number of Criteria Met (Maximum-4)	Improvement		End-State Functioning	
	N	%	*N*	%
0	2	8	5	19
1	3	12	2	8
2	2	8	4	15
3	11	42	6	23
4	8	31	9	35

Chi-squares were then performed to compare patients scoring low (0-2) vs. those scoring high (3-4) on improvement and end-state functioning across the four experimental treatment conditions. The results were statistically significant (improvement: Chi-square = 14.14, 4 *df*, $p < .01$, ETA = .74; end-state: Chi-square = 17.26, 4 *df*, $p < .001$, ETA = .81) and revealed that the three active treatments were superior to the NS group. Indeed, none of the active groups had cases of low improvement in contrast to the NS group where the majority of patients (e.g., 75 percent), evidenced a low level of improvement.

Finally, the presence (+) or absence (−) of spontaneous panic attacks (SPA) was assessed. At pretreatment, 69 percent of the patients were SPA (+), while at 1-month posttreatment this had declined to 27 percent. Furthermore, interesting differences emerged between the four experimental conditions. Sixty percent of the patients in the IF group were SPA (+) at pretreatment, which declined to 0 percent at 1-month followup. The figures were identical, pre-50 percent and 1-month followup 17 percent SPA (+), for both the I and F conditions. In the NS group, 75 percent were SPA (+) at pretreatment and this had declined to only 50 percent at 1 month followup.

Process Analyses

To ascertain during which assessment phase(s) significant changes occur, sequential *t*-tests were performed comparing pre-4, 4-8, 8-12, and 12 weeks-1 month posttreatment segments in the overall group and within each experimental condition.

Table 4 presents the results which reveal that significant changes occur early on many measures and that there is a reduction in the number of measures reaching significance in subsequent phases of treatment. It is interesting to note that in the first month of treatment, 11 out of the 14 measures achieved significant changes with the combined treatment. The same effect was obtained with imipramine, whereas only seven measures reached significance with flooding. The notable difference between I and F were measures of anxiety and depression. Furthermore, four of the central measures of agoraphobia also show significant improvement with the nonspecific treatment in the first month of treatment, supporting the therapeutic usefulness of providing rationale and instructions to agoraphobic patients.

The second and third months of treatment seem to be a period of consolidation of gains, with fewer measures reaching significance. This would suggest that with the active treatments, major gains occurred in the first month of treatment, with improvement continuing to occur up to 1 month posttreatment. Interestingly, measures of agoraphobia as well as depression and performance improved significantly in the second month of treatment even with the nonspecific treatment. However, little change occurred after this period with this treatment, suggesting that its effectiveness is limited to the initial phase of the intervention.

In contrast, significant improvement on measures of phobia and anxiety continued to take place with flooding in the posttreatment phase. This would suggest that patients treated with flooding continue their treatment, on a self-directed basis, thus consolidating gains after formal termination of therapy. In addition, the imipramine group, far from relapsing, seems to experience further reduction in the severity of their agoraphobic condition.

Table 1 also illustrates the Neuman-Keuls posthoc comparisons of the experimental treatment conditions at each assessment. Two comparisons at Week 4 reached significance, indicating that the imipramine condition alone was superior to the control treatment on clinical anxiety and depression measures. However, there were no significant differences between the three active groups. By Week 8 the three active treatments still did not differ significantly, although imipramine and flooding treatments differed significantly from nonspecific treatment on a clinical anxiety measure and flooding, in addition, differed significantly from the nonspecific group on a depression measure. At the 12-week assessment, and at the 1 month posttreatment assessment, the three active treatments did not differ significantly from one another but achieved significantly greater results compared to the nonspecific group on most measures.

The Figure illustrates these differential patterns of change and underscores the marked and rapid improvement in mood which imipramine induces and which is apparent by Week 4. It also shows that similar changes occur with flooding but that this treatment may require up to 8 weeks to equal the changes seen with imipramine. On both measures of anxiety and panic, rate of improvement levels off with imipramine between 4-8 weeks of treatment, whereas improvement maintains a steady pace with flooding. Moreover, improvement in depression is rapid and equivalen for both imipramine and flooding treatments i the first month. Further improvements continu with both treatments, albeit more gradually wit flooding. Finally, on the measure of agoraphobi anxiety and avoidance, the course of improvement with both treatments is identical. Interestingly, improvement in subjective anxiety experienced during the behavioral avoidance te does not improve in the first 4 weeks of treatmen except with the combined imipramine/floodin treatment. This is puzzling, because in the same period flooding remains unchanged and imipramine induces a worsening on this measure. Furthermore, this apparent advantage of the combined group is lost by Week 8. On this measure, and in contrast to the other measures of mood, major changes seem to occur in the later phases o treatment and appear to be associated mor strongly with flooding.

Table 4

Sequential T-Test Comparisons of Pre-4-8-12 Weeks and 1-Month Posttreatment Assessments for Overall Sample, Imipramine and Flooding, Imipramine, Flooding, and Nonspecific Control Conditions

	GAS	SRS	HSCL	MHQ	FSS	FQ-T	FQ-AG	PAA	SAS	MAS	PANIC	BDI	SDS	S-BAT	S-SUDS	I-BAT	I-SUDS
Pre to 4	IF O	IF F O I NS	(—)	IF F O I	IF F O I	IF F O I	IF F O I NS	IF F O I NS	O I	IF O I	O I F NS	IF O I	IF O I	O	IF	(—)	(—)
4 to 8	IF O F		(—)	O I	I		O	F O I NS	F	O	F	O NS			O NS	(—)	(—)
8 to 12	O NS	IF O I	IF O F NS		IF	O	IF O I	IF O I		O			O I		O F	I O	IF F O
12 to One Month Post		I	NS sig. worsen-ing			F	F	O		F							I

Note: Presence of group code indicates statistically significant differences between the previous assessment phase and the assessment where the code app

O = Overall Group
I = Imipramine Group
IF = Meds/Flooding Group
F = Flooding Group
NS = Placebo/Discussion Group
(—) = No data for these measures at 4-and 8-week assessment
(p < .05)

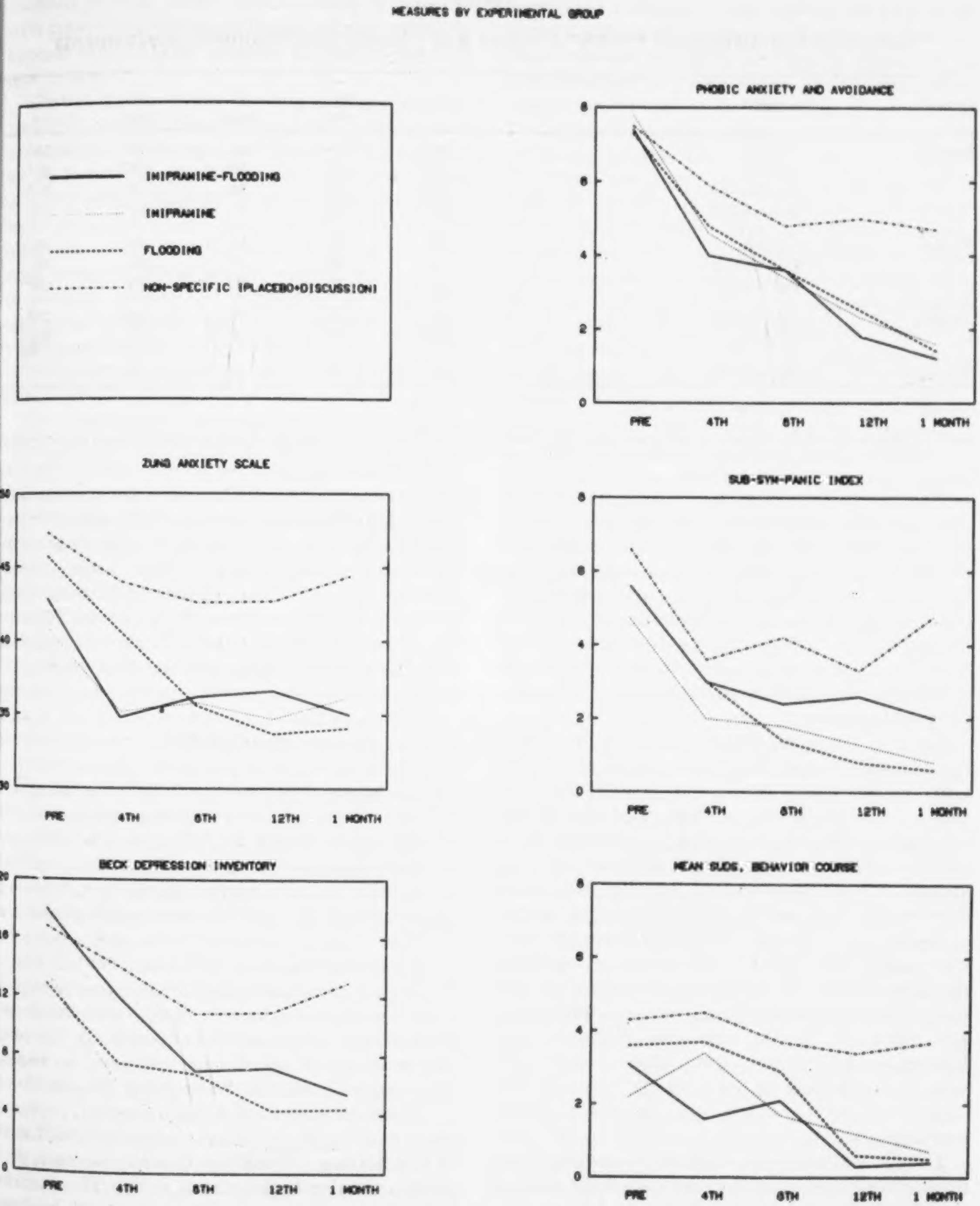


FIGURE. Measures of anxiety, depression, phobic anxiety and avoidance, panic, and distress during the behavioral ourse across the four experimental treatment conditions.

Table 5

Canonical Correlations at Pre-4-8-12 Weeks and 1-Month Posttreatment Assessments

Domain I	Domain II	Pre	4th Week	8th Week	12th Week	1 Mo Pos
Severity	Phobia	.89[c]	.87[a]	.91	.97[a]	.92[a]
	Anxiety	.82[a]	.80	.95	.95[a]	.89[a]
	Depression	.84[b]	.74	.80	.76	.84[a]
	Behavioral	.56	.78[a]	.91	.97[c]	.92[b]
Phobia	Anxiety	.69	.68	.98	.86	.89[b]
	Depression	.63	.79	.72	.80	.70
	Behavioral	.51	.58	.95	.95	.95[c]
Anxiety	Depression	.53	.84[a]	.85	.90[b]	.79[b]
	Behavioral	.73[a]	.69	.66	.81	.75
Depression	Behavioral	.46	.19	.55	.83	.74

[a] $p < .05$ [b] $p < .01$ [c] $p < .001$

Note: The size of the correlation needed to achieve statistical significance may differ across assessments due to varying sample sizes. Thus, the absolute lev correlation in addition to the resultant significance level, should be considered.

Next, multivariate canonical correlation analyses were performed to evaluate the patterns of relationship between the different domains of assessment in the course of treatment. Based on hypothesis of differential rates and patterns of change across treatments and measures earlier in treatment, the authors expected to find low correlations among the various domains earlier in treatment, and higher correlations in the later phases of treatment.

Table 5 presents the domains, their constituents, and the results of the canonical correlations at all assessments. The results depict a steady increase in the percent of domains correlating significantly as well as a parallel rise in the strength of the correlations as treatment progresses. These results strongly support the idea of differential rates and patterns of change across measures occurring in the early phases of treatment and justify further explorations in regard to the phenomena of synchrony/desynchrony and concordance/disconcordance across treatments and domains, as discussed by Hodgson and Rachman (1974). Moreover, these results add support to the use of multiple process/outcome measures with which to delineate these phenomena.

Finally, patients were divided into two groups, depending on whether they met 0-2 (LEF) or 3-4 (HEF) of the end-state functioning criteria (*see* Table 3) and compared across each assessment phase. The results of the *t*-tests showed no pr treatment differences between HEF and LEF pa tients. However, by Week 4, significant dif ferences emerged on many of the major depen dent measures, in favor of the HEF group. Thi pattern continued at Week 8, and by the 12-wee assessment showed increases strength in regard t both the number and size of the differences.

Discussion

The degree of improvement found in the entir sample reflects the overall effectiveness of th clinical research project. Despite the inheren methodological constraints (nine patients receive nonspecific control treatment), the overall level o improvement compares favorably with previousl reported outcome studies with imipramine o flooding (Mavissakalian & Barlow 1981a). Thus the magnitude of change on the clinical scales (2- point decrease on 9-point scales are considere marked improvement in the literature), the co sistent statistical significancy obtained on near all measures, and the finding that 73 percent o the patients witnessed a high level of impro ment with nearly 60 percent enjoying a high leve of functioning, all indicate that the research pro gram was also highly therapeutic. The autho believe this is an important point becau agoraphobic patients, like most chronicall disabled groups, enter clinical research projects with great expectations of being helped—which it appears were in great measure fulfilled in the current project.

The results show that flooding and imipramine are highly and equally effective in the treatment of agoraphobia. Although was found partial support for the hypothesis predicting earlier improvement in mood with imipramine, mood was also found very responsive to flooding and the two treatments did not differ from Week 8 of treatment onward. These results suggest the exercise of extreme caution in attributing an exclusive etiological treatment status to pharmacotherapy which purportedly would treat the core problem of "endogenous anxiety" in agoraphobia (Sheehan et al. 1980).

The results did not support the hypothesis which predicted that phobic avoidance and anxiety would improve earlier with flooding. In fact, there was suggestive evidence that anxiety, experienced during the behavioral testing, improved in the later phases of treatment, even in those patients treated with flooding. In a recent study, (Mavissakalian & Michelson, in press) which investigated differential rates and patterns of change between the three response systems of behavioral performance, subjective anxiety, and physiological responsiveness measured by heart rate, it was found that clinical and behavioral improvement occured early in treatment followed by improvement in subjective anxiety and heart rate in the intermediate and later phases of treatment. These results were interpreted as supporting the hypothesis advanced by Hodgson and Rachman (1974) predicting that psychophysiological improvement would lag behind behavioral improvement in flooding or similar behavioral treatments with high demand characteristics. Such high demand characterized the treatment of all the patients who were repeatedly instructed to practice self-directed flooding. The increased concordance between all domains of assessment in the later phases of treatment adds further support to the predictions of change advanced by Hodgson and Rachman concerning treatments with high demand characteristics.

A major and unexpected finding was the failure of the combined imipramine flooding treatment to show a clear superiority over the individual treatments. *Therefore, when therapeutic rationale and instructions to practice in vivo exposure are given to patients, it appears that imipramine, flooding, or their combined treatment are highly and equally effective in the short-term outcome of agoraphobia.* This finding raises serious questions as to the need for combined treatments in agoraphobia and suggests that the primarily clinical advantage stemming from the combined treatment would be the possibility of reduced relapse rates, compared to pharmacotherapy alone. The prolonged followup phase planned in the completed research project will address this question. However, preliminary findings of a 6-month followup reported by Zitrin et al. (1980) are not encouraging since they revealed that 27 percent of agoraphobic women treated with combined imipramine and flooding relapsed, a figure which is as high as those encountered with antidepressants alone (Sheehan et al. 1980).

Therapeutic rationale and instructions to practice *in vivo* exposure, even though systematically prescribed over a 3-month period, seem to be inadequate by themselves. In this condition, some improvement seems to take place in the first 8 weeks of treatment but subsequently levels off. This contrasts with the marked improvement noted in the earlier phases as well as the continuing improvement in the later phases of active treatments, and suggests that this is a weak and time-limited treatment. However, the observation that two out of the nine patients in this group showed high levels of improvement suggests that in a small percentage of agoraphobics these nonspecific treatment factors can be sufficiently effective in their own right and, furthermore, that in this weaker treatment certain patient characteristics might prove crucial in determining substantial degrees of improvement.

In regard to the differential patterns of change between low end-state and high end-state functioning patients, it was observed that more rapid treatment gains occurred among the high end-state functioning group. Indeed, these patients were already showing significant improvement by the 4th week and continued to accelerate their therapeutic responses across subsequent assessment phases. Conversely, the low end-state functioning group showed significantly slower and smaller treatment gains. These findings suggest that early changes in treatment could be extremely useful in identifying responders, and that clinicians might incorporate these findings into their treatment by considering alternative interventions for patients who fail to show gains by Weeks 4 or 8. On the other hand, pretreatment baseline measures did not differ between responders and nonresponders and therefore do not seem likely to provide prognostically helpful information at this time.

If the completed projects' results confirm these preliminary findings, it would raise the question and search for a common factor to explain the similarity of outcome between the active treatments. Since all patients in all groups received the same therapeutic rationale and instructions to practice, it is conceivable that the degree of self-practiced exposure is a major mediating factor in these treatments. If this is truly the case, one would expect to find less practice in the nonspecific group than in the other three treatment groups which, in addition, would not differ significantly in this respect. The authors plan to examine the role of self-directed practice in the various treatments, using continuous naturalistic data collected by means of diaries.

In summary, these preliminary results indicated that imipramine, flooding, and their combination treatment are equally effective in the treatment of agoraphobia, given that rational and basic instructions to practice *in vivo* are present. Clearly, these findings need replication on larger samples. Likewise, the numerous questions raised, relating to both process and long-term outcome, require further elucidation. What seems likely, however, is that self-help groups relying solely on discussion and providing support and information as well as instructions to face phobic situations may be of limited effectiveness in the treatment of chronic agoraphobia.

References

Barlow, D.H., Agras, W.S., Leitenberg, H., and Wincze, J.P. An experimental analysis of the effectiveness of 'shaping' in reducing maladaptive avoidance behavior: An analogue study. *Behav. Res. Ther.*, 8:165-173, 1970.

Barlow, D.H., Leitenberg, H., Agras, W.S., and Wincze, J.P. The transfer gap in systematic desensitization: An analogue study. *Behav. Res. Ther.*, 7:191-196, 1969.

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., and Erbaugh, J. An inventory for measuring depression. *Arch. Gen. Psychiatry*, 4:561-571, 1961.

Colgan, A. A pilot study of Anafranil in the treatment of phobic states. *Scot. Med. J.*, 20:55-60, 1975.

Crowe, M.J., Marks, I.M., Agras, W.S., and Leitenberg, H. Time-limited desensitization, implosion and shaping for phobic patients: A crossover study. *Behav. Res. Ther.*, 10:319-328, 1972.

Crown, S. and Crisp, A.H. A short clinical diagnostic self-rating scale for psychoneurotic patients: The Middlesex Hospital Questionnaire (M.H.Q.). *Br. J. Psychiatry*, 112:917-923, 1966.

Derogatis, L.R., Lipman, R.S., Rickels, K., Uhlenhuth, E.H., and Covi, L. The Hopkins Symptom Checklist (HSCL): A self-report symptom inventory. *Behav. Sci.*, 19:1-15, 1974.

Emmelkamp, P.M.G. Self-observation versus flooding in the treatment of agoraphobia. *Behav. Res. Ther.*, 12:229-237, 1974.

Emmelkamp, P.M.G. and Kuipers, A.C.M. Agoraphobia: A follow-up study four years after treatment. *Br. J. Psychiatry*, 134:342-355, 1979.

Emmelkamp, P.M.G. and Ultee, K.A. A comparison of 'successive approximation' and 'self-observation' in the treatment of agoraphobia. *Behav. Ther.*, 5:606-613, 1974.

Emmelkamp, P.M.G. and Wessels, H. Flooding in imagination versus flooding *in vivo:* A comparison with agoraphobics. *Behav. Res. Ther.*, 13:7-15, 1975.

Everaerd, W.T.A.M., Rijken, H.M. and Emmelkamp, P.M.G. A comparison of 'flooding' and 'successive approximation' in the treatment of agoraphobia. *Behav. Res. Ther.*, 11:105-117, 1973.

Gelder, M.G., Bancroft, J.H.J., Gath, D.H., Johnston, D.W., Mathews, A.M., and Shaw, P.M. Specific and nonspecific factors in behaviour therapy. *Br. J. Psychiatry*, 123:445-462, 1973.

Hafner, H., and Marks, I. Exposure *in vivo* of agoraphobics: Contributions of diazepam, group exposure, and anxiety evocation. *Psychol. Med.*, 6:71-88, 1976.

Hallam, R.S., and Hafner, R.J. Fears of phobic patients: Factor analyses of self-report data. *Behav. Res. Ther.*, 16:1-6, 1978.

Hand, I., Lamontagne, Y., and Marks, I.M. Group exposure (flooding) *in vivo* for agoraphobics. *Br. J. Psychiatry*, 124:588-602, 1974.

Hodgson, R., and Rachman, S. II. Desynchrony in measures of fear. *Behav. Res. Ther.*, 12:319-326, 1974.

Jannoun, L., Munby, M., Catalan, J., and Gelder, M.G. A home-based treatment program for agoraphobia: Replication and controlled evaluation. *Behav. Ther.*, 11:294-305, 1980.

Kelly, D., Guirguis, W., Frommer, E., Mitchell-Heggs, N., and Sargent, W. Treatment of phobic states with antidepressants. A retrospective study of 246 patients. *Br. J. Psychiatry*, 116:387-398, 1970.

King, A. Phenelzine treatment of Roth's Calamity Syndrome. *Med. J. Aust.*, 6:879-883, 1962.

Klein, D.F. Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia (Berlin)*, 5:397-408, 1964.

Klein, D.F. Importance of psychiatric diagnosis in prediction of clinical drug effects. *Arch. Gen. Psychiatry*, 16:118-126, 1967.

Klein, D.F. Delineation of two drug-responsive anxiety syndromes. *Psychopharmacologia (Berlin)*, 5:397-408, 1964.

Klein, D.F. Importance of psychiatric diagnosis in prediction of clinical drug effects. *Arch. Gen. Psychiatry*, 16:118-126, 1967.

Klein, D.F. and Fink, M. Psychiatric reaction patterns to imipramine. *Am. J. Psychiatry*, 119:432-438, 1962.

Lipsedge, M.S., Hajioff, J., Huggins, P., Napier, L., Pearce, J., Pike, D.J., and Rich, M. The management of severe agoraphobia: A comparison of iproniazid and systematic desensitization. *Psychopharmacologica (Berlin)*, 32:67-80, 1973.

Marks, I.M. *Fears and Phobias*. London: Heineman Medical Books, 1969.

Marks, I.M. Phobic disorders four years after treatment: A prospective follow-up. *Br. J. Psychiatry*, 118:683-688, 1971.

Marks, I.M. & Gelder, M.G. A controlled retrospective study of behavior therapy in phobic patients. *Br. J. Psychiatry*, 11:561-573, 1965.

Marks, I.M. & Mathews, A.M. Brief standard self-rating for phobic patients. *Behav. Res. Ther.*, 17:263-267, 1979.

Marshall, W.K. and Micev, V. The role of intravenous clomipramine in the treatment of obsessional and phobic disorders. *Scot. Med. J.*, 20:49-53, 1975.

Mathews, A.M., Johnston, D.W., Lancashire, M., Munby, M., Shaw, P.M., and Gelder, M.B. Imaginal flooding and exposure to real phobic situations: Treatment outcome with agoraphobic patients. *Br. J. Psychiatry*, 129:362-371, 1976.

Mathews, A.M., Teasdale, J., Munby, M., Johnston, D.W., and Shaw, P.M. A home-based treatment program for agoraphobia. *Behav. Ther.*, 8:915-924, 1977.

Mavissakalian, M., and Barlow, D.H. (eds.) *Phobia: Psychological and Pharmacological Treatment*. New York:Guilford Press, 1981a.

Mavissakalian, M., and Barlow, D.H. Phobia: An overview. In *Phobia: Psychological and Pharmacological Treatment*. Mavissakalian, M., and Barlow, D.H. (eds.), New York:Gilford Press, 1981b.

Mavissakalian, M., and Michelson, L. Patterns of psychophysiological change in the treatment of agoraphobia. *Behav. Res. Ther.* (In press)

McDonald, R., Sartory, G., Grey, S.J., Cobb, J., Stern, R., and Marks, I. The effects of self-exposure instructions on agoraphobic outpatients. *Behav. Res. Ther.*, 17:183-185, 1979.

McPherson, F.M., Brougham, L., and McLaren, S. Maintenance of improvement in agoraphobic patients treated by behavioural methods — A four-year followup. *Behav. Res. Ther.*, 18:150-152, 1980.

Mountjoy, C.Q., Roth, M., Garside, R.F., and Leitch, I.M. A clinical trial of phenelzine in anxiety depressive and phobic neuroses. *Br. J. Psychiatry*, 131:486-492, 1977.

Sheehan, D.V., Ballenger, J., and Jacobsen, G. Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms. *Arch. Gen. Psychiatry*, 37:51-59, 1980.

Snaith, R.P. Clinical investigation of phobias. *Br. J. Psychiatry*, 114:673-698, 1968.

Solyom, L., Heseltine, G.F.D., McClure, D.J., Solyom, C., Ledwidge, B., and Steinberg, G. Behaviour therapy versus drug therapy in the treatment of phobic neurosis. *Can. J. Psychiatry*, 18:23-32, 1973.

Stern, R., and Marks, I. Brief and prolonged flooding: A comparison in agoraphobic patients. *Arch. Gen. Psychiatry*, 28:270-276, 1973.

Taylor, J.A. A personality scale of manifest anxiety. *J. Abnorm. Soc. Psychol.*, 48:285-290, 1953.

Teasdale, J.D., Walsh, P.A., Lancashire, M., and Mathews, A.M. Group exposure for agoraphobics: A replication study. *Br. J. Psychiatry*, 130:186-193, 1977.

Tyrer, P., Candy, J., and Kelly, D. Phenelzine in phobic anxiety: A controlled trial. *Psychol. Med.*, 3:120-124, 1973a.

Tyrer, P., Candy, J, and Kelly, D. A study of the clinical effects of phenelzine and placebo in the treatment of phobic anxiety. *Psychopharmacologia (Berlin)*, 32:237-254, 1973b.

Tyrer, P., and Steinberg, D. Symptomatic treatment of agoraphobia and social phobias: A follow-up study. *Br. J. Psychiatry*, 127:163-168, 1975.

Watson, J.P., and Marks, I.M. Relevant and irrelevant fear in flooding: A crossover study of phobic patients. *Behav. Ther.*, 2:275-295, 1971.

Waxman, D. An investigation into the use of Anafranil in phobic and obsessional disorders. *Scot. Med. J.*, 20:61-66, 1975.

Wolpe, J., and Lang, P.J. A fear survey schedule for use in behaviour therapy. *Behav. Res. Ther.*, 2:27-30, 1964.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Behavior therapy, supportive psychotherapy, imipramine, and phobias. *Arch. Gen. Psychiatry*, 35:307-316, 1978.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Treatment of agoraphobia with group exposure *in vivo* and imipramine. *Arch. Gen. Psychiatry*, 37:63-72, 1980.

Zung, W.W.K. A self-rating depression scale. *Arch. Gen. Psychiatry*, 12:63-70, 1965.

Zung, W.W.K. A rating instrument for anxiety disorders. *Psychosomatics*, 12:371-379, 1971.

Comparison of Generalized Anxiety Disorder With Panic Disorder Patients

Rudolf Hoehn-Saric, M.D.[1]

Few attempts were made to distinguish subgroups of patients with the broad diagnosis of "anxiety neurosis" prior to the reclassification of anxiety disorders in the Diagnostic and Statistical Manual-III (DSM-III). The discovery that antidepressants prevent the reoccurrence of panic attacks but do not affect anticipatory anxiety (Klein 1981), led to the division of anxiety neurosis into panic disorder and generalized anxiety disorder. Several studies have investigated panic disorders (Klein et al. 1978; Mountjoy et al. 1977; Sheehan et al. 1980), however, the description of generalized anxiety disorders in DSM-III was based on clinical impression rather than on systematic data. In an earlier study, Hoehn-Saric (1981) reported that generalized anxiety disorder patients differed from those with panic disorders mainly in physical symptoms. Generalized anxiety disorder patients also rated themselves more introverted than those with panic disorder. Recently, a survey which examined symptomatic volunteers found those who were diagnosed as having panic disorder rated themselves higher on the anxiety subscale and the panic anxiety subscale of the Hopkins Symptom Checklist than volunteers who were classified as generalized anxiety disorder (Barrett 1981). This paper presents a more extensive comparison between the two disorders, based on a multi-axial approach, which describes state measures, personality measures, social adjustment, and disturbance during childhood.

Method

Subjects

The population consisted of 133 patients who were admitted to the Anxiety Clinic at the Johns Hopkins Hospital. All patients suffered persistent anxiety for at least 6 months, had no history of psychotic disorder, were not substance abusers, and were sufficiently educated to rate various questionnaires. Criteria for panic disorders followed the guidelines of DSM-III; however, it included patients who experienced panic attacks only once a month. Patients who had experienced panic attacks in the past but, in spite of lack of adequate treatment were free of panic attacks for at least 6 months, were placed in the category of Generalized Anxiety Disorder.

Of the 133 patients examined, 48 percent were diagnosed Generalized Anxiety Disorder and 52 percent Panic Disorder. The average age was 33.9 years, ranging between 18 and 58. Eight-two percent were white and 18 percent black, 60 percent female and 40 percent male, 45 percent were married and the others were single, separated, or divorced. The average education was 13 years, with 8th grade as minimal education. There were no significant differences on any of the demographic data between the two diagnostic conditions.

Measures

At the time of admission to the Anxiety Clinic, patients filled out four types of questionnaires covering present state (symptoms), personality traits, social and personal adjustment, and behavioral disturbances during childhood. The following measures were employed:

---

[1] Johns Hopkins School of Medicine, Baltimore, MD 20205.

State Measures

Physician Ratings. 1) *Hamilton Anxiety Scale* (Hamilton 1959): This scale describes psychic and somatic symptoms associated with anxiety. 2) *Global Rating of Generalized Anxiety:* A 4-point scale describing the general level of anxiety. 3) *Global Rating of Anxiety Attacks:* A 4-point scale describing sudden emergence of anxiety, including panic attacks. 4) *Global Neurotic Scale:* A 4-point scale rating psychic symptoms of anxiety. 5) *Global Somatic Scale:* A 4-point scale rating physical symptoms of anxiety.

Patient Ratings. 1) *State- Trait Anxiety Inventory, State Form* (Spielberger et al. 1970): This form describes the present level of psychic anxiety. 2) *Affects Balance Scale* (Derogatis 1975): A self-rating scale of four positive and four negative affects. 3) *Somatic Symptoms Scale* (Hoehn-Saric 1981): Describes somatic symptoms that frequently accompany anxiety. 4) *Zung Scale of Depression* (Zung 1965): Describes symptoms associated with depression.

Personality Measures

1) *Eysenck Personality Questionnaire Form A* (Eysenck & Eysenck 1975): Measures two personality dimensions: extraversion, which describes the person's sociability and impulsivity, and b) neuroticism, which measures trait anxiety, dysphoria, and lability. 2) *Mastery-Powerlessness Scale* (Frank et al. 1978): This modification of Rotter's Locus of Control Scale (Rotter 1966) rates the person's perception of internal control, i.e., the degree to which he is in control of himself and his environment, as opposed to external control, i.e., seeing himself at the mercy of fate and other forces. 3) *State-Trait Anxiety Inventory, Trait Form* (Spielberger et al. 1970): This scale describes a person's general tendency to respond to anxiety.

Social Adjustment

Clark Personal and Social Adjustment Scale (Clark 1968): This scale appraises the effectiveness and satisfaction at work, interpersonal relationships, feeling of optimism, and feeling of mastery.

Childhood Behavior Disturbance Measure

Childhood History (Tarter et al. 1977): This is a 50-item checklist of behaviors associated with children diagnosed as "minimal brain disorder."

Statistics

Student's *t*-tests were used to compare the differences between scale values in Generalized Anxiety Disorder patients from those of Panic Disorder patients. In addition, discriminant analyses (Wilks) were calculated to identify items differentiating the two disorders.

Results

Table 1 summarizes the differences between the Generalized Anxiety Disorder and Panic Disorder groups. Patients with a Panic Disorder rated significantly higher on the total score of the Hamilton Anxiety Scale ($p < .005$) and, as expected, on the Global Rating of Anxiety Attacks ($p < .001$). The reason that patients diagnosed as Generalized Anxiety Disorder also scored on anxiety attacks was due to the vagueness of the scale which included not only panic attacks, but also strong, rapidly increasing fluctuations of anxiety levels. Ratings on the Zung Scale of Depression and the Global Rating of Generalized Anxiety failed to discriminate between the two groups. Additionally, none of the psychic subscales discriminated significantly between the two groups. However, all of the somatic scales, including the somatic subscale of the Hamilton Anxiety Scale ($p < .001$), the Global Somatic Scale ($p < .003$), and Somatic Symptoms Scale ($p < .05$), differentiated between the two groups. None of the personality measures, the social adjustment ratings, or the Childhood History differed between the two disorders.

Symptoms of the Somatic Symptoms Scale were subdivided into classes describing muscular symptoms, symptoms associated with hyperventilation, cardiovascular symptoms, and gastrointestinal and genital symptoms. Only symptoms

Table 1

Comparison of Generalized Anxiety Disorder With Panic Disorder Patients

STATE MEASURES		Generalized Anxiety Disorders	Panic Disorder	Signifi
General Scales				
Hamilton Anxiety Scale	67[a]	19.8 ± 7.1	25.0 ± 7.0	.005
Global Ratings of Generalized Anxiety	129	1.8 ± 0.7	1.8 ± 0.9	.10
Global Ratings of Anxiety Attacks	129	1.2 ± 1.1	2.0 ± 0.9	.001
Zung Scale of Depression	131	56.5 ± 14.5	58.1 ± 13.4	-
Psychic Subscales				
Hamilton Anxiety Scale, Psychic Subscale	67	11.2 ± 4.0	12.1 ± 3.5	-
Global "Neurotic" Scale	104	2.5 ± 0.8	2.7 ± 0.9	-
STAI, State Form	134	52.0 ± 14.8	56.0 ± 12.00	.10
Affects Balance Scale	133	0.04 ± 1.1	-0.28 ± 0.9	.10
Somatic Subscales				
Hamilton Anxiety Scale, Somatic Subscale	67	8.7 ± 4.4	13.2 ± 4.9	.001
Global "Somatic" Scale	104	2.1 ± 1.0	2.6 ± 0.9	.003
Somatic Symptoms Scale	133	19.2 ± 12.7	23.7 ± 11.4	.05
SOCIAL ADJUSTMENT				
Clark Scale	113	31.7 ± 8.0	33.4 ± 9.0	-
PERSONALITY INVENTORY				
Eysenck Personality Questionnaire	116			
Extraversion		9.5 ± 4.1	9.6 ± 4.5	-
Introversion		16.3 ± 4.9	16.9 ± 4.5	-
STAI, Trait Form	121	51.8 ± 11.3	54.8 ± 11.1	-
Mastery-Powerlessness Scale	112	13.2 ± 4.4	12.2 ± 4.3	-
CHILDHOOD DISTURBANCES				
Childhood Scale	107	7.4 ± 6.2	9.1 ± 6.6	-

[a] Number of patients with completed scales

associated with hyperventilation and the cardiovascular system differentiated significantly between the two disorders ($p < .05$ for each symptom subclass). On individual physical symptoms, patients with panic disorder rated significantly higher ($p < .05$ or higher) on the following subscales: fatigue, sweating, heart pounding, difficulty breathing, having a lump in the throat, headaches, attacks of irritability, attacks of depression, and lower degree of vigor.

Table 2 outlines the results of the discriminant analysis. Only patients with complete records were included. The Hamilton Anxiety Scale, which was introduced after collection of half of the population, was excluded from the analysis. Since highly correlated items are automatically eliminated from the discriminant analysis, the state form of the State-Trait Anxiety Scale whi correlated with the Zung Depression Sca ($r = 0.69$, $p < .001$), does not appear on Table The analysis discriminated to a significant deg between the two disorders ($p < .001$). The analy indicated that in addition to physical symptom the lack of positive affects, the presence negative affects, and general "neurotic" symp toms, differentiated between patients with pa disorders and generalized anxiety disorders. discriminant analysis of the subscales of Somatic Symptoms Scale (*see* Table 3) confirm that symptoms associated with the cardiovascu system and hyperventilation also differentia the two groups ($p < .04$). Furthermore, insomn and loss of sex drive were strongly represented the Panic Disorder patients.

Table 2

Generalized Anxiety Disorder vs. Panic Disorder Discriminant Analysis (Wilks) $N = 87$, (GAD:43, PD:44)

Standardized Canonical Discriminant Function Coefficients:	
Zung Depression Scale (PD higher)	1.25
Affects Balance Scale, Total Positive (PD lower)	1.00
Physicians' Ratings of Anxiety Attacks (PD higher)	−0.68
Affects Balance Scale, Total Negative (PD higher)	−0.59
Global Neurotic Symptoms Scale (PD higher)	0.49
STAI, Trait Form (PD higher)	−0.47
Physicians' Ratings of Generalized Depression (PD higher)	0.45
EPI, Extraversion (PD higher)	−0.36
Physicians' Ratings of Irritability Attacks (PD higher)	−0.36
Physicians' Ratings of Generalized Anxiety (PD lower)	0.34
Global Somatic Symptoms Scale (PD higher)	−0.26
Somatic Symptoms Scale, Muscular Symptoms (PD higher)	−0.24
Group Centroids	
Generalized Anxiety Disorder	0.89
Panic Disorder	−0.87

Canonical discriminant function: Wilks lambda 0.55, *df* = 12, sig. = 0.000

Table 3

Generalized Anxiety Disorder vs. Panic Disorder Discriminant Analysis of Items of the Somatic Symptoms Scale (Wilks) $N = 124$ (GAD: 60/PD: 64)

Standardized Canonical Discriminant Function Coefficients:[a]	
Tingling in arms and legs	0.57
Difficulties sleeping	0.57
Loss of sex drive	−0.57
Heart pounding or racing	−0.51
Sweating	−0.48
Headaches	−0.43
Group Centroids:	
Generalized Anxiety Disorder	−0.35
Panic Disorder	−0.32

[a] Panic disorder group rating higher on all symptoms

Canonical discriminant function: Wilks lambda 0.90, *df* = 6, sig. = 0.04

Discussion

The study confirmed previous findings that patients with Panic Disorder diagnosis score higher on somatic, but not on psychic anxiety scales than patients with a Generalized Anxiety Disorder diagnosis (Hoehn-Saric 1981). In addition, it was demonstrated that the groups differed predominantly in symptoms describing hyperventilation and cardiovascular changes rather than symptoms relating to the muscular and gastrointestinal systems. The results also showed that Panic Disorder patients tend to experience more negative affects, such as depression and irritability. The extended survey failed to replicate the previous finding that Generalized Anxiety Disorder patients are more introverted (Hoehn-Saric 1981). Moreover, the extraversion dimension of the Eysenck Personality Questionnaire correlated poorly with the other measures ($r = \leq .35$), indicating a weak relationship to psychopathology. The neuroticism dimension of the Eysenck Scale was significantly correlated with all psychic scales, the Zung Depression Scale, and the Somatic Symptoms Scale ($r = .43$ to $.69$, $p < .001$), but failed to differentiate between the two diagnostic groups.

The lack of relationship between the diagnostic categories and personality variables, social state, and childhood history suggests that the primary difference between patients who develop panic attacks and those who experience generalized anxiety may lie in their physical response to stress. However, an examination of the population suggests that patients with the diagnosis of Generalized Anxiety Disorder may form a heterogeneous group. Some patients who had experienced panic attacks in the past changed into having generalized anxiety without further panic attacks, while other patients who had suffered from generalized anxiety for years eventually developed a panic disorder. The latter sequence has also been reported by Cloninger et al. (1981). Moreover, in a previous study, Hoehn-Saric and Masek (1981), discovered a group of patients who corresponded to the description of Generalized Anxiety Disorder except that they lacked autonomic hyperactivity. These patients had a significantly higher degree of forehead muscle tension than normal controls. However, heart rate and skin conductance remained comparable to the control group. A pilot study, which the investigator is conducting at the present time, suggests that within moderate degrees of anxiety, some patients experience pronounced autonomic symptoms such as increased diastolic and systolic blood pressure, while others exhibit pronounced muscular symptoms without excessive cardiovascular changes.

Further investigations will be necessary to determine if patients with a Generalized Anxiety Disorder constitute a continuum whose symptoms relate directly to the severity of anxiety, or if they represent distinct subgroups with different constitutionality, one being autonomically labile and the other autonomically stable. If this should be the case, one would expect that under sufficient stress the autonomically labile group would develop panic attacks, while the autonomically stable group may exhibit various psychic symptoms, insomnia, and somatic symptoms associated with increased muscle tension, but would not develop a panic disorder. A dichotomy of patients diagnosed as Generalized Anxiety Disorder into those with high and low levels of cardiovascular symptoms was not helpful, because patients who scored high on cardiovascular symptoms also rated high on all other psychic and somatic measures. Thus, it appears that patients with high levels of anxiety experience all types of somatic symptoms. This does not exclude the possibility of a distinct subgroup of anxiety disorders which, due to their greater autonomic stability, remain within moderate levels of anxiety ratings. A clarification of the existence of such subgroups will be of importance in the pharmacotherapy of anxiety disorders.

References

Barrett, J. Psychiatric diagnoses (Research Diagnostic Criteria) in symptomatic volunteers. *Arch. Gen. Psychiatry*, 38:153-157, 1981.

Clark, A.W. The personality and social network adjustment scale. *Hum. Relat.*, 21:85-96, 1968.

Cloninger, C.R., Martin, R.L., Clayton, P., and Guze, S.B. A blind follow-up and family study of anxiety neurosis: A preliminary analysis of the St. Louis 500. In: Klein, D.F., and Rabkin, J. (eds.), *Anxiety: New Research and Changing Concepts*. New York: Raven Press, 1981, pp. 137-154.

Derogatis, L.R. *Affects Balance Scale (ABS)*. Baltimore: Clinical Psychometric Research, 1975.

Eysenck, S.B.G., and Eysenck, H.J. *Manual of the Eys* *Personality Questionnaire*. London: Hodder and Stoughto 1975.

Frank, J.D., Hoehn-Saric, R., Imber, S.D., et al. *Effe* *Ingredients of Successful Psychotherapy*. New York: Brunne Mazel, 1978, pp. 202-206.

Hamilton, M. The assessment of anxiety states by rating *Br. J. Med. Psychol.*, 32:50-55, 1959.

Hoehn-Saric, R. Characteristics of chronic anxiety patien In: Klein, D.F., and Rabkin, J.G. (eds.) *Anxiety: Ne* *Research and Changing Concepts*. New York: Raven Pres 1981, pp. 399-409.

Hoehn-Saric, R., and Masek, B.J. Effects of naloxone o normals and chronically anxious patients. *Biol. Psychiatry* 16:1041-1049, 1981.

Klein, D.F. Anxiety reconceptualized. In: Klein, D.F. and Rabkin, J.G. (eds.), *Anxiety: New Research and Chang* *Concepts*. New York: Raven Press, 1981, pp. 235-263.

Klein, D.F., Zitrin, C.M., and Woerner, M. Antidepre sants, anxiety, panic and phobias. In: Lipton, M.A. DiMascio, A., and Killam, K.F. (eds.), *Psychopharmacolog* *A Generation of Progress*. New York: Raven Press, 1978, pp 1401-1410.

Mountjoy, C.Q., Roth, M., Garside, R.F., and Leitc I.M. A clinical trial of phenelzine in anxiety depressiv and phobic neuroses. *Br. J. Psychiatry*, 131:486-492, 197

Rotter, J.B. Generalized expectancies for internal vs. exte nal control of reinforcement. *Psychol. Monogr.*, 80(1):1-2 1966.

Sheehan, D.V., Ballenger, J., and Jacobsen, G. Treatme of endogenous anxiety with phobic, hysterical an hypochondriacal symptoms. *Arch. Gen. Psychiatry* 37:51-59, 1980.

Spielberger, C.S., Gorsuch, R.L., and Lushene, R.E. *Manual for the State-Trait Anxiety Inventory*. Palo Alt Psychologists Press, 1970.

Tarter, R.E., McBride, H., Buonpane, N., and Schneide D.U. Differentiation of alcoholics. *Arch. Gen. Psychiat* 34:761-768, 1977.

Zung, W.W.K. A self-rating depression scale. *Arch. Ge* *Psychiatry* 12:63-70, 1965.

Unresolved Issues in the Treatment of Agoraphobia With Panic Attacks

Michael R. Liebowitz, M.D.,[1] **and Donald F. Klein, M.D.**[1]

There is at present considerable confusion in the treatment for agoraphobia regarding the respective roles of various forms of psychotherapy and medication. A number of self-help phobia groups specifically eschew the use of medication. Even groups (Chambless 1981) who recognize the utility of antidepressant medication first recommend extensive, complex courses of psychotherapeutic treatment and consider medication only if such treatment fails. A literature review to determine the relative utility of pharmacological and behavioral forms of treatment and the specific impact of each upon the various components of the agoraphobic syndrome reveals the need for further comparative trials.

As defined in the Diagnostic and Statistical Manual-III (DSM-III), Panic Disorder is a condition characterized by the sudden and unprovoked occurrence of severe anxiety which can border on terror, and which is usually accompanied by such symptoms as palpitations, breathlessness, sweating, faintness or dizziness, nausea, or diarrhea. The attacks usually last only 20-30 minutes, but become the source of great concern to patients who fear they are going crazy, having a heart attack, or about to lose control of themselves in some socially embarrassing way. What usually follows is the development of great anticipatory anxiety, which is often treated or self-treated with tranquilizers or alcohol. A third stage involves phobic avoidance of places where panic attacks typically occur or where rapid exit to seek help is difficult, such as public transportation, heavy auto traffic, bridges, tunnels, restaurants, theaters, churches, or crowded stores. When a widespread, disabling avoidance pattern becomes established, the patient meets DSM-III criteria for Agoraphobia with Panic Attacks.

Pharmacotherapy

The pharmacotherpay of panic attacks has advanced greatly in the past two decades. Of major importance was the recognition that panic attacks, although not the accompanying anticipatory anxiety, could be effectively blocked by the tricyclic antidepressant imipramine, but not by minor tranquilizers such as the benzodiazepines (Klein & Fink 1962; McNair & Kahn 1981). On the other hand, benzodiazepines but not tricyclics appeared to be effective for the anticipatory anxiety that often develops as a consequence of panic attacks. This led Klein to hypothesize that panic attacks and non-panic anxiety represent two distinct pathophysiological entities. However, a recent report (Lipman et al. 1980) that non-panic chronic anxiety states also respond preferentially to tricyclics over benzodiazepines, and that the benzodiazepine alprazolam may effectively block panic attacks (Sheehan 1982); suggests that further studies are required before firm boundaries between panic anxiety and non-panic anxiety conditions are drawn.

Extending these findings were studies that demonstrated that the monoamine oxidase inhibitors (MAOI) were also highly efficacious for panic attacks (Tyrer et al. 1973). Phenelzine was also shown to block the ability of sodium lactate to precipitate panic attacks in Panic Disorder patients (Kelly et al. 1971), a phenomenon also recently demonstrated for imipramine by the authors' research group. The ability of sodium lactate to induce severe anxiety attacks in patients vulnerable to spontaneous episodes but not in normal controls was first demonstrated by Pitts and McClure (1967) and later replicated by several other investigative groups (Fink et al. 1969) including work done by the authors.

---

[1] College of Physicians and Surgeons, Columbia University and New York State Psychiatric Institute, New York, NY 10032.

A recent double-blind, placbo-controlled study comparing the efficacy of the tricyclic imipramine and the MAOI phenelzine in patients with panic attacks found both drugs to be highly effective with a trend to superiority for phenelzine (Sheehan et al. 1980). One problem that limits the generalizability of these findings is that dosages of both active drugs used in the study were fixed and low, phenelzine being limited to 45 mg/day and imipramine to 150 mg/day, while in the authors' experience some panic patients require phenelzine doses of up to 90 mg/day or imipramine doses of 300 mg/day or more.

Behavior Therapy

Paralleling the progress in clinical psychopharmacology was the recognition that many agoraphobic individuals could be markedly helped by behavior therapy, coupled with a gradual refinement of those techniques. The modern era of behavior therapy of phobias actually dates back to the late 1950s with Wolpe's reports of the use of systematic desensitization, which involved having patients go through an imagined hierarchy of fear-producing situations while practicing deep muscle relaxation (Wolpe 1958). A variant of this technique developed by Stampfl and called imaginal flooding, has patients begin by imagining themselves confronting their most feared situation rather than slowly building up from non-feared situations as Wolpe had them do (Stampfl 1970).

While much debate occurred over the actual therapeutic mechanisms of these behavioral techniques, a central principle of all therapists who treat phobias is that to overcome the fear a patient must actually confront phobically avoided objects or activities. Given this, beha therapists began to wonder if it did not more sense to directly try systematic densensiti tion or flooding in live situations rather than imagination. From this evolved several *in viv* posure techniques (prolonged exposure, cessive approximations, therapist-assiste homework assignments, individual or group) a variety of investigators in short-term stu have found to be more quickly effective than posure in imagination for treating agoraphobic well as simple phobics (Mathews et al. 1981). the studies by Zitrin et al. (1978, 1980) expos *in vivo* was faster-acting but did not improve greater proportion of the patients than o techniques over 26 weeks.

Pharmacotherapy vs. Behavior Therapy

With the emergence and proven efficacy of easily applied treatment techniques, one ph macological and the other behavioral, the n question to be asked was: "How do these forms of treatment compare with each other patients with panic attacks and agoraphobi Recently, several studies have attempted answer this question, but a number of importa issues have not been satisfactorily resolved.

One study by Solyom et al. (1981) compar phenelzine and exposure in a 2 × 2 double-bli design involving 40 patients who were eit agoraphobic or socially phobic. Phenelzine w given for 6 weeks in doses up to 45/mg day, wh exposure appears to have involved therapist structions for patients to confront anxiety-elicit situations bolstered by three telephone calls week to the patient. Patients who did not rece exposure were not "systematically encouraged confront phobic situations."

While the authors concluded that exposu with or without phenelzine, was the supe treatment, there are a number of issues whi limit the generalizability of this conclusion. On that, as acknowledged by the authors, phenel doses of 45 mg or less are below the 60-90 mg le now found effective with depressed patien Secondly, 6 weeks of medication treatment much less than the 26 weeks found optimally fective for agoraphobics in other studies (Soly et al. 1981; Zitrin et al. 1980). Thirdly, social phobics, who have not generally shown to be responsive to antipanic medications, are mixed in with agoraphobics without separate pretreatment stratification or even independent reporting of the results. Also, no mention is made about how many patients in either group had spontaneous panic attacks; while most agoraphobic patients do, this is not always the case. For this reason, DSM-III distinguishes between Agoraphobia with Panic Attacks and Agoraphobia without Panic Attacks. Finally, one might reasonably argue that the investigators in this study are not comparing clinically meaningful modes of treatment. Pharmacologists familiar with treatment of phobias will tell their patients that in addition to taking medication they must push themselves to confront feared situations; where they differ in practice from behavior therapists is by not offering a structured program to bring this about. The clinically relevant comparison is how drugs plus such informal "exposure instructions" compare to formal exposure programs without drugs, and the Solyom study cannot answer this question.

At approximately the same time Zitrin et al. (1980) reported a study of 76 agoraphobic women randomly assigned to imipramine or placebo while all received group *in vivo* exposure for a 10-week period. Medication was started first; from weeks 5-14, patients received one exposure session per week lasting 3 hours. Medication was continued until week 26; the maximum possible dose of imipramine was 300 mg.

This study found imipramine plus exposure superior to placebo plus exposure at both 14 and 26 weeks in terms of clinical global improvment, primary phobia, and spontaneous panic. Interestingly, the active drug group continued to improve between weeks 14 and 26. At 26 weeks the imipramine patients tend to be markedly improved, while more placebo patients tended to register moderate improvements, although some were also markedly improved. (According to the independent evaluator, 62 percent of imipramine patients were markedly improved on clinical global ratings at 26 weeks, while 28 percent were moderately improved and 10 percent showed no or only minimal improvement; for the placebo group, 29 percent were markedly improved, 42 percent moderately better, and 29 percent only minimally better or unimproved.) An interesting finding was that panic attacks increased between weeks 14 and 26 (after discontinuation of exposure) in the placebo but not in the active drug groups. Given these findings, it makes sense that future studies should extend the drug treatment period to 26 weeks, far beyond the usual 6 to 8 weeks. It also makes sense now to try extending the exposure treatment period to 26 weeks as well, since a once-weekly group session for 6 months is not an impractical form of clinical treatment.

While the dropout rate was the same for the two treatment groups (29 percent), eight of twelve active drug dropouts left because of a refusal to take medication, while only one could not keep up with the exposure program. For the placebo group, three of ten refused to continue medication, while five of ten were unable to keep up with the group. Whether dropouts (and nonresponders) unwilling to comply or unable to benefit from one type of treatment would do well with the other is an open question.

At 6 months posttreatment, 27 percent of the imipramine and 6 percent of the placebo group had relapsed. While these differences were not statistically significant, they have been cited by other investigators to show that drug treatment is less durable, even when combined with exposure. However, the data can be looked at another way, namely, that a certain percentage of agoraphobics require continued medication to maintain their gains, and will relapse when medication is withdrawn even after 6 months of treatment.

This study also found that the more depressed patients were at the beginning of treatment, the worse they did, which weighs against Marks' argument that imipramine's effect is confined to agoraphobics with associated depression (Marks et al., unpublished). Zitrin et al. (1978, 1980) believe that the dysphoria often seen in agoraphobics is symptomatic of antidepressant unresponsive demoralization rather than tricyclic responsive endogenous depression, since they found no drug specific antidepressant effect. Scientific progress since the time the Zitrin et als.'s study was begun now allows investigators to also distinguish signs of frequently associated atypical depression (Liebowitz et al. 1981) in agoraphobic or panic patients. On the basis of preliminary evidence, panic patients with associated atypical depressions may not do particularly well on tricyclics (Liebowitz et al. 1982).

Zitrin et al. had earlier reported a 26-week study comparing systematic desensitization plus imipramine, systematic desensitization plus placebo, and supportive psychotherapy plus imipramine in 218 patients (Zitrin et al. 1978). Diagnostically the patients were divided into agoraphobics, simple phobics, and mixed phobics (who had circumscribed phobias, panic attacks, and no travel restrictions). Overall, imipramine was found superior to placebo in the agoraphobic and mixed phobic groups in reducing overall severity of illness, improvement in phobias, reducing severity, and frequency of panic attacks and reducing other anxiety symptoms, while no differences were found between behavioral and supportive psychotherapy for any diagnostic group. In addition, for the agoraphobic group ($N = 77$), behavior therapy plus imipramine was clearly superior to behavior therapy plus placebo in reducing the frequency and severity of anxiety attacks, as measured by the Acute Panic Inventory and the Taylor Manifest Anxiety Scale, for the travel and panic symptom clusters on the Wolpe-Lang Fear Survey Schedule, and for independent evaluators rating of primary phobia improvement.

Marks and colleagues also recently compared imipramine (up to 200 mg/day for 28 weeks), placebo, therapist-aided exposure, and therapist-aided relaxation for 45 agoraphobic patients in a 2 × 2 design (Marks et al., unpublished). All patients were given systematic self-exposure homework including an instruction manual. No significant effects were found for imipramine, while significant but limited effects were found for therapist-aided exposure. Marks et al. concluded that self-exposure homework is a powerful therapeutic device, that imipramine adds nothing for agoraphobics who are not depressed, and that therapist-aided exposure is helpful for some patients.

One limit on the generalizability of Marks' conclusions is low medication dosages; mean doses were 124 mg at Week 6, 158 mg at Week 14, and not reported at Week 26. (Mean drug plasma levels were in the antidepressant range, but inflated by several outliers.) In addition, a number of patients previously shown not to respond to antidepressants were taken into the study. Also, among the patients counted as dropouts were two who showed rapid improvement with imipramine. One other interesting point was that patients were put on imipramine during the ad treatment followup period, including 8 who h been on imipramine before. However, no me tion is made as to whether these individua deteriorated when taken off medication the fir time.

However, comparison of Marks' sample sel ratings of "feeling blue" are almost identical wi the Zitrin-Klein sample; therefore, the differenc in drug effects is unlikely to be due to lesse depression in Marks' sample. Further, Zitrin Klein specifically barred acceptance of any pa tient with diagnosable depression.

Mavissakalian and Michelson (1981) hav recently reported the preliminary results of a ongoing comparison of imipramine, placebo flooding, and nonspecific psychosocial treatmen in agoraphobic patients using a 2 × 2 design. Al patients were given weekly therapeutic instructio on the importance of trying to enter fear situations. Maximum imipramine dose was 200 m and duration of treatment was 12 weeks. The control for *in vivo* exposure was a group discussion o illness and progress. Patients previously treated with antidepressants were not excluded; in fact all 32 patients reported in the pilot study ha previously received antidepressants of some type although drug dosage, duration, and previou response are not indicated. Average dose of imipramine in the last month of treatment was 12 mg/day. A behavioral performance test was used as an outcome measure, as was an overall judgment about degree of improvement.

What is reported are the results obtained at month posttreatment. Both imipramine and exposure were found to be active treatments, with no significant differences between them and no additional benefits seen in the combined group No predictors are offered as to which patients d well with one or another form of treatment, although the investigators speculated that imipramine may stabilize mood (block panic?) which leads to behavioral change, while *in vivo* exposure may produce behavioral and then mood improvement.

Conclusion

What are needed are drug versus exposur studies that exclude patients previously show unresponsive to either test treatment, use of adequate doses and duration of medication, continue exposure treatment for patients who respond, test nonresponders for their responsivity to other forms of treatment, and rigorously evaluate both type and degree of associated depression. Hopefully, this will generate clinical predictors of who responds best to pharmacological or behavioral treatment of agoraphobia. Among the specific hypotheses that require testing are the following:

1. That patients whose panic attacks are in remission or on the wane but who still have high anticipatory anxiety will do well with group *in vivo* exposure without accompanying drug treatment.

2. That patients with severe or frequent ongoing panic attacks will do better with antipanic drug treatment, and may become more phobic or demoralized if treated with an *in vivo* exposure program unaccompanied by drug treatment.

3. That patients with frequent or severe panic and high anticipatory anxiety may require both forms of treatment but will do better if drugs are offered first, to be followed by a formal exposure program once panic attacks are blocked.

4. That some of the agoraphobic patients who improved with exposure, unaccompanied by drug, may overcome their phobic avoidance but still continue to experience panic attacks that they have now learned to tolerate or "float through." This could be assessed by self-report, by *in vivo* physiological monitoring, and by pre- and post-treatment challenges with sodium lactate infusions to test changes in panic vulnerability.

5. That many agoraphobic patients will respond to drug treatment without any concomitant psychotherapy except simple encouragement of self-exposure. This has never been examined in a formal study; previous trials of antidepressant medication in agoraphobics that have employed adequate dosage and duration of treatment have embedded these trials within various forms of psychotherapy. Thus, it remains unclear whether psychotherapy is necessary to help patients reduce anticipatory anxiety and avoidant behavior once panic attacks have been blocked by medication. Clinical anecdotal evidence indicates that many patients can rid themselves completely of the agoraphobc syndrome by simple drug treatment accompanied by encouragement of self-exposure activity (Muskin & Fyer 1981).

6. That depressive features are not necessary for imipramine's anti-panic effects and, in the case of associated atypical depression, may impede it. On the other hand, demoralization may impede self-exposure and extinction of anticipatory anxiety.

7. That imipramine's principal effect in agoraphobia is to block panic attacks, and that the lessening of anticipatory anxiety occurs after the antipanic effects. This could be assessed by having patients keep daily logs and ratings of frequency and intensity of episodes of panic and anticipatory anxiety as well as frequent investigative assessments of both types of symptomatology.

The authors now have in hand two relatively effective modes of treatment for Agoraphobia with Panic Attacks, but further comparative trials are required before they can fully identify the mechanisms by which each works, or say which is preferable as a first try for any particular patient.

References

Chambless, D. (ed). Agoraphobia: An integrated treatment approach. In: *Phobia: Psychological and Pharmacological Treatment.* New York, London:Guilford Press, 1981.

Fink, M., Taylor, M.A., and Volavka, J. Anxiety precipitated by lactate. *N. Engl. J. Med.*, 281:1429, 1969.

Kelly, D., Michell-Heggs, N., and Sherman, D. Anxiety and the effects of sodium lactate assesses clinically and physiologically. *Br. J. Psychiatry*, 119:129-141, 1971.

Klein, D.F., and Fink, M. Psychiatric reaction patterns to imipramine. *Am. J. Psychiatry*, 119:432-438, 1962.

Liebowitz, M.R., Quitkin, F.M., Stewart, J.W., McGrath, P.J., Harrison, W., Schwartz, D., Rabkin, J., Tricamo, E., and Klein, D.F. Phenelzine and imipramine in atypical depression. *Psychopharmacol. Bull.*, 17(3):159-161, 1981.

Liebowitz, M.R., Quitkin, F.M., Stewart, J.W., McGrath, P.J., Harrison, W., and Rabkin, J. Atypical depression: Clinical description and treatment specificity. Presented at the Annual Meeting of the American Psychiatric Association, Toronto, Canada, 1982.

Lipman, R.S., Covi, L., Downing, R.W., Fisher, S., Kahn, R.J., McNair, D.M., Rickels, K., and Smith, V.K. Pharmacotherapy of anxiety and depression: Rationale and study design. *Psychopharmacol. Bull.*, 17(3):91-94, 1981.

Marks, I.M., Gray, S., Cohen, S.D., et al. Imipramine and brief therapist-aided exposure in agoraphobics having self-exposure homework: A controlled trial. March 1981. (Unpublished manuscript)

Mathews, A.M., Gelder, M.G., and Johnson, D.W. (eds). The behavioral treatment of agoraphobia. In: *Agoraphobia: Nature and Treatment.* New York,London:Guilford Press, 1981, pp. 71-98.

Mavissakalian, M., and Michelson, L. Agoraphobia: Behavioral and pharmacological treatments. I: Short-term outcome with 32 patients. Presented at the American Psychiatric Association meeting, New Orleans, May 1981.

McNair, D.M., and Kahn, R.J. Imipramine compared with a benzodiazepine for agoraphobia. In: Klein, D.F., and Rabkin, J.G. (eds.), *Anxiety: New Research and Changing Conceptions*. New York:Raven Press, 1981.

Muskin, P.R., and Fyer, A.J. Treatment of panic disorder. *J. Clin. Pharmacol.*, 1:81-90, 1981.

Pitts, F.N., and McClure, J.N. Lactate metabolism in anxiety neurosis. *N. Engl. J. Med.*, 227:1329-1336, 1967.

Sheehan, D.V. Panic disorders: A treatment overview. Presented at the Annual Meeting of the American Psychiatric Association, Toronto, Canada, 1982.

Sheehan, D.V., Ballenger, J., and Jacobsen, G. Treatment of endogenous anxiety with phobic, hysterical, and hypochondriacal symptoms. *Arch. Gen. Psychiatry*, 37:51-59, 1980.

Solyom, C., Solyom, L., LaPierre, Y., Pecknold, J., and Morton, L. Phenelzine and exposure in the treatment of phobics. *Biol. Psychiatry*, 16(3):239-247, 1981.

Stampfl, T.G. Implosive therapy: An emphasis on covert stimulation. In: Lewis, D.J. (ed.), *Learning Approaches to Therapeutic Behavior Change*. Chicago:Aldine Press, 1970, pp. 182-204.

Tyrer, P., Candy, J., and Kelly, D.A. A study of the clinical effects of phenelzine and placebo in the treatment of phobic anxiety. *Psychopharmacologia (Berlin)*, 32:237-254, 1973.

Wolpe, J. *Psychotherapy by Reciprocal Inhibition*. Palo Alto, Cal.: Stanford University Press, 1958.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Behavior therapy, supportive psychotherapy, imipramine, and phobias. *Arch. Gen. Psychiatry*, 35:307-316, 1978.

Zitrin, C.M., Klein, D.F., and Woerner, M.G. Treatment of agoraphobia with group exposure *in vitro* and imipramine. *Arch. Gen. Psychiatry*, 37:63-72, 1980.

Vol. 18, No. 4, October 1982

Antiobsessional and Antidepressant Effects of Clomipramine in the Treatment of Obsessive-Compulsive Disorder

Thomas R. Insel, M.D.,[1] Ina Alterman, M.A.,[1] and Dennis L. Murphy, M.D.[1]

Two treatments for obsessive-compulsive disorder (OCD) have recently been demonstrated to be effective. A particular form of behavior therapy using exposure and response prevention techniques has prompt and lasting effects for OCD patients who ritualize (Foa & Goldstein 1978; Marks et al. 1980). Pharmacologic treatment, in particular, treatment with clomipramine, has also been shown to be effective, although less information is available about the magnitude and duration of the effects (Insel & Murphy 1981; Thorén et al. 1980). One promising aspect of clomipramine treatment is that patients without rituals or avoidant behavior and patients with secondary depressions, i.e., groups for whom behavioral interventions may be less effective (Foa 1979), may be drug responders. Whether all categories of obsessional patients are likely to respond to clomipramine remains controversial. For instance, Marks (1981) has recently noted, after reviewing several studies, that clomipramine was less effective for nondepressed OCD patients in one study than in comparable studies using somewhat more depressed OCD patients.

The authors attempted to evaluate both antiobsessional and antidepressant effects in an ongoing double-blind study of clomipramine, clorgyline, and placebo for OCD. While much of the data from this study have yet to be analyzed, a preliminary comparison of a few rating scales yielded data pertinent to the following questions: Do baseline depression ratings in OCD patients predict response to clomipramine? Are changes in obsessional and depression rating scale scores correlated during clomipramine treatment? Are the time courses for antiobsessional and antidepressant changes different and, if so, which effect occurs first?

Method

The authors studied 12 OCD patients, fulfilling Diagnostic and Statistical Manual-III (DSM-III) criteria and Research Diagnostic Criteria (RDC) and including both ritualizers and pure obsessionals at the Clinical Center of the National Institutes of Health. The patients (age 19-45, mean 29.9 years) included seven males and five females. The double-blind study involved crossover trials of clorgyline and clomipramine, although only clomipramine results were analyzed for this report (trend effects within the crossover were not significant). Daily clomipramine dosage ranged from 100 to 300 mg (mean 220 mg). The following clinical ratings were scored for this analysis: Hamilton Depression Scale (18 items) (Hamilton 1967); the Comprehensive Psychiatric Rating Scale-Obsessive compulsive (CPRS-OC) subscale, (Thorén et al. 1980); the CPRS-OC subscale modified to include only primary obsessional symptoms (compulsive thoughts, rituals, concentration difficulty, indecision, lassitude); and global assessment scale for depression and obsessions (each requiring a single number rating between 1 (no symptoms) and 15 (maximum symptoms). These ratings were completed at least every 2 weeks and in many cases weekly. Not all patients had the same rater, although each patient had the same rater throughout the study. The authors calculated percent clinical response by comparing scores at the end of 6 weeks on drug with baseline values (i.e., the end of 4 weeks on placebo).

---

[1] Clinical Neuropharmacology Branch, National Institute of Mental Health, Bethesda, MD 20205.

Results

The entire sample improved after 6 weeks of clomipramine treatment with mean percent change from baseline of 32 percent on the modified CPRS-OC subscale, 33 percent on the Global O-C Scale, and 35 percent on the full CPRS-OC subscale. To answer the question of the influence of baseline depression on clomipramine response, the authors separated the group into more depressed or less depressed subgroups, using the mean Hamilton Depression Score of 12.2 as the dividing point. Judged by changes after 6 weeks of treatment in ratings of obsessions (*see* Table), the less depressed group appeared to show a superior response as shown in the Table, although this difference was not statistically significant. The depression changes were actually greater for the less depressed group, reflecting the greater magnitude of percent changes with a lower baseline.

To augment the group data, the authors used an intensive design for the study of a single case who became depressed in the course of the study. This patient's progress (*see* Figure), followed during two successive double-blind trials, of clomipramine, showed a similar change in obsessional ratings, although baseline Hamilton scores were 300 percent higher on the second trial.

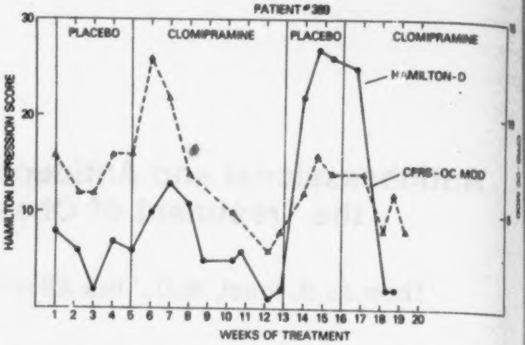


FIGURE. Progress for one subject on two successive double-blind trials of clomipramine.

While it does not appear that response to clomipramine requires or is even favored by high depression scores, is the antiobsessional response correlated with changes in mood? To answer this question the authors compared changes in the global ratings of obsessions and depression following 6 weeks of clomipramine treatment. The correlation for percent change from baseline for these two scales (completed simultaneously by the same rater) was nearly 0 ($r = -.03$), even though the means for percent change for these scales were nearly equal (34.9 ± 7.7 percent for depression, 32.6 ± 4.5 percent for obsessions).

Are the time courses for the two effects different? This question could not be answered comprehensively, as the authors had data at 2-week intervals in six subjects and weekly intervals in the remaining six. Still, the time of the peak change in global ratings of mood and obsessional symptoms could be compared in each subject. For six of the subjects, the peak change in mood was simultaneous with the improvement in obsessional symptoms. For five of the remaining six, the peak mood change preceded the peak change

Table

Baseline Scores and Percent Change on Clomipramine for More-Depressed and Less-Depressed Subgroups of Obsessive-Compulsive Patients

Groups		Baseline			Percent Change at 6 Weeks			
	N	Ham-D Range	Ham-D Mean	MOD CPRS-OC	CPRS-OC	MOD CPRS-OC	Global OC	Global Dep.
More Depressed	5	13-20	15.6	7.6	30.4	24.8	23.7	15.7
Less Depressed	7	7-11	9.7[a]	7.9	39.0	37.7	38.9	48.7[a]

[a] $p < .05$, two-tailed *t*-test for group means.

in obsessional symptoms by 2 to 4 weeks. In one subject, obsessional changes preceded the antidepressant effect. The overall mean for number of weeks to peak change was 3.8 for antidepressant effect and 4.7 for antiobsessional effect.

In summary, the evidence from this trial of clomipramine in OCD patients suggests:
1) Clomipramine's effectiveness for obsessional symptoms is independent of baseline depression ratings;
2) Changes in obsessional symptoms do not uniformly correlate with changes in mood, either in magnitude or time of occurrence;
3) Clomipramine's antiobsessional effects may occur slightly later than its antidepressant effects.

These results are surprising, in view of the accepted nosology that depressive symptoms in OCD are secondary. Indeed, in a separate study using a single dose of *d*-amphetamine, the authors showed a possible correlation between the changes in obsessional and depressive ratings (unpublished data). The lack of such a relationship with clomipramine may reflect the increasing number of confounding variables within a several weeks' trial as opposed to a few hours of treatment in the amphetamine study. Another possibility is that clomipramine, unlike *d*-amphetamine, works through two independent pharmacologic mechanisms to ameliorate a disorder of mood and a disorder of cognition and behavior.

Certainly the distinction between depressive and obsessional symptoms is not always clear. Exhaustion, self-reproach, and preoccupation with guilt are part of both affective and obsessional disorders. While these two disorders have been previously distinguished by different clinical courses (Welner et al. 1975), different rates of suicide (Goodwin et al. 1969), and different family incidences of affective illness (Coryell 1981), individual patients can have both OCD and severe depression. In general, if the depression begins subsequent to the obsessional complaints, it is considered a complication of OCD and, hence, a secondary depression. However, in some cases the depression seems to become autonomous, overtaking the obsessional symptoms.

Furthermore, the authors have reported a higher incidence of some of the psychobiologic manifestations of depressive disorders in OCD patients even without severe or even moderate affective symptoms. These variables include dexamethasone suppression tests (6 or 16 OCD patients escaped) and sleep electroencephalograph (EEG) records (OCD patients show reduced rapid-eye-movement latency and reduced Stage 4 sleep) (Insel et al. 1982). It may be that OCD biologically represents a variant of affective illness which is responsive to antidepressant treatment even in the absence of overt depression. Alternatively, these biological markers may be correlated with some phenomenon that the two syndromes have in common (e.g., anxiety or preoccupation with guilt). A third and not mutually exclusive hypothesis is that OCD is a chronic disorder that predisposes to affective illness, much as an immune deficiency state might predispose to infection. Perhaps the depression brings the patient to treatment, but because of the chronic obsessional disorder the usual affective manifestations are not evident, except as an exacerbation of ruminating or ritualizing. Thus, one would expect the biological manifestations of affective illness and response to antidepressant treatment independent of manifest depression.

References

Coryell, W. Obsessive compulsive disorder and primary unipolar depression. *J. Nerv. Ment. Dis.*, 169:220-224, 1981.

Foa, E.B. Failure in treating obsessive-compulsives. *Behav. Res. Ther.*, 17:169-176, 1979.

Foa, E.B., and Goldstein, A. Continuous exposure and complete response prevention treatment of obessive-compulsive neurosis. *Behav. Ther.*, 9:821-830, 1978.

Goodwin, D.W., Guze, S.B., and Robins, E. Followup studies in obsessional neurosis. *Arch. Gen. Psychiatry*, 20:182-187, 1969.

Hamilton, M. Development of a rating scale for primary depressive illness. *Br. J. Soc. Clin. Psychol.*, 6:278-296, 1967.

Insel, T.R., and Murphy, D.L. The psychopharmacological treatment of obsessive-compulsive disorder: A review. *J. Clin. Psychopharm.*, 1:304-311, 1981.

Insel, T.R., Kalin, N., Guttmacher, L., Cohen, R.M., and Murphy, D.L. The dexamethasone suppression test in patients with primary obsessive compulsive disorder. *Psychiatry Res.*, 6:153-160, 1982.

Mark, I.M. Are there anticompulsive or antiphobic drugs? *Psychopharmacol. Bull.*, 18(4):78-84, 1982.

Marks, I.M., Stern, R.S., Mawson, D., Cobb, J., and McDonald, R. Clomipramine and exposure for obsessive-compulsive rituals. *Br. J. Psychiatry*, 136:1-25, 1980.

Thorén, P., Åsberg, M., Cronholm, B., Jörnstedt, L., and Träskman, L. Clomipramine treatment of obsessive-compulsive disorder. A controlled clinical trial. *Arch. Gen. Psychiatry*, 37:1281-1289, 1980.

Welner, A., Reich, T., Robins, E., Fishman, R., and van Doren, T. Comprehensive compulsive neurosis. *Compr. Psychiatry*, 17:527-539, 1975.

20th Annual Meeting of the ACNP—Poster Sessions

The following are papers based on poster sessions presented at the American College of Neuropsychopharmacology (ACNP) (December 1981) meeting. Abridged proceedings of papers presented at panels and workshops of the ACNP were included in Vol. 18, No. 3 of the *Psychopharmacology Bulletin*.

Evaluation of Alpha-Adrenergic Responsiveness to Clonidine Challenge and Noradrenergic Metabolism in the Affective Disorders and Their Treatment

Larry J. Siever, M.D.,[1] Thomas W. Uhde, M.D.,[2] Edward K. Silberman, M.D.,[3] Charles R. Lake, M.D.,[4] David C. Jimerson, M.D.,[5] S. Craig Risch, M.D.,[6] Ned H. Kalin, M.D.,[1] and Dennis L. Murphy, M.D.[1]

Introduction

The dysregulation of noradrenergic activity hypothesized to be associated with the affective disorders and the alterations of activity accompanying antidepressant treatment may depend on the functional state of noradrenergic receptors. The physiologic and biochemical responses to the administration of clonidine, a selective α_2-adrenergic agonist, may permit an indirect evaluation of the responsiveness of these receptors. The growth hormone response to clonidine appears to be mediated by postsynaptic α_2-adrenergic receptors in the hypothalamus and in animal studies, its magnitude may be correlated with α^2-adrenergic receptor sensitivity. The hypotensive response may provide a means of assessing the responsiveness of α_2-adrenergic autoreceptors. These and other responses to clonidine, as well as noradrenergic metabolites in controls and depressed patients before and during antidepressant treatment have been evaluated in an attempt to characterize noradrenergic receptor function in depression and its treatment.

Methods

Clonidine was administered to 19 depressed patients (off all medications for 3 weeks) and 20 controls (including 14 age- and sex-matched patient-control pairs) and to 9 patients before and during the administration of clorgyline, a selective monoamine oxidase (MAO)-A inhibitor. All women were tested within the 10 days following menses. Clonidine was administered intravenously over 5 minutes to subjects in the morning following an overnight fast, with plasma samples drawn at 15-minute intervals and blood pressure monitored at 5-minute intervals before and after clonidine administration. The averaged growth hormone response to clonidine during the first hour following clonidine administration was compared between the depressed patients and controls by the Mann-Whitney U Test. The averaged mean arterial pressure (MAP) between 45 and 60 minutes following the infusion was subtracted from the averaged MAP in the 20 minutes prior to the infusion. The magnitude of the MAP decrement after chronic (greater than 21 days) treatment with clorgyline was compared by Student's t-test to the hypotensive decrease before treatment in the nine patients and to the hypotensive decrease after acute (2-3 days) and intermediate (10-14 days) treatment in three of these patients. Noradrenergic availability was indirectly assessed by determining plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) and norepinephrine levels before and during the infusion, as well as urinary metabolite levels excreted over 24 hours prior to the clonidine study.

---

[1] Clinical Neuropharmacology Branch, National Institute of Mental Health, Bethesda, MD 20205.

[2] Section on Psychobiology, Biologic Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205.

[3] Laboratory of Psychology, National Institute of Mental Health, Bethesda, MD 20205.

[4] University of the Health Sciences Medical School, Department of Psychiatry and Pharmacology, Bethesda, MD 20814.

[5] Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20205.

[6] Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093.

Table

Percent Fall of MAP Following Clonidine in Patients on Placebo and Long-term Clorgyline

Placebo	Clorgyline
11.7 ± 6.3 (S.D.)	2.4 ± 5.3 (S.D.)

Results

The growth hormone response to clonidine was significantly decreased in all ($p < .001$) subjects compared to controls as well as between age- and sex- matched depressed patients and controls ($p < .05$). This finding held up when subjects with elevated baseline growth hormone levels were either included or excluded. This response was negatively correlated ($r = -0.32, p < .05$, one-tailed test) with baseline plasma MHPG.

The hypotensive response to clonidine was significantly decreased after chronic clorgyline treatment ($p < .05$). No attenuation of the response was observed in the three patients tested after acute clorgyline treatment, with a slight apparent attenuation after intermediate duration treatment. The author's preliminary results do not suggest a consistent enhancement of the growth hormone response to clonidine after chronic clorgyline treatment.

Conclusions

The diminished growth hormone response to clonidine in depression is consistent with the results of other investigators (Checkley et al. 1981; Matussek et al. 1980) and raises the possibility that decreased postsynaptic α_2-adrenergic responsiveness may be associated with depression. Postsynaptic noradrenergic subsensitivity could conceivably contribute to a functional decrease in noradrenergic activity in depressed patients. The degree to which noradrenergic receptor responsiveness may be reciprocally related to presynaptic noradrenergic availability in depression deserves further exploration.

The attenuated hypotensive response to clonidine following chronic MAO inhibitor treatment is consistent with reports of a decreased hypotensive fall following chronic administration of the tricyclic desipramine (Charney et al. 1981; Checkley et al. 1981) and a previous report of patients on clorgyline and imipramine (Siever et al. 1981) and suggests that α_2-adrenergic autoreceptors may become subsensitive decreasing feedback inhibition of noradrenergic release, after chronic antidepressant treatment. The apparent lack of effect of acute treatment in our study suggests that this reflects a slow adaptive change rather than an acute effect such as α_2-adrenergic blockade. The time course of the decreased response to clonidine parallels that of the onset of clinical efficacy and of the decrease in blood pressure accompanying MAO inhibitor treatment, thus suggesting an important role for this adaptation in the MAO inhibitors and perhaps tricyclics' mechanism of action.

References

Charney, D.S., Heninger, G.R., Sternberg, D.E., Redmond, D.E., Leckman, J.F., Maas, J.W., and Roth, R.H. Presynaptic adrenergic receptor sensitivity in depression. *Arch. Gen. Psychiatry,* 38:1334-1340, 1981.

Checkley, S.A., Slade, A.P., and Shur, E. Growth hormone and other responses to clonidine in patients with endogenous depression. *Br. J. Psychiatry,* 138:51-55, 1981.

Checkley, S.A., Slade, A.P., Shur, E., and Dowling, S. A pilot study of the mechanism of action of desipramine. *Br. J. Psychiatry,* 138:248-251, 1981.

Matussek, N., Ackenheil, M., Hippius, H., Müller, F., Schroder, H.-Th., Schultes, H., and Wasilewski, B. Effect of clonidine on growth hormone release in psychiatric patients and controls. *Psychiatry Res.,* 2:25-36, 1980.

Siever, L.J., Cohn, R.M., and Murphy, D.L. Antidepressants and α_2-adrenergic autoreceptor desensitization. *Am. J. Psychiatry,* 138:681-682, 1981.

Biological Markers for Depressive Illness

Alan G. Robertson, M.D.,[1] Betty Jo Tricou, M.D.,[1] Victor S. Fang, Ph.D.,[1,2] and Herbert Y. Meltzer, M.D.[1]

Introduction

Numerous investigators have reported a blunted thyroid stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) in major depression (Extein et al. 1981; Gold et al. 1981; Kirstein et al. 1981).

There is evidence for the regulation of the hypothalamic-pituitary-thyroid axis by serotonergic neurons (Morley et al. 1981). Meltzer et al. (1981) reported a significant decrease in the number of serotonin (5-HT) uptake sites (V_{max}) in the blood platelets of unmedicated depressed patients.

This study investigated the TSH response to TRH and its relationship to ^{14}C-5-HT uptake in patients with major depressive illness, other psychiatric disorders, and controls.

Method

The subjects in these studies were newly admitted psychiatric patients and normal controls. Diagnoses were established according to Research Diagnostic Criteria (RDC).

The TRH test was carried out in 58 euthyroid patients and 19 euthyroid controls. All patients were drug-free for at least 7 days prior to testing and none had a history of lithium carbonate use within the preceding 6 months. After three baseline samples were obtained (-30′, -15′, 0′), 500 μg of TRH was infused at 10 a.m. over a 30-second period with subsequent blood samples taken at 15, 30, 60, 90, and 120 minutes. TSH was determined in duplicate by radioimmunoassay. Maximal TSH response (peak minus t_o baseline) was determined for each subject. The TSH response to TRH was considered blunted for all subjects with $\Delta TSH \leq 7$ μU/ml and in a separate statistical analysis for all subjects with $\Delta TSH < 5.0$μU/ml.

The method of 5-HT uptake determination has been previously reported (Arora & Meltzer 1981). V_{max} and K_m were determined on two occasions in patients who had been drug-free for at least 7 days. Results were averaged.

Table 1

Comparison of Mean ΔTSH Following TRH in Unipolar Depression, Other Diagnostic Groups, and Controls

Diagnosis	*N*	ΔTSH[a]	*t*
Males and Females			
Unipolar depression	12	6.8 ± 4.2	–
Bipolar depression	6	11.8 ± 4.7	2.28[b]
Schizoaffective depression	13	13.5 ± 9.7	2.20[b]
Bipolar, minor, and schizoaffective depression	23	12.8 ± 7.9	2.43[b]
All diagnoses other than unipolar depression	46	12.0 ± 7.3	2.63[b]
Controls	13	11.6 ± 7.2	2.00[c]
Males			
Unipolar depression	8	4.6 ± 2.8	–
Bipolar, minor, and schizoaffective depression	9	8.8 ± 4.8	2.22[b]
All diagnoses other than unipolar depression	22	10.6 ± 5.6	2.80[b]
Controls	8	10.8 ± 7.2	2.24[b]

[a] μU/ml (Mean ± S.D.)
[b] Compared to unipolar depression, $p < .05$.
[c] Compared to unipolar depression, $p < .10$.

Results

Of 19 nonpatient controls given TRH, 500 μg, i.v., six had a personal history of previous minor depression, excess alcohol use, or a family history of treated depressive disorders. Five of these six controls had a blunted TSH response ($\Delta TSH < 5$ μU/ml), whereas none of the other 13 did.

The proportion of patients and controls with a blunted TSH response varied greatly depending upon which criterion ($\Delta TSH < 5$ or $\Delta TSH \leq 7$ μU/ml) was used because the response of many subjects fell within the 5-7 μU/ml range. Eight of 12 (66.7%) unipolar depressed patients had a significantly ($p < .05$) greater proportion of blunted responses (ΔTSH ≤ 7 μU/ml) than the combined group of bipolar, minor, and schizoaffective depressed patients (6/23, 26.1%). Fifteen of 46 (32.6%) patients with other psychiatric disorders (schizophrenia, mania, schizoaffective mania, unspecified functional psychosis, personality disorder, generalized anxiety disorder, obsessive compulsive disorder, anorexia nervosa, and drug use disorder) also had a blunted TSH response. The sensitivity of the TRH test for unipolar depression (primary and secondary) was 66.7 percent and the specificity 67.4 percent, using ΔTSH ≤ 7 μU/ml as the criterion.

---

[1] Department of Psychiatry, University of Chicago Pritzker School of Medicine and the Illinois State Psychiatric Institute, Chicago, IL 60612.

[2] Department of Medicine, University of Chicago Pritzker School of Medicine, and the Illinois State Psychiatric Institute, Chicago, IL 60612.

The unipolar depressives had a significantly lower mean ΔTSH response than the 1) bipolar depressives, 2) schizoaffective depressives, 3) bipolar, minor, and schizoaffective depressives, and 4) patients with diagnoses other than unipolar depression (Table 1). Male unipolar depressives had a significantly lower mean ΔTSH response than male controls (Table 1). Secondary major depressives ($N=5$) had a significantly ($p < .05$) lower mean ΔTSH response than patients with primary major depression ($N=7$). There was no significant correlation between the severity of depression as measured by Hamilton scores and the ΔTSH response to TRH.

Peak TSH levels after TRH infusion were reassayed in duplicate by the thyroid laboratory of the University of Chicago Medical Center in 22 patients and controls. Although there was good correlation between both assays ($r=0.953$), the absolute levels differed by 1.5-2 μU/ml in the critical 5-7 μU/ml range.

Table 2

Relationship of TSH Response to TRH and ^{14}C-5-HT Uptake in Major Depressed and Schizoaffective Depressed, Mainly Affected Patients

		Mean ± S.D.	
	N	K_m[a]	V_{max}[b]
Patients	20	0.43 ± 0.16[e]	10.94 ± 3.10[c]
ΔTSH ≤ 7 μU/ml	11	0.37 ± 0.12[d,e]	10.16 ± 2.60[c]
ΔTSH > 7 μU/ml	9	0.52 ± 0.16	11.88 ± 3.54
Controls	55	0.51 ± 0.14	12.74 ± 3.08

[a] K_m indicates the apparent Michaelis constant; the values are micromolar.
[b] V_{max} indicates maximum velocity; the values are picomoles per 10^7 platelets per minute.
[c] $p < .05$ compared to controls.
[d] $p < .05$ compared to patient group ΔTSH > 7 μU/ml.
[e] $p < .005$ compared to controls.

Results of the TSH response to TRH and platelet 5-HT uptake were available for 20 patients with major depression or schizoaffective depression, mainly affective type (Table 2). V_{max} of 5-HT uptake was significantly decreased in patients with a ΔTSH response of ≤ 7 μU/ml compared to normal controls. K_m of 5-HT uptake was significantly lower in patients with a ΔTSH response of ≤ 7 μU/ml compared to patients with a ΔTSH response of > 7 μU/ml and to normal controls.

Discussion

The sensitivity (66.7%) of a blunted TSH response to TRH to identify unipolar depression using a criterion of ΔTSH ≤ 7 μU/ml was in the range as previously reported by Extein et al. (1981), Gold et al. (1981), and Kirstein et al. (1981) who found the TSH response to TRH was useful in confirming the diagnosis of major unipolar depression. The finding of a lower specificity (67.4%) may be due to differences in studies in the diagnostic compositions of patient groups with diagnoses other than unipolar depression.

The finding of a significantly lower mean ΔTSH response in unipolar depression compared to bipolar depression has been previously reported by Gold et al. (1980), but was not confirmed by Bjørum and Kirkegaard (1979). The finding of a significantly lower mean ΔTSH response in secondary major depression compared to primary major depression is opposite to the results reported by Gold et al. (1980).

Finding blunted TSH responses in five of six volunteers with previous minor depression, excess alcohol use, or family history of treated depression indicates the need for careful evaluation of control subjects and their families. This study also indicates the need for an extremely reliable and reproducible means of TSH determination and for each laboratory to determine the limit of the normal TSH response to TRH.

Decreased V_{max} of platelet 5-HT uptake appears to have great promise as a marker of vulnerability to major depressive illness (Meltzer et al. 1981). The association between a blunted TSH response to TRH and decreased V_{max} and K_m values provides some clue to the nature of a blunted TSH response which may be related to an abnormality of the serotonergic system.

References

Arora, R.C., and Meltzer, H.Y. A modified assay method for determining serotonin uptake in human platelets. *Clin. Chim. Acta.*, 112:225-233, 1981.

Bjørum, N., and Kirkegaard, C. Thyrotropin-releasing hormone test in unipolar and bipolar depression. *Lancet*, 2:694, 1979.

Extein, I., Pottash, A.L.C., and Gold, M.S. The thyrotropin-releasing hormone test in the diagnosis of unipolar depression. *Psychiatry Res.*, 5:311-316, 1981.

Gold, M.S., Pottash, A.L.C., Ryan, N., Sweeney, D.R., Davies, R.K., and Martin, D.M. TRH-induced TSH response in unipolar, bipolar, and secondary depressions: Possible utility in clinical assessment and differential diagnosis. *Psychoneuroendocrinology*, 5:147-155, 1980.

Gold, M.S., Pottash, A.L.C., Extein, I., Martin, D.M., Howard, E., Mueller, E.A., and Sweeney, D.R. The TRH test in the diagnosis of major and minor depression. *Psychoneuroendocrinology*, 6:159-169, 1981.

Kirstein, L., Gold, M.S., Pottash, A.L.C., and Extein, I. Thyrotropin-releasing hormone test and male unipolar depression. *Biol. Psychiatry*, 16:819-824, 1981.

Meltzer, H.Y., Arora, R.C., Baber, R., and Tricou, B.J. Serotonin uptake in blood platelets of psychiatric patients. *Arch. Gen. Psychiatry*, 38:1322-1326, 1981.

Morley, J.E., Brammer, G.L., Sharp, B., Yamada, T., Yuwiler, A., and Hershman, J.M. Neurotransmitter control of hypothalamic-pituitary-thyroid function in rats. *Eur. J. Pharmacol.*, 70:263-271, 1981.

Relationship of Dexamethasone (2 mg) and Plasma Cortisol Hypersecretion in Depressive Illness: Clinical and Neuroendocrine Parameters

Gregory M. Asnis, M.D.,[1] Uriel Halbreich, M.D.,[2] Edward J. Sachar, M.D.,[1] R. Swami Nathan, M.D.,[3] Mark Davies, M.P.H.,[1] Hana Novacenko, M.S.,[1] Lynn C. Ostrow, R.N., M.A.,[1] Jean Endicott, Ph.D.,[1] and Joaquim Puig-Antich, M.D.[1]

Dexamethasone (2 mg) resistance and cortisol hypersecretion are two neuroendocrine abnormalities seen in approximately 1/3 to 1/2 of endogenously depressed patients (Brown et al. 1979; Carroll et al. 1976a, 1976b; Sachar et al. 1970; Stokes et al. 1975). Both neuroendocrine disturbances are presumed to reflect increased hypothalamic-pituitary-adrenal activity. The investigators studied the above neuroendocrine assessments in the same group of endogenously depressed patients. The focus was upon the relationship of various clinical correlates with dexamethasone resistance and plasma cortisol hypersecretion; the main hypthesis was that if both tests of cortisol abnormality were associated with specific depressive symptoms, then they were more likely to reflect similar underlying mechanisms.

Method

Thirty depressed patients (10 men and 20 women, mean age ± SD = 44.2 ± 14.4 years, range = 18-64 years) were admitted to an inpatient research ward where they were evaluated with the Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott & Spitzer 1978), and were diagnosed according to the Research Diagnostic Criteria (RDC) (Spitzer et al. 1978) as having a major depressive disorder, endogenous subtype; patients had to have at least a moderately severe depression (Hamilton ≥ 18) (Endicott, et al. 1981). All subjects were free of psychotropic medication for a minimum of 10 days prior to being studied, were medically healthy, and were not taking any hormone pills.

---

[1] New York State Psychiatric Institute and College of Physicians and Surgeons of Columbia University, New York, NY 10032.

[2] Present Address: Montefiore Hospital and Medical Center, Bronx, NY 10467.

[3] Western Psychiatric Institute and Clinic, Pittsburgh, PA 15261.

Demographic data, RDC depressive subtypes, SADS-C scales (symptom clusters relating to the past week), and a scale constructed by the authors of "Hypothalamic Signs" (insomnia, poor appetite, psychomotor retardation, worsening of mood in the morning) were systematically obtained on all subjects.

All subjects received the 2 mg dexamethasone suppression test (DST)* and a mean 1 to 4 p.m. plasma cortisol assessment. Two mg of dexamethasone were taken orally at 11 p.m. with postdexamethasone plasma cortisol assessed at 4 and 11 p.m. the following day. Resistance to dexamethasone was defined as a postdexamethasone plasma cortisol value of > 5 μg/dl. Plasma cortisol was analyzed by a modified competitive protein binding method as described by Novacenko et al. (1980). Subjects received a basal plasma cortisol assessment prior to the DST. An angiocatheter was inserted in the antecubital vein at 9 a.m. with blood sampling (3 cc) every 30 minutes for 24 hours; 26 or the 30 subjects had a complete study while 4 subjects had their study terminated prematurely (but after 4 p.m.) due to subcutaneous infiltration of the angiocatheter. Thus, all subjects had a 1 to 4 p.m. study, and the mean plasma cortisol for this period was used as an integrated measure of plasma cortisol secretion. This was done because the mean 1 to 4 p.m. plasma cortisol has been shown to highly correlate with the mean 24-hour cortisol in normals and depressives (Halbreich et al. 1981, 1982). In the 26 subjects who had a complete 24-hour study, the mean 1 to 4 p.m. plasma cortisol was also highly correlated to the mean 24-hour plasma cortisol, $r = 90$, $p < 0.001$.

A more extensive evaluation of the mean 1 to 4 p.m. plasma cortisol was undertaken in 32 normal volunteers and 52 endogenously depressed patients in order to determine a satisfactory cortisol level to define cortisol hypersecretion (*see* Figure 1). A mean 1 to 4 p.m. plasma cortisol of > 10 μg/dl was used to define cortisol hypersecretion. This criterion was met in 2 of 32 normals (6 percent) and 20 of 52 (40 percent) depressives (Fisher Exact Probability Test, $p = 0.027$).

Results

Eight of 30 (27%) patients were dexamethasoneresistant and 12 of 30 (40%) patients were defined as cortisol hypersecretors.

Age

Patients with dexamethasone resistance were not significantly different in age from suppressors (45.0 SD 14.2 years vs. 42.2 SD 15.8 years, $F = 0.02$, NS); however, cortisol hypersecretors were significantly older than cortisol normosecretors (51.7 SD 12.7 years vs. 39.3 SD 13.7 years, $F = 6.25$, $p < .02$). A positive relationship between age and cortisol hypersecretion in endogenous depressives had been reported previously by Asnis et al. (1981). Subsequent analyses reported below controlled for age.

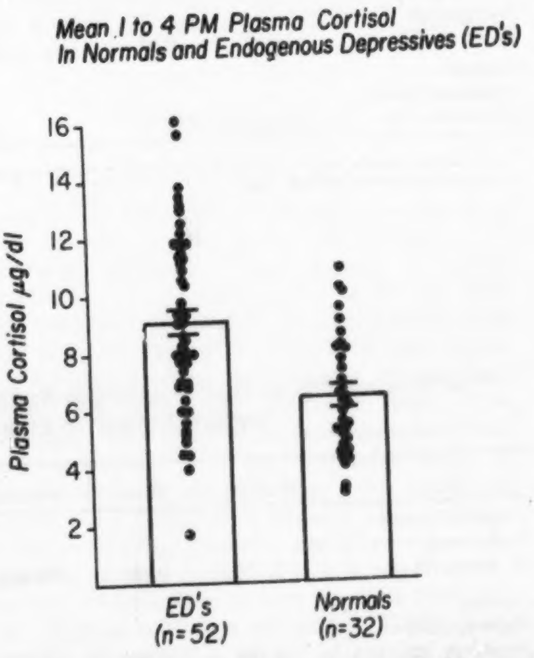


FIGURE 1. Mean 1 to 4 p.m. plasma cortisol in normals and endogenous depessions (EDs).

---

*There are two versions of the DST: one uses 1 mg, the other uses 2 mg.

Sex

Two of 10(20%) men vs. 6 of 20(30%) women were dexamethasone resistant (Fisher exact test, NS); 4 of 10 (40%) men vs. 8 of 20 (27%) women were cortisol hypersecretors (Fisher exact test, NS).

SADS-C Scales

As can be seen in Table 1, the patients wit dexamethasone resistance had significantly highe scores on the scale "Hypothalamic Signs"; the symptom of this scale which was significantl associated with dexamethasone resistance wa

Table 1

The Relationship of SADS-C and Summary Scales to Dexamethasone Resistance and Cortisol Hypersecretion in Endogenously Depressed Patients

	Depressive Syndrome	Endogenous Features	Manic Syndrome	Anxiety	Delusions-Hallucinations Disorganization	GAS Score
Dexamethasone Resistance ($N = 8$ vs. 22)	4.01	3.90	2.76	0.09	0.01	0.08
Cortisol Hypersecretion ($N = 12$ vs. 18)	0.47	0.02	2.86	1.26	0.69	0.12

	Extracted Hamilton	Miscellaneous Psychopathology	Social Functioning	Suicidal Behavior	Hypothalamic[a] Signs
Dexamethasone Resistance ($N = 8$ vs. 22)	0.66	2.49	0.92	0.09	7.20[b]
Cortisol Hypersecretion ($N = 12$ vs. 18)	0.03	4.51[c]	0.98	0.01	0.03

[a] Hypothalamic signs consist of a cluster of symptoms from endogenous feature scale (insomnia, poor appetite, psychomotor retardation, worse in morning) felt be specific for hypothalamic dysfunction.

[b] $p < .01$

[c] $p < .05$

Table 2

The Relationship of RDC Depressive Subtypes to Dexamethasone Resistance and Cortisol Hypersecretion in Endogenously Depressed Patients

	Psychotic	Bipolar	Retarded	Agitated	Simple	Situational	Primary	Incapacitat
Dexamethasone Resistance ($N = 8$ vs. 22)	0.175	0.056	[a]0.018	0.574	0.637	0.426	0.548	0.282
Cortisol Hypersecretion ($N = 12$ vs. 18)	0.455	0.350	0.132	0.251	0.197	0.206	0.350	0.586

[a] Statistically significant

psychomotor retardation ($F = 10.12$, $p < .004$). In contrast, patients with cortisol hypersecretion had significantly higher scores on the scale Miscellaneous Psychopathology (the significant symptom in this scale was subjective anger) ($F = 10.83$, $p < .003$).

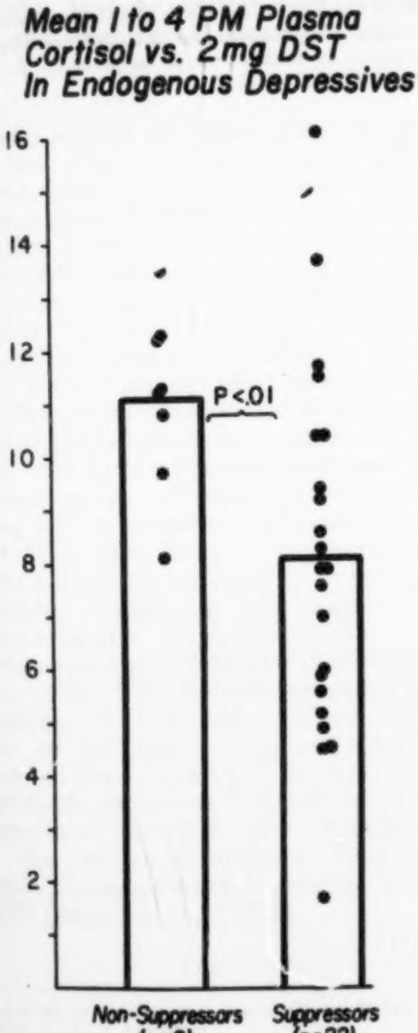


FIGURE 2. Mean 1 to 4 p.m. plasma cortisol vs. 2 mg DST in endogenous depressives.

RDC Subtypes

As can be seen in Table 2, dexamethasone resistance was significantly associated with retarded depression (trend for bipolar depression) while cortisol hypersecretion was not significantly associated with any depressive subtype.

The Association of the 2 Mg DST and Mean 1 to 4 P.M. Plasma Cortisol

As can be seen in Figure 2, nonsuppressors had a significantly higher mean 1 to 4 p.m. plasma cortisol (11.1 ± 1.6 μg/dl) than the suppressors (8.1 ± 3.4 μg/dl) ($F = 8.24$, $p < .01$). Six of 8 nonsuppressors were cortisol hypersecretors in comparison to 6 of 22 suppressors (Fisher exact test, $p = .027$). Although there is an association of the 2 mg DST and plasma cortisol hypersecretion, only 50 percent of the cortisol hypersecretors (6 of 12 patients) were identified by the 2 mg DST. On the other hand, two dexamethasone nonsuppressors were normosecreters.

Within the 12 cortisol hypersecretors, mean 1-4 p.m. cortisol did not predict DST−2 mg. nonsuppression ($r = -.14$, NS).

Discussion

The phenomenon of dexamethasone resistance (2 mg DST) and plasma cortisol hypersecretion were studied in the same 30 endogenously depressed patients. The clinical correlates associated with dexamethasone resistance were RDC subtype (retarded depression) and the summary scale of "Hypothalamic Signs" (the significant symptom being psychomotor retardation). These correlates were different from those associated with plasma cortisol hypersecretion, i.e., older age and the summary scale of Miscellaneous Psychopathology (the significant symptom was subjective anger). These clinical correlates need replication and may reflect the particular sample studied. Thus, a larger sample size may be necessary to firm up these findings.

In addition with two exceptions, DST−2 mg basically identified a subset of cortisol hypersecretors, although the mean 1-4 p.m. plasma cortisol within the group of hypersecretors did not predict DST−2 mg resistance. Dexamethasone

(2 mg) does not simply inhibit "milder" cortisol hypersecretors. Even some normosecretors may escape the suppressant effect of DST–2 mg.

The implication of these clinical/neuroendocrine findings is that the complexity of dysregulation of cortisol secretion in major depressives is not fully understood. Interestingly, both measures of cortisol secretion are associated with depressive illness, but the data reported here do not in any way fit a linear univariate model nor do they identify underlying mechanisms for DST– 2 mg and cortisol hypersecretion.

Several measures (DST–1 mg, *d*-amphetamine test) of cortisol secretion in the same sample of depressives and both normal and pathological controls should illuminate further the pathophysiology of depressive illness and the diagnostic utility of one (or several) tests of cortisol secretion.

References

Asnis, G.M., Sachar, E.J., Halbreich, U., Nathan, J.S., Novacenko, H., and Ostrow, L.C. Cortisol secretion in relation to age in major depression. *Psychosom. Med.*, 43:235-246, 1981.

Asnis, G.M., Halbreich, U., Nathan, R.S., et al. The dexamethasone suppression test in depressive illness: Clinical correlates. *Psychoneuroendocrinology.* (In press)

Brown, W.A., Johnston, R., and Mayfield, D. The 24-hour dexamethasone suppression test in a clinical setting: Relationship to diagnosis, symptoms, and response to treatment. *Am. J. Psychiatry*, 136:543-547, 1979.

Carroll, B.J., Curtis, G.C., and Mendels, J. Neuroendocrine regulation in depression: II. Discrimination of depressed from nondepressed patients. *Arch. Gen. Psychiatry*, 33:1051-1058, 1976a.

Carroll, B.J., Curtis, G.C, Davies, B.M., Mendels, J., and Sugarman, A.A. Urinary free cortisol excretion in depression. *Psychol. Med.*, 6:43-50, 1976b.

Endicott, J., and Spitzer, R.L. A diagnostic interview: The Schedule for Affective Disorders and Schizophrenia. *Arch. Gen. Psychiatry*, 35:837-844, 1978.

Endicott, J., Cohen, J., Nee, J., Fleiss, J., and Saxantakos, S. Hamilton Depression Rating Scale: Extracted from regular and change versions of the Schedule for Affective Disorders and Schizophrenia. *Arch. Gen. Psychiatry*, 38:98-103, 1981.

Halbreich, U., Sachar, E.J., Asnis, G.M., Nathan, R.S., and Halpern, F., Studies of cortisol diurnal rhythm and cortisol response to *d*-amphetamine in depressed patients. *Psychopharmacol. Bull.*, 17:114-116, 1981.

Halbriech, U., Zumoff, B., Kream, J., and Fukushima, D. The mean 1 to 4 p.m. plasma cortisol concentration as a diagnostic test for hypercortisolism. *J. Clin. Endocrinol. Metab.* (In press)

Novacenko, H., Halpern, F., and Sachar, E.J. Improved protein-binding radioassay for plasma cortisol. *Clin. Chem.* 26:312-313, 1980.

Sachar, E.J., Hellman, L., Fukushima, D., and Gallagher, T.F. Cortisol production in depressive illness. *Arch. Gen. Psychiatry*, 23:289-298, 1970.

Schlesser, M.A., Winokur, G., and Sherman, B.M. Genetic subtypes of unipolar primary depressive illness distinguished by hypothalamic-pituitary-adrenal axis activity. *Lancet*, 1:739-741, 1979.

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry*, 35:773-782, 1978.

Stokes, P.E., Pick, G.R., Stoll, P.M., and Nunn, W.D. Pituitary-adrenal function in depressed patients: Resistance to dexamethasone suppression. *J. Psychiatr. Res.*, 12:271-281, 1975.

Melatonin Secretion as a Neurobiological "Marker" and Effects of Light in Humans

Alfred J. Lewy, M.D.,[1] Thomas A. Wehr, M.D.,[2] Norman E. Rosenthal, M.D.,[2] John I. Nurnberger, M.D.,[2] Larry J. Siever, M.D.,[2] Thomas W. Uhde, M.D.,[2] David A. Newsome, M.D.[3] Leslie E. Becker, M.D.,[2] Sanford P. Markey, Ph.D.,[2] Irwin J. Kopin, M.D.,[2] and Frederick K. Goodwin, M.D.[2]

Development of the highly accurate and sensitive gas chromatographic-negative chemical ionization mass spectrometric assay for plasma melatonin (Lewy & Markey 1978) has facilitated evaluation of pineal function in humans. The pineal gland synthesizes and secretes melatonin in response to stimulation of its beta-adrenergic receptors by norepinephrine released by postganglionic sympathetic neurons, the nervi conarii (Ariëns Kappers 1960; Deguchi & Axelrod 1972). Beta-adrenergic stimulation initiates a sequence of biochemical events, culminating in increased activity of N-acetyltransferase, which converts serotonin to N-acetylserotonin, the rate-limiting step in melatonin synthesis (Klein & Weller 1970). The firing of these sympathetic neurons is discretely regulated by an endogenous pacemaker, thought to be located in the suprachiasmatic nucleus (SCN) of the hypothalamus (Moore & Eichler 1972; Stephan & Zucker 1972). The endogenous pacemaker is responsible for a circadian (about 24-hour) rhythm in the activity of these sympathetic neurons. The circadian rhythm in the hypothalamic pacemaker is synchronized to the environmental light/dark cycle, through input from the retinohypothalamic tract which transmits photic information from the retina to the SCN (Moore & Lenn 1972).

There are essentially two effects of light on the circadian system, one, the light/dark cycle entrains (synchronizes) circadian rhythms (Aschoff 1981) and two, the changing length of darkness throughout the year cues seasonal rhythms (Pittendrigh 1981). An additional unique effect of light (specific to the pineal) is that acute exposure to light suppresses melatonin production (Minneman et al. 1974). It is assumed that all three effects of light are mediated by the same neural pathways. Consequently, measurement of light suppression of melatonin may be a "marker" for the effects of light on the circadian system.

The human pineal appears to be regulated in the same way as is the pineal of other mammalian species, because nighttime secretion of melatonin is suppressed by bright artificial light and sunlight in humans (Lewy et al. 1980). Light also appears to be important for the proper synchronization of the circadian rhythm of melatonin secretion, because some blind people have unusual circadian secretory rhythms (Lewy & Newsome 1982).

Manic-depressive patients seem to be supersensitive to light (Lewy et al. 1981). Four patients (taking no medications in seven out of eight instances) were studied in both mood states. Exposure to 500 lux Vita-Lite suppressed the patients by 50 percent; this intensity had little or no effect in a normal control group ($N = 6$). This difference was statistically significantly different ($p < .02$, by analysis of variance). An additional group of five euthymic manic-depressive patients were also studied. Melatonin secretion was suppressed by 50 percent with 500 lux light in this group as well. Thus, supersensitivity to light may be a "trait marker" for manic-depressive illness. Supersensitivity to light is consistent with, and could possibly explain, phase-advanced circadian rhythms observed in these patients (Wehr & Goodwin 1981). More subjects, including a group of unipolar patients, are currently being studied. Also, preliminary evidence suggests that there may be a seasonal rhythm in light sensitivity in both patients and normal controls, because subjects appear to suppress more during the winter than during the summer.

Light supression of melatonin secretion has some potentially important implications—the circadian rhythms of humans may be synchronized by the light/dark cycle and humans may have seasonal rhythms that are affected by the changing length of daylight Ordinary artificial light apparently does not affect human melatonin secretion (Lewy et al. 1980), implying that human circadian and seasonal rhythms may not be perturbed by indoor lighting under usual circumstances. Consequently, humans may be similar to other species in that they may be affected by the 24-hour rhythm of sunlight and by the length of natural daylight as it changes throughout the year (Aschoff 1981).

---

[1] Sleep and Mood Disorders Laboratory, Oregon Health Sciences University, Portland, OR 97201.
[2] National Institute of Mental Health, Bethesda, MD 20205.
[3] National Eye Institute, Bethesda, MD 20205.

Send reprint requests to: Dr. A.J. Lewy, Department of Psychiatry, Oregon Health Sciences University, Portland, OR 97201.

Photoperiodic effects of light were evaluated in humans by exposing a man with winter depression to "long days" of light during the winter of 1980 (Lewy et al. 1982a). A manic-depressive patient with a well-documented 13-year history of winter depressions and springtime remissions was exposed to 2000 lux Vita-Lite between 6 and 9 a.m. and between 4 and 7 p.m. for 10 days. Within 4 days his winter depression remitted. Although this is an $N = 1$ study, it is the first attempt to use light to treat a manic-depressive patient with a disorder that appears to be related to the circadian system. More patients were studied during the winter of 1981 using a modified crossover design with dim light as a placebo control. (Ordinary dim room light would not be expected to directly affect the circadian system of humans.) Bright light combined with sleep deprivation as a treatment for depression is also being evaluated.

Melatonin levels are also a marker for adrenergic function. Human melatonin secretion appears to be regulated by beta-adrenergic receptors. Transection of the spinal cord abolishes the circadian melatonin secretory rhythm (Kneisley et al. 1978). Sympatholytic diseases, such as Shy Drager Syndrome and idiopathic orthostatic hypotension, result in either reduced plasma melatonin and urinary 6-hydroxymelatonin levels or disrupted secretory rhythms Tetsuo et al. 1981; Vaughan et al. 1979). Administration of propranolol reduces the nighttime rise in melatonin levels (Hanssen 1977; Vaughan 1976). Bedtime administration of 120 mg daily (p.o.), can completely reduce nighttime melatonin levels (authors' unpublished data).

Clonidine can also reduce nighttime levels (Lewy et al. 1982b). Clonidine was administered intraventricularly (i.v.) to four normal volunteers around midnight at doses of 2.0, 2.5, and 3.0 μg/kg. There was a linear log dose reduction of plasma melatonin levels 1 hour after administration of clonidine compared to the same time on a baseline night ($r = -.986$, $p < .01$). Oral administration of clonidine is also effective; administration by this route has a delayed onset of action and a longer duration of action than after i.v. administration. Measurement of urinary 6-hydroxymelatonin may also be a useful way of quantifying the effects of clonidine on melatonin production. Presumably, clonidine acts on an alpha-adrenergic receptor, although the exact location of this receptor has yet to be identified. [The only alpha-receptor localized so far in the retino-hypothalamic-pineal system has been a presynaptic alpha-2-autoadrenoceptor on the sympathetic neuron innervating the pineal (Pelayo et al. 1977).]

Summary

Plasma melatonin levels are a marker for adrenergic function; the rhythm of melatonin production is a marker for the phase and period of its endogenous pacemaker; suppression of melatonin secretion by light is a marker for the effects of light in humans. Bright light appears to have similar biological effects in humans as does ordinary room light in other species. Light suppression of melatonin may prove to be a valuable research tool; light may also have potential as a therapeutic modality for certain circadian and seasonal disorders.

References

Ariëns Kappers, J. The development, topographical relations, and innervation of the epiphysis cerebri in the albino rat. *Z. Zellforsch. Mikrosk. Anat.*, 52:163-215, 1960.

Aschoff, J. (ed.), *Handbook of Behavioral Neurobiology, Biological Rhythms.* Vol 4. New York: Plenum Press, 1981.

Deguchi, T., and Axelrod, J., Control of circadian change of serotonin N-acetyltransferase in the pineal organ by the beta-adrenergic receptor. *Proc. Natl. Acad. Sci. USA*, 69:2547-2550, 1972.

Hanssen, T. Heyden, T., Sundberg, T., and Wetterberg, L. Effect of propanolol on serum-melatonin. *Lancet*, 2:309-310, 1977.

Klein, D.C., and Weller, J., Indole metabolism in the pineal gland: A circadian rhythm in N-acetyltransferase. *Science*, 169:1093-1095, 1970.

Kneisley, L.W., Moskowitz, M.H., and Lynch, H.J. Cervical spinal cord lesions disrupt the rhythm in human melatonin excretion. *J. Neurol. Transm.* (Suppl.), 13:311-323, 1978.

Lewy, A.J., and Markey, S.P. Analysis of melatonin in human plasma by gas chromatography-negative chemical ionization mass spectrometry. *Science*, 201:741-743, 1978.

Lewy, A.J., and Newsome, D.A. Unusual melatonin secretion in some blind subjects. (Submitted, 1982)

Lewy, A.J., Kern, H.A., Rosenthal, N.E., and Wehr, T.A. Bright artificial light treatment of a manic-depressive patient with a seasonal mood cycle. *Am. J. Psychiatry*, 139:1496-1498, 1982a.

Lewy, A.J., Siever, L., Uhde, T.W., Goodwin, F.K., Murphy, D.L., Post, R.M., and Markey, S.P. Clonidine reduces human melatonin secretion. (Submitted, 1982b)

Lewy, A.J., Wehr, T.A., Goodwin, F.K., Newsome, D.A., and Markey, S.P. Light suppresses melatonin secretion in humans. *Science*, 210:1267-1269, 1980.

Lewy, A.J., Wehr, T.A., Goodwin, F.K., Newsome, D.A., and Rosenthal, N.E. Manic-depressive patients may be supersensitive to light. *Lancet*, 1:383-384, 1981.

Minneman, K.P., Lynch, H., and Wurtman, R.J. Relationship between environmental light intensity and retina-mediated suppression of rat pineal serotonin-N-acetyltransferase. *Life Sci.*, 15:1791-1796, 1974.

Moore, R.Y., and Eichler, V.B. Loss of circadian adrenal corticosterone rhythm following suprachiasmatic lesions in the rat. *Brain Res.*, 42:201-206, 1972.

Moore, R.Y., and Lenn, N.J. A retinohypothalamic projection in the rat. *J. Comp. Neurol.*, 146:1-14, 1972.

Pelayo, F., Dubocovich, M.L., and Langer, S.Z. Regulation of noradrenaline release in the rat pineal through a negative feedback mechanism mediated by presynaptic alpha-adrenoceptors. *Eur. J. Pharmacol.*, 45:317-318, 1977.

Pittendrigh, C.S. Circadian systems: Entrainment. In: Aschoff, J. (ed.), *Handbook of Behavioral Neurobiology, Biological Rhythms.* Vol. 4. New York:Plenum Press, 1981, pp. 95-124.

Stephan, F.K., and Zucker, I. Circadian rhythms in drinking behavior and locomotor activity of rats are eliminated by hypothalamic lesions. *Proc. Natl. Acad. Sci. USA*, 69:1583-1586, 1972.

Tetsuo, M. Polinsky, R.J., Markey, S.P., and Kopin, I.J. Urinary 6-hydroxymelatonin excretion in patients with orthostatic hypotension. *J. Clin. Endocrinol. Metab.*, 53:607-610, 1981.

Vaughan, G.M., McDonald, S.D., Bell, R., and Stevens, E.A. Melatonin, pituitary function, and stress in humans. *Psychoneuroendocrinology*, 4:351-362, 1979.

Vaughan, G.M., Pelham, R.W., Pang, S.F., Loughlin, L.L., Wilson, K.M., Sandock, K.L., Vaughn, M.K., Koslow, S.H., and Reiter, R.J. Nocturnal elevation of plasma melatonin and urinary 5-hydroxy-indoleacetic acid: Attempts at modification by brief changes in environmental lighting and sleep and by autonomic drugs. *J. Clin. Endocrinol. Metab.*, 42:752-754, 1976.

Wehr, T.A., and Goodwin, F.K. Biological rhythms and psychiatry. In: Arieti, S., and Brodie, H.K.H. (eds.), *American Handbook of Psychiatry.* Vol. 7, 2nd ed. New York:Basic Books, 1981, pp. 46-74.

The Relationship of Plasma-Free MHPG to Anxiety and Psychophysical Pain in Normal Volunteers

Thomas W. Uhde, M.D.,[1] Larry J. Siever, M.D.,[2] Robert M. Post, M.D.,[1] David C. Jimerson, M.D.,[3] Jean-Philippe Boulenger, M.D.,[1] and Monte S. Buchsbaum, M.D.[1]

Alterations in noradrenergic function have been postulated in theories of anxiety and pain. In animals, lesions of the noradrenergic nucleus locus coeruleus produce decreased fear-associated behaviors (Redmond & Huang 1979) and analgesia (Bodnar et al. 1978). Pharmacologic inhibition of the locus coeruleus also produces effects in a similar direction. That is, morphine (Korf et al. 1974) and clonidine (Aghajanian 1978) inhibit locus coeruleus activity, reduce fear-associated behaviors (Redmond 1977; Redmond & Huang 1979), and have potent analgesic (Fielding et al. 1981; Paalzow 1974) properties. Tricyclic antidepressants decrease locus coeruleus firing (Redmond 1977; Redmond & Huang 1979), produce analgesia in some animals, and potentiate morphine-induced antinociception (Malseed & Goldstein 1979). Although electrical and pharmacologic (Redmond 1977; Redmond & Huang 1979) activation of the locus coeruleus is associated with increased fear-associated behaviors, the effect of increased noradrenergic function on antinociception remains uncertain (Pert 1980). These observations may suggest a linkage between the biological functions of anxiety and pain. It is interesting in this regard that morphine is generally accepted to have analgesic and antianxiety properties in man. Furthermore, tricyclic antidepressants are effective in the treatment of patients with panic disorder (Klein 1964)

---

[1] Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20205.

[2] Clinical Neuropharmacology Branch, National Institute of Mental Health, Bethesda, MD 20205.

[3] Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20205.

Address reprint requests to: Uhde, M.D., Biological Psychiatry Branch, Building 10, Room 3S-239, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20205.

and certain pain syndromes (Merskey & Hestes 1972). Clonidine also has antianxiety effects in depressed (Uhde et al. 1981) and anxious patients (Hoehn-Saric et al. 1981; Liebowitz et al. 1981; Uhde et al. 1982), but not normal volunteers (Leckman et al. 1980; Uhde et al. 1981, 1982). Although clonidine at low doses does not produce analgesic effects in human controls as a group (Uhde et al. 1980, 1982), both clonidine and morphine produce predictable changes in a subgroup of insensitive subjects in the direction of increased analgesia as reflected by somatosensory evoked potentials (Buchsbaum et al. 1982). Benzodiazepines, which decrease locus coeruleus firing (Grant et al. 1980), recently have been reported to influence endogenous opioid systems (Duka et al. 1979; Soubrie et al. 1980).

Together, these data may suggest a functional relationship between the noradrenergic system and the experience of anxiety and pain. In attempts to collect data pertinent to these variables the authors have investigated the relationship among plasma free 3-methoxy-4-hydroxyphenylethylene glycol (MHPG), state anxiety, and psychophysical pain in 12 normal volunteers.

Method

Psychophysical Pain

Using previously described methods (Davis et al. 1978), an index of pain insensitivity was obtained in 12 normal volunteers 1-1½ hours after the blind administration of a placebo infusion which had been randomly paired with an active medication. Subjects received shocks at each milliamperage (mA) increment from 1 to 31, for a total of 93 randomly presented shocks. Subjects judged each shock as noticeable, distinct, unpleasant, or very unpleasant. An index of pain insensitivity was obtained by threshold and signal detection analysis. This index is derived from the subject's ability to distinguish between distinct and unpleasant sensations. Increases in this measure have been associated with morphine and aspirin analgesia (Buchsbaum & Davis 1979; Davis et al. 1980), and decreases with naltrexone-induced hyperalgesia in schizophrenics (Davis et al. 1979).

State Anxiety

The Spielberger State Trait Anxiety Invento (range 20-80) was administered 1-1½ hours af the placebo infusion (just prior to the administ tion of the shocks).

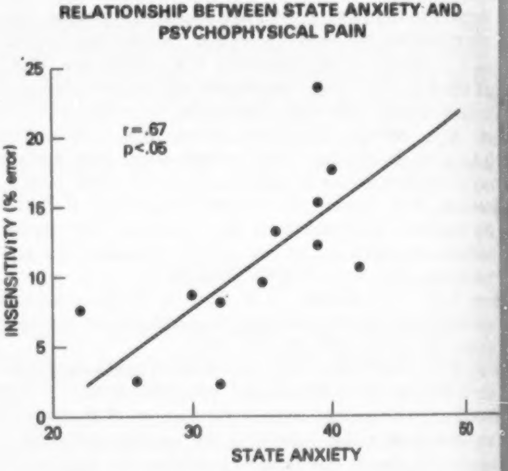


FIGURE 1. Those normal volunteers with higher rati of state anxiety demonstrated increased pain insensitiv as measured by threshold and signal detection analysi

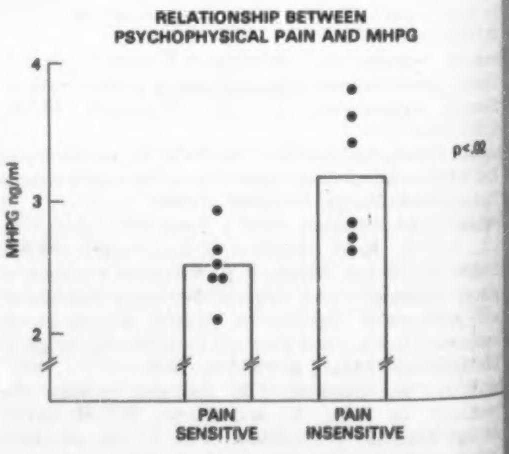


FIGURE 2. In the first 12 normal subjects studied, th most pain-sensitive subjects had lower values of plas free MHPG than the six most pain-insensitive subje

ological Measures

Plasma-free MHPG was measured by gas romatography-mass spectrometry (Jimerson et . 1981). All results refer to data obtained after e placebo infusion and, therefore, just prior to e administration of shocks.

Results

There were significant correlations between ate anxiety and scores on the insensitivity index $= .67, N = 12, p < .05$) (Figure 1) and state nxiety and plasma-free MHPG ($r = .59, N = 12$, $< .05$). Thus, the subjects with the highest tings of state anxiety had the greatest plasma-ee MHPG and were least able to discriminate etween distinct and unpleasant sensations. By edian split, the six most pain insensitive in-ividuals had significantly higher levels of lasma-free MHPG (3.2 ng/ml ± 0.2 S.E.) Figure 2) and anxiety (39.1 ± 1.8) compared to e six least pain insensitive individuals (MHPG .5 ± 0.1, $p < .02$; anxiety 27.8 ± 1.6, $p <$ 001).

Discussion

Our data suggest that the greater the state anx-ety, the greater the insensitivity and inability to iscriminate among randomly administered hocks. Individuals with low MHPG were less nxious and more pain sensitive than those sub-ects with relatively higher MHPG. These find-ngs support previous observations of a relation-hip between anxiety and noradrenergic function nd suggest that high anxiety in normal controls nay reduce the ability to discriminate the amount f pain an individual feels. This rather unique elationship in normals is opposite the usual ex-ectation of clinicians treating patients with hronic pain. That is, pathological anxiety in hronic pain patients is often thought to decrease ain thresholds. Preliminary evidence from the uthors' laboratory also suggest that patients with hronic pathological anxiety may become more ain sensitive with increasing degrees of state nxiety. Increases in state anxiety, therefore, may ave opposite effects on pain discriminability in normal controls compared to patients with chronic anxiety disorders, suggesting that the relationship between anxiety and pain may be nonlinear.

The authors' findings suggest that reducing some patients' anxiety with anxiolytics might intensify, rather than decrease, the amount of pain experienced as measured by the insensitivity index. If this hypothesis is correct it might explain why clonidine, which has acute antianxiety effects in depressed and phobic anxious patients, lacked group analgesic activity in normal human volunteers as measured by the insensitivity index (Uhde et al. 1980, 1981, 1982). These findings in man support and extend previous animal research suggesting an important role for noradrenergic systems in the modulation of anxiety and pain.

References

Aghajanian, G.K. Tolerance of locus coeruleus neurons to morphine and suppression of withdrawal response by clonidine. *Nature*, 276:186-187, 1978.

Bodnar, R.J., Ackerman, R.F., Kelly, D.D., and Grusman, N. Elevations in nociceptive thresholds following locus coeruleus lesions. *Brain Res. Bull.*, 3:125-130, 1978.

Buchsbaum, M.S., and Davis, G.C. Application of somatosensory event-related potentials to experimental pain and the pharmacology of analgesia. In: Lehmann, D., and Collaway, E. (eds.), *Human Evoked Potentials: Applications and Problems.* New York: Plenum Press, 1979, pp. 43-54.

Buchsbaum, M.S., Davis, G.C., Uhde, T.W., Siever, L.J., and Naber, D. Individual differences in pain sensitivity determine pharmacological response to morphine, naloxone, and clonidine. (Submitted, 1982)

Davis, G.C., Buchsbaum, M.S., and Bunney, W.E., Jr. Naloxone decreases diurnal variation in pain sensitivity and somatosensory-evoked potentials. *Life Sci.*, 23:1449-1460, 1978.

Davis, G.C., Buchsbaum, M.S., van Kammen, D.P., and Bunney, W.E., Jr. Analgesia to pain stimuli in schizophrenics and its reversal by naltrexone. *Psychiatry Res.*, 1:61-69, 1979.

Davis, G.C., Buchsbaum, M.S., Naber, D., and van Kammen, D.P. Effects of opiates and opiate antagonists on somatosensory-evoked potentials in patients with schizophrenia and normal adults. In: Perris, C., von Knorring, L., and Kemali, D. (eds.), *Recent Advances in Biological Psychiatry.* Basel, Switzerland: S. Karger, 1980, pp. 73-80.

Duka, T., Wüster, M., and Herz, A. Rapid changes in enkephalin levels in rat striatum and hypothalamus induced by diazepam. *Naunyn-Schmiedeberg's Arch. Pharmacol.*, 309:1-5, 1979.

Fielding, S., Spaulding, T.C., and Lal, H. Antinociceptive actions of clonidine. In: *Psychopharmacology of Clonidine.* New York:Alan R. Liss, Inc., 1981, pp. 225-242.

Grant, S.J., Huang, Y.H., and Redmond, D.E., Jr. Benzodiazepines attenuate single unit activity in the locus coeruleus. *Life Sci.*, 27:2231-2236, 1980.

Hoehn-Saric, R., Merchant, A.F., Keyser, M.L., and Smith, V.K. Effects of clonidine on anxiety disorders. *Arch. Gen. Psychiatry*, 38:1278-1282, 1981.

Jimerson, D.C., Markey, S.P., Oliver, J.O., and Kopin, I.J. Simultaneous measurement of plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) and 3,4-dihydroxyphenylglycol (DHPG) by gas chromatography-mass spectrometry (6 CMS). *Biomed. Mass Spectrom.*, 8:256-259, 1981.

Klein, D.F. Delineation of two drug-response anxiety syndromes. *Psychopharmacologia (Berlin)*, 5:397-408, 1964.

Korf, J., Bunney, B.S., and Aghajanian, G.K. Noradrenergic neurons: Morphine inhibition of spontaneous activity. *Eur. J. Pharmacol.*, 25:165-169, 1974.

Leckman, J.F., Maas, J.W., Redmond, D.E., Jr., and Heninger, G.R. Effects of oral clonidine on plasma 3-methoxy-4-hydroxy-phenylethyleneglycol (MHPG) in man: Preliminary report. *Life Sci.*, 26:2179-2185.

Liebowitz, M.R., Fyer, A.J., McGrath, P., and Klein, D.F. Clonidine treatment of panic disorder. *Psychopharmacol. Bull.*, 17:122-123, 1981.

Malseed, R.T., and Goldstein, F.J. Enhancement of morphine analgesia by tricyclic antidepressants. In: *Neuropharmacology*. Vol. 8. Great Britain:Pergamon Press, 1979, pp. 827-829.

Merskey, H., and Hestes, R.A. The treatment of chronic pain with psychotropic drugs. *Postgrad. Med. J.*, 48:594-598, 1972.

Paalzow, L. Analgesia produced by clonidine in mice and rats. *J. Pharm. Pharmacol.*,26:361-363, 1974.

Pert, A. Psychopharmacology of analgesia and pain. In: Ng/Bonica (eds.), *Pain, Discomfort, and Humanitarian Care*. North Holland:Elsevier, 1980.

Redmond, D.E., Jr. Alterations in the function of the nucleus locus coeruleus: A possible model for studies of anxiety. In: Hanin, I. and Usdin, E. (eds.), *Animal Models of Psychiatry and Neurology*. Oxford/New York:Pergamon Press, 1977, pp. 293-305.

Redmond, D.E., Jr., and Huang, Y.H. Current concepts. II. New evidence for a locus coeruleus-norepinephrine connection with anxiety. *Life Sci.*, 25:2149-2162, 1979.

Soubrie, P., Jobert, A., and Thiebot, M.H. Differential effects of naloxone against the diazepam-induced release of behavior in rats in three aversive situations. *Psychopharmacology (Berlin)*, 69:101-105, 1980.

Uhde, T.W., Siever, L.J., and Post, R.M. Clonidine: Acute challenge and clinical trial paradigms for the investigation and treatment of anxiety disorders, affective illness, and pain syndromes. In: Post, R.M., and Ballenger, J.C. (eds.), *Neurobiology of the Mood Disorders*. Baltimore:Williams and Wilkins, 1982. (In press)

Uhde, T.W., Post, R.M., Siever, L.J., and Buchsbaum, M.S. Clonidine and psychophysical pain. *Lancet*, 2:1375, 1980.

Uhde, T.W., Post, R.M., Siever, L.J., Buchsbaum, M.S., Jimerson, D.C., Silberman, E.K., Murphy, D., and Bunney, W.E., Jr. Clonidine: Effects on mood, anxiety, and pain. *Psychopharmacol. Bull.*, 17:125-126, 1981.

Current Knowledge of Tricyclic Antidepressant Response Indicators

David H. Tilley, M.P.H.,[1] Solomon C. Goldberg, Ph.D.,[1] and Robert O. Friedel, M.D.[1]

Since the early 1960s, a substantial amount o clinical research has been aimed at refining an targeting the therapeutic application of tricycli antidepressants (TCA). Attempts to detect meaningful correlations between patient characteristi and treatment response have been an importan aspect of this work. Symptoms, patient history personality variables, and biological markers hav been and are currently being studied for thei response indicator value.

In order to characterize the current state o knowledge of TCA response indicators, th authors have reviewed the literature (controlle clinical research and nodal review articles) an polled substantial panels for expert and practitioner opinion among psychiatrists. The expe panel consisted of productive and widely accepte researchers in the field drawn from the America College of Neuropsychopharmacology (ACNP membership roster and literature citation. Th practitioner panel consisted of members of th Virginia Neuropsychiatric Society who "frequently" use TCA in the treatment of depressed patients. Panel respondents were presented with a list of 41 proposed response indicators and asked to classify each item as 1) indicative of positiv clinical response to TCA, 2) indicative of non response (no better than placebo), or 3) of no indicative value with respect to TCA response.

The authors consider both homogeneity and diversity among sources helpful in understanding their current state of knowledge, in identifying areas which merit further research attention, and in forming research questions and hypotheses The following tables display the more interesting areas of agreement and disagreement among sources, and provide some insight with respect t currently important questions:

---

[1] Medical College of Virginia, Richmond, VA 23298.

1. Does the expert panel agree on anything or is there no consensus on the state-of-the-art regarding TCA response indicators?
2. To what extent do general psychiatric practitioners agree or disagree with expert opinion?
3. How does accumulated clinical wisdom compare with findings reported in the literature?

Areas of Agreement

Agreement among panel members and between panels is so strong with respect to the first 10 indicators shown in Table 1, that they might reasonably be considered current clinical knowledge. The virtual coincidence of these items and Diagnostic and Statistical Manual-III (DSM-III) criteria for melancholia supports the proposition that TCA therapy is an appropriate treatment for the disorder.

Table 1

Positive Response Indicators on Which Experts and Practitioners Agree

Indicator	Expert Panel (% +)	Practitioner Panel (% +)
Weight loss	82	92
Early morning awakening	79	97
Psychomotor retardation	89	94
Loss of appetite	82	94
Primary depression	86	93
Prior episodes	82	90
Poor concentration	68	88
Anhedonia	75	68
Better in evening	68	78
Blames self	68	83
Midnight awakening	64	76
Fatigue and lethargy	61	75

Table 2

Nonresponse Indicators on Which Experts and Practitioners Agree

Indicator	Expert Panel (% –)	Practitioner Panel (% –)
Inadequate personality	71	83
Secondary to antisocial personality	72	86
Hallucinations	75	83
Energetic	64	86
Delusions	75	63

While Table 2 (nonresponse indicators) shows substantial agreement on three items (inadequate personality, secondary to antisocial personality disorder, and hallucinations), no nonresponse indicator achieved the level of concurrence demonstrated for the six leading positive indicators (Table 1). Both panels responded with more agreement to positive indicators than to nonresponse indicators. In addition to the items shown in Table 2, there was fair concurrence on the nonresponse indicative value of other items describing "secondary depression" (secondary to alcoholism, secondary to schizophrenia, and secondary to obsessive-compulsive disorder).

Table 3 compares panel results with results cited in literature reviews. The positive indicative value of vegetative signs of depression (weight loss, early morning awakening, and psychomotor retardation) is strongly and consistently supported by the literature. Anhedonia, anorexia, and self-reproach are supported by panel responses as indicators of positive TCA response, but the literature is less conclusive. The literature is of little help in verifying the indicative value of primary depression, prior episodes, poor concentration, and diurnal variation. *None of the nonresponse indicators selected by the authors' panels showed consistent results in the literature.*

Table 3

Concensus Indicators Compared to the Literature

Indicator	Bielski and Friedel[a]	Nelson and Charney[b]
Weight loss +	+	slight +
Early morning awakening +	+	slight +
Psychomotor retardation +	+	strong +
Primary depression +	-----	-----
Prior episodes +	-	-----
Poor concentration +	-----	-----
Anhedonia +	-----	moderate +
Better in evening +	-----	-----
Loss of appetite +	+	-----
Blames self +	-----	moderate +
Inadequate personality -	-----	-----
Secondary to antisocial personality -	-----	-----
Energetic -	-----	-----
Hallucinations -	-----	-----

[a] Bielski, R.J., and Friedel, R.O. Prediction of tricyclic antidepressant response: A critical review. *Arch. Gen. Psychiatry*, 33:1497-1400, 1976.

[b] Nelson, J.C., and Charney, D.S. The symptoms of major depressive illness. *Am. J. Psychiatry*, 138:1-13, 1981.

Table 4

Indicators in the Literature Not Supported by Expert/Practitioner Panels

Indicator	Bielski and Friedel	Nelson and Charney	Experts			Practitioners		
			% +	% −	%Non-indicator	% +	% −	%No- Indicat
Insidious onset	+	---	18	21	61	56	36	8
Agitated	+	mod. +	43	29	29	73	22	5
Delusional	mod. −	mod. −	0	75	25	30	63	7
Abnormal MHPG	+	---	39	0	61	54	24	22
Hypochondriasis	−	---	18	39	43	42	47	11
Somatic anxiety	−	---	18	25	57	66	27	7
Rejection sensitivity	−	---	3	43	54	64	31	5

Table 5

Expert and Practitioner Opposing Views

Indicator	Expert Panel	Practitioner Panel
Irritable	25% +	79% +
Somatic anxiety	18% +	66% +
Rejection sensitivity	3% +	64% +
Blames others	0% +	76% +
Craving for sweets	21% −	75% −

Table 6

Items of Greatest and Least Agreement

Greatest Agreement	Least Agreement
Weight loss	Agitated
Early morning awakening	Hypochondriasis
Psychomotor retardation	Blames others
Anhedonia	Rejection sensitivity
Anorexia	Somatic anxiety
Self-Reproach (blames self)	Irritability
	Craving for sweets

Areas of Disagreement

Table 4 shows a series of items alluded to in the literature which are either contradicted (insidious onset) or not substantially supported by panel responses.

Marked response differences between expe and practitioner panels are noted with respect t items listed in Table 5. All of these items have appeared in the literature as descriptive of "atypica depression" and attempts have been made t associate them with positive response t monoamine oxidase inhibitors (MAOIs).

In reviewing these data, it is interesting to distinguish items of greatest and least agreement. Table 6 displays the six items which stimulate th most consistent responses, and the seven item which stimulate the most diverse responses. Th diversity of response to these latter items ma serve to identify areas where research might b most useful in improving our ability to distingui TCA responders and nonresponders. Conversely, there seems to be little need to further documen the indicative value of weight loss, early mornin awakening, psychomotor retardation, anhedoni anorexia, or self-reproach.

Comment on Individual Items

"Abnormal MHPG"—Recent research whic tends to devalue MHPG as an indicator seem not to have penetrated the practitioner panel a well as it has the expert panel.

"Precipitant".—So few experts value the presenc or absence of a precipitant to episode as t response indicator that it might be worthwhi to counsel practitioners to ignore the matter.

"Blames other"—This item produced the greate net variance between expert and practitione opinion in that practitioners felt it was a positive indicator and the experts felt it wa worthless.

"Craving for sweets"—Much more significance as a nonresponse indicator is ascribed by practitioners than by experts. (75/21%)

"Delusional"—The relatively high valuation of this item as a nonresponse indicator may be impeding the concurrent use of TCA and a neuroleptic in the treatment of depression with delusions. Recent literature supports concurrent TCA/neuroleptic therapy as the treatment of choice.

Effects of Membrane Fluidity on Secretion and Receptor Stimulation

Fulton T. Crews, Ph.D.[1]

Introduction

The secretion of hormones and neurotransmitters as well as receptor mediated signal transduction are processes involving membranes. The initial secretory event involves a stimulus which causes a change in membrane permeability and/or other factors which lead to an increase in the intraneuronal calcium concentration. The increase in intraneuronal calcium concentration activates exocytosis, i.e., a mechanism where the membrane of the transmitter containing granule fuses with the neuronal plasma membrane releasing the granule contents extracellularly. This change in membrane permeability, which is necessary for secretion, is dependent on a change in membrane properties.

Once hormones or neurotransmitters are released, they carry out their specific functions by interacting with nerves or other target tissues. The initial event is the recognition of the hormone or transmitter by a receptor macromolecule on the outer surface of the cell membrane. The binding of the transmitter to its receptor then triggers a series of complex chemical and physical reactions in the membrane which permits the cell to carry out its specific function. Each of these reactions, i.e., receptor binding and coupling to ion channels and/or enzymes, is dependent on a suitable membrane environment. Thus, the metabolism of lipids as well as the lipid composition of the membrane plays an important role in the transduction of neurotransmitter, hormone, and other signals through the cell membrane.

Method

Membrane Fluidity

According to the now generally accepted fluid-mosaic model of membrane structure (Singer & Nicolson 1972), integral membrane proteins have hydrophobic ends embedded in the lipid matrix of the membrane which is at least in some parts fluid. The fluid properties of the lipid matrix have been suggested to play an important role in membrane transport (Coleman 1973), enzyme activity (Melchoir & Stein 1976), and other cell functions including receptor binding and stimulation (Rimon et al. 1978). Many membrane-bound enzymes and receptors have several subunits which interact within the membrane. Thus, the rate of subunit diffusion, rotation, and collision, as well as the maximal activity of enzymes, can be directly effected by the fluid properties of the lipid matrix in the membrane.

Phospholipid Methylation and Membrane Fluidity

Recent studies on enzymes altering membrane fluidity have centered on two methyltransferase enzymes that methylate phosphatidylethanolamine to form phosphatidylcholine. Although the methylation pathway is a minor pathway for the synthesis of phosphatidylcholine, evidence suggests that it is involved in both secretion and receptor-mediated membrane signal transduction. The two phospholipid methyltransferases have only recently been found to be present in rat brain and have their highest specific activity in the synaptosomal plasma membrane (Crews et al. 1980a; Mozzi & Porcellati 1979). The first enzyme, phospholipid methyltransferase I (PMT I), methylates phosphatidylethanolamine one time to form phosphatidyl-N-monomethyl-ethanolamine. PMT I has an optimum pH of 7.5 and a low apparent K_m for S-adenosyl-L-methionine (SAM), the methyl donor. The second enzyme, phospholipid methyltransferase II (PMT II), catalyzes two successive methylations of phosphatidyl-N-monomethyl-ethanolamine to form phosphatidylcholine. PMT II has an optimum pH of 10.5, a high apparent K_m for SAM, and can be differentially solubilized by sonication. These observations suggest that the synaptosomal fraction of rat brain contains at least two methyltransferases which catalyze the synthesis of phosphatidylcholine. Blusztajn et al. (1979) have demonstrated the formation of phosphatidylcholine by the methylation pathway in calf caudate nucleus. In addition, this group has demonstrated the *in vitro* formation of free choline from phosphatidylcholine synthesized through the methylation pathway (Blusztajn & Wurtman 1981). Since these enzymes have been shown to affect transmitter-receptor stimulation in erythrocytes (Hirata et al. 1979b), astrocytoma cells (Strittmatter et al. 1979), and many other cell types (Hirata & Axelrod 1980), it seems likely they are involved in synaptic transmission.

---

[1] Department of Pharmacology, University of Florida College of Medicine, Gainesville, FL 32610.

Evidence for the asymmetric localization of phospholipid methyltransferases in synaptosome membranes has been obtained by selective proteolytic digestion using trypsin in intact and lysed synaptosomes (Crews et al. 1980c). Trypsin treatment caused a small reduction, about 13 percent, in PMT I activity in intact synaptosomes, while in lysed synaptosomes it destroyed 83 percent of the activity. This suggests PMT I mainly faces the cytoplasmic side of the plasma membrane where trypsin cannot penetrate. Trypsin treatment reduced PMT II activity by 57 percent in intact synaptosomes, and by 95 percent in lysed synaptosomes (Figure 1). The loss of PMT II in intact synaptosomes after trypsin treatment represents the fraction of the enzyme localized on the exterior side of the plasma membrane and indicates that PMT II is mainly present on the outer surface of the membrane. The additional loss of PMT II activity in lysed preparations probably represents PMT II present on vesicles, mitochondria, and other intrasynaptosomal particles.

Similar experiments using phospholipase C suggested that in intact synaptosomes phosphatidyl-N-monomethylethanolamine is buried within the membrane or located on the cytoplasmic side, whereas phosphatidylcholine and phosphatidyl-N,N-dimethylethanolamine are exposed to the outer surface of the membrane (Crews et al. 1980c). The phospholipid methyltransferase enzymes have also been found to be asymmetrically distributed in liver microsomal membranes (Higgins 1981) and in rat erythrocyte ghosts (Hirata & Axelrod 1978a). These data suggest the stepwise methylation and translocation of a fraction of the methylated phospholipids from the cytoplasmic side to the outside of the membrane (Figure 2).

The methylation and rapid vectorial rearrangement of phospholipids has been shown to affect membrane fluidity. Using varying concentrations of SAM, it was observed in rat erythrocyte ghosts that the membrane viscosity, as measured by fluorescent polarization, using diphenylhexatriene (DPH), decreased in parallel with the synthesis of phosphatidyl-N-monomethylethanolamine (Hirata & Axelrod 1978b). Other studies on chicken erythrocytes have found that concanavalin A will increase phospholipid methylation and simultaneously decrease membrane viscosity (Nakajima et al. 1981). This study used the electron spin resonance spectra of a stearic acid spin label to estimate membrane viscosity and found that methylation inhibitors could block the concanavalin A-induced change in fluidity. These studies suggest that the methylation of phosphatidylethanolamine and the rapid translocation of the methylated phospholipid has an important influence on membrane fluidity.

Phospholipid Methylation, Ca^{2+} Flux and Exocytosis

Mast cells and basophils have been used to study the cellular mechanisms involved in secretion (Douglas 1978; Kazimiercyak & Diamant 1978). The normal stimulus for mast cell secretion is the reaction of a specific antigen with antibodies, i.e., immunoglobulin E (IgE), which are bound to the cell surface. Mast cells exposed to antigen accumulate $^{45}Ca^{2+}$. Furthermore, antigen-stimulated $^{45}Ca^{2+}$ accumulation occurs even when the secretory response is inhibited by the cell being deprived of energy (Foreman et al. 1977), thereby supporting the hypothesis that calcium influx is an early event in the secretory response

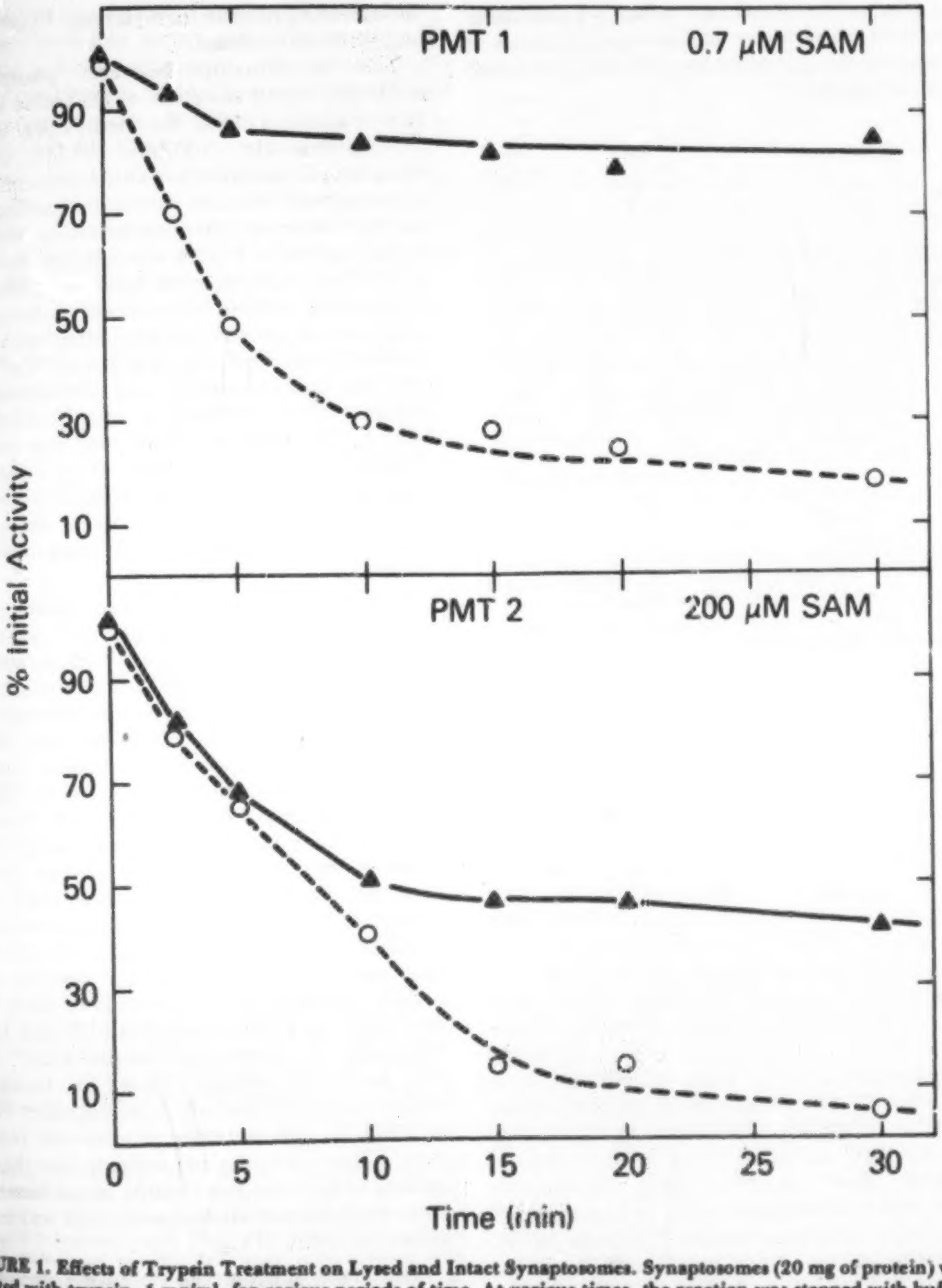


FIGURE 1. Effects of Trypsin Treatment on Lysed and Intact Synaptosomes. Synaptosomes (20 mg of protein) were incubated with trypsin, 1 mg/ml, for various periods of time. At various times, the reaction was stopped with buffer containing 5 mg/ml pancreatic trypsin inhibitor with 2 percent nonident and assayed for phospholipid methyltransferase I (PMT I) or phospholipid methyltransferase (PMT II) activity as described in Crews et al. (1980c). (▲ – ▲) Intact synaptosomes, (○ – ○) lysed synaptosomes.

The mechanism of calcium influx is particularly important, since many endogenous regulators of release are thought to act by inhibiting the initial influx of calcium.

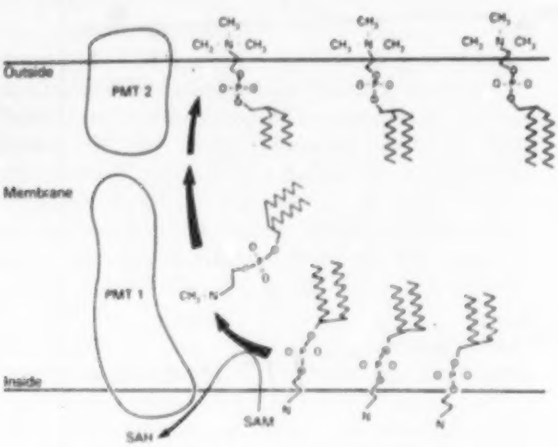


FIGURE 2. Schematic Diagram of Methylation and Translocation of Phospholipids in Synaptosomal Membranes. SAM is S-adenosyl-L-methionine, SAH is S-adenosyl-L-homocysteine.

The relationship between phospholipid methylation and histamine release was first studied using rat mast cells. Concanavalin A (Con A), a lectin which binds membrane glycoproteins (Siraganian 1976) was initially used to stimulate the secretion of histamine. Stimulating rat mast cells with Con A resulted in a rapid increase in methylated phospholipids which was followed by the release of histamine (Hirata et al. 1979a). After about 3 minutes, there was a fall in the methylated phospholipids suggesting further metabolism of these lipids. More recent studies on phospholipid methylation have used antibodies raised against IgE receptors on rat basophilic leukemia cells (anti-RBL). It is known that F(ab')$_2$ fragments of anti-RBL cause an influx of ^{45}Ca^{2+} and release histamine by bridging IgE receptors. F(ab')$_2$ fragments of anti-RBL also induce a rapid increase in phospholipid methylation which precedes ^{45}Ca^{2+} influx and histamine release (Ishizaka et al. 1980). Monovalent Fab' fragments failed to increase phospholipid methylation, induce ^{45}Ca^{2+} uptake, and release histamine. These findings suggest bridging of IgE receptors is necessary to initiate phospholipid methylation, ^{45}Ca^{2+} in
and histamine release.

The relationship between phosphol
methylation and secretion of histamine was
ther established using the methylation inhi
3-deazaadenosine (3-DZA). 3-DZA inhi
phospholipid methylation and histamine rel
in an almost identical concentration-depend
manner whereas other methylations were
slightly affected. 3-DZA also blocked the rel
of [^{14}C]-arachidonic acid from prelabeled c
(Crews et al. 1980b). More recent studies on R
cells have shown that antigen stimulation of
sensitized cells results in an influx of ^{45}Ca^{2+} w
precedes both histamine and arachidonic a
release. When methylation was inhibited w
3-DZA, the influx of ^{45}Ca^{2+} was also inhib
(Figure 3) (Crews et al. 1981). These findings a
consistent with the hypothesis that the initial i
crease in phospholipid methylation alters me
brane viscosity following the opening of the C
channel.

Additional evidence for the critical role
phospholipid methylation in Ca^{2+} influx a
histamine release was obtained with mutant R
cells (McGivney et al. 1981). Two variant clo
of RBL cells were found which in response to a
tigen did not release histamine and had
calcium influx. However, stimulation with
calcium ionophore did induce calcium flux a
histamine release. Both mutant cell lines we
found to have IgE receptors suggesting a def
between the receptor and the calcium chann
One cell line was found to have PMT I a
almost no PMT II activity. A second variant ha
PMT II activity and no PMT I activity. Fusion
each cell line at a ratio of 1:1 resulted in t
growth of independent hybrids. Hybrids had no
mal levels of PMT I and PMT II activity a
responded to antigen-IgE mediated Ca^{2+} infl
and histamine release. Thus, by fusing t
nonsecreting cell lines which lacked either PMT
or PMT II, the secretory process was recon
tuted. These observations indicate that the cr
linking of IgE receptors results in an increase
both phospholipid methytransferases which th
allows an influx of Ca^{2+}.

The data suggest the following hypoth
(Figure 4): Antigen stimulation of the cells cro
links and aggregates IgE receptors which incre
the methylation of phospholipids resulting in

decrease in membrane viscosity. This decrease in viscosity probably occurs primarily in a specific domain where receptors, the phospholipid methyltransferases, the calcium ion channel, and other enzymes are localized. The change in viscosity could allow the opening of the Ca^{2+} channel. Thus, rapid changes lipid metabolism may alter the membrane fluidity in a highly localized domain within the membrane and thereby cause changes in the activity and coupling of proteins within this domain.

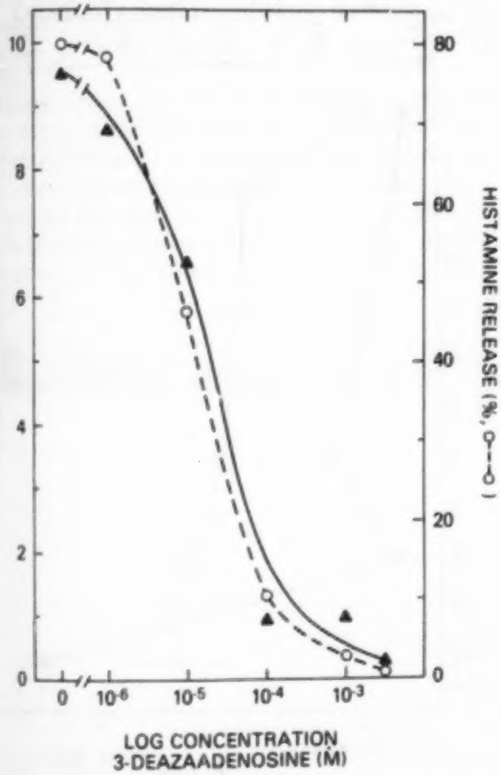


FIGURE 3. Effects of Various Concentrations of 3-Deazaadenosine (3-DZA) and Homocysteine Thiolactone on $^{45}Ca^{2+}$ Flux and Histamine Release. Rat basophilic leukemic cells (2 × 10^6 cells/well) sensitized with ovalbumin specific IgE were preincubated with various concentrations of 3-DZA and 2 × 10^{-4} M homocysteine thiolactone for 90 min. Cells were challenged with 10 µg/ml ovalbumin for 30 min. as described in Crews et al. (1981a).

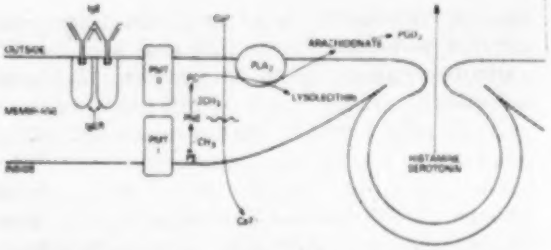


FIGURE 4. Schematic Diagram of Events During Antigen IgE Mediated Stimulation of Histamine and Arachidonic Acid Release. IgE is immunoglobin E and IgER is immunoglobin E Receptor. PE is phosphotidylethylnolamine which is methylated to PNE, i.e., phosphatidyl-N-monomethylmethanolamine, which would alter local membrane microviscosity allowing calcium influx. PC is phosphatidylcholine which can be hydrolyzed by PLA_2, i.e., phospholipase A_2 to lysolecithin, and arachidonate which is metabolized to PGD2, postaglandin D2.

Cholesterol/Phospholipid Molar Ratio and Membrane Fluidity

Although receptor stimulation may rapidly alter membrane fluid properties, the viscosity of the membrane is also affected by relatively low changes in composition. One change in composition that is known to alter membrane viscosity is the cholesterol to phospholipid molar ratio (C/P ratio). The interaction of the rigid backbone of cholesterol with phospholipid acyl chains increases the degree of order and restricts movement in the membrane interior (Cantor & Schimmel 1980). This increased order tends to increase viscosity (i.e., decrease fluidity), to abolish any phase transitions in membrane phospholipids and to alter the rotational freedom and position of proteins within the membrane lipid matrix (Shinitzky & Inbar 1976).

Studies of the synaptosomal plasma membrane (SPM) prepared from rats treated with ethanol have found changes in the C/P ratio. Ethanol and other anesthetics are thought to affect the nervous system by disrupting excitable membranes (Seeman 1972). This suggested that tolerance and physical dependence upon ethanol could be the result of an alteration in neuronal membranes during chronic exposure. The SPM from control rats, rats acutely treated with ethanol, rats dependent and intoxicated with ethanol, i.e., prodromal dependent rats, and rats undergoing ethanol withdrawal were prepared and the C/P ratio determined (Crews, Majchrowicz, & Meeks, submitted). There was a significant increase in the C/P ratio of SPM from rats dependent and intoxicated with ethanol as compared to the SPM of control and rats acutely treated with ethanol (Figure 5). Cholesterol incorporation into membranes has been shown to increase membrane organization (Shinitzky & Berenholz 1978). An increased C/P ratio has also been found in the membranes of ethanol tolerant mice (Chin et al. 1978). Synaptic membranes prepared from tolerant mice are resistant to ethanol-induced fluidization in vitro, i.e., they have become tolerant to the disruptive effects of ethanol (Chin & Goldstein 1977). The disruptive affects of ethanol on membranes are to some extent opposite to those of cholesterol. Cells may respond to the disruptive effects of ethanol by increasing the C/P ratio in their membranes. It is possible that under certain conditions cells can regulate their membrane fluidity by altering the C/P ratio. Certainly, the evidence suggests that tolerance and dependence to ethanol are related to alterations in nerve cell membrane organization and composition.

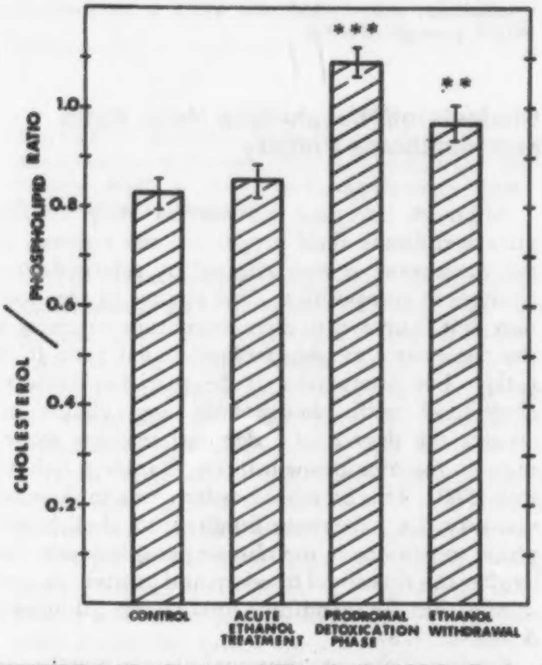


FIGURE 5. The Cholesterol/Phospholipid Molar Ratio of SPM Prepared from Rats after Various Alcohol Treatments. Controls were treated with water. Acute ethanol treatment involved a group of nonfasted animals given a single dose of ethanol (5 g/kg) 4 hrs prior to sacrifice. Prodromal detoxication phase group consisted of animals rendered physically dependent upon ethanol but were sacrificed while still intoxicated. The animals undergoing ethanol withdrawal syndrome were treated with ethanol as the prodromal group and were then decapitated at least 6 hrs after the onset of overt signs and symptoms of the ethanol withdrawal syndrome as described by Majchrowicz (1975).

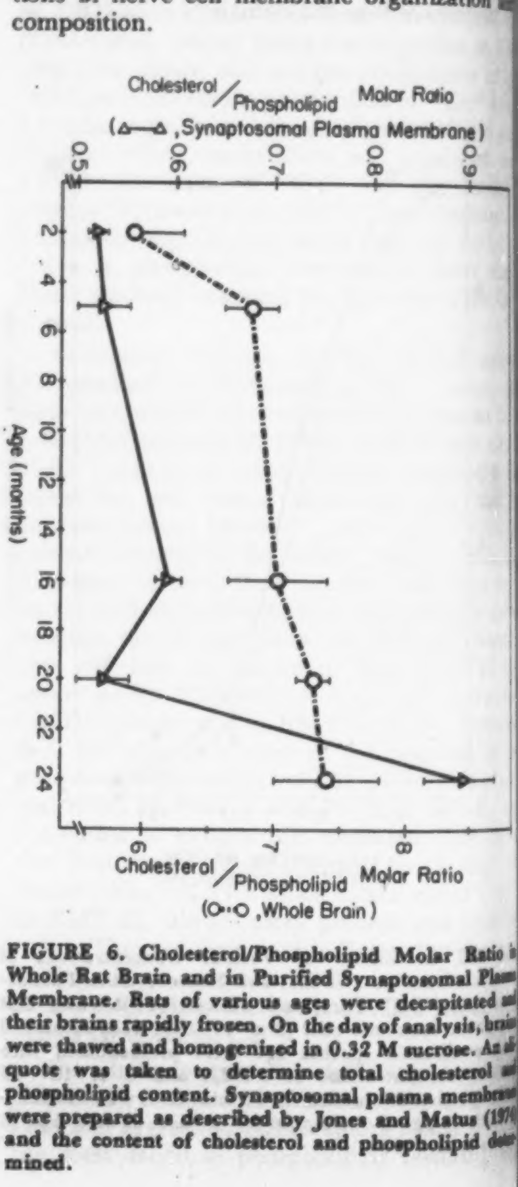


FIGURE 6. Cholesterol/Phospholipid Molar Ratio in Whole Rat Brain and in Purified Synaptosomal Plasma Membrane. Rats of various ages were decapitated and their brains rapidly frozen. On the day of analysis, brains were thawed and homogenized in 0.32 M sucrose. An aliquote was taken to determine total cholesterol and phospholipid content. Synaptosomal plasma membranes were prepared as described by Jones and Matus (1974) and the content of cholesterol and phospholipid determined.

In addition to the ethanol-induced changes in the C/P ratio of SPM, we have found that during aging there are changes in membrane C/P ratio. The SPM from rats of various ages was prepared and its lipid composition compared to that of whole brain. In whole brain the C/P ratio increased in young rats between 2 and 5 months of age and then remained relatively constant. In contrast, the C/P ratio of SPM changed very little in rats 2 to 20 months of age. However, the C/P ratio in SPM of rats 24 months of age was increased almost twofold over the C/P ratio of SPM in 20-month-old rats (Figure 6). This alteration in the SPM composition would be expected to alter synaptic transmission and may be related to changes in brain function which occur during aging.

To investigate the effects of changes in the C/P ratio on synaptic transmission, we studied carbachol stimulation of pyramidal neurons in the CA1 region of rat hippocampal brain slices. Since cholesterol transfer occurs between proteins rich in cholesterol to membranes containing smaller amounts, we incorporated cholesterol into hippocampal slices by perfusing them with buffered Yamamoto's solution containing 1 percent bovine serum albumin saturated with cholesterol (Figure 7). Recordings were made through a glass micropipette filled with 3 M NaCl saturated with fast green dye as described previously (Camacho & Phillips 1982). The cholineric agonist carbachol consistently excited cells in the hippocampus. Atropine blocked carbachol, suggesting muscarinic receptor mediated stimulation of firing. Incorporation of cholesterol markedly reduced carbachol induced firing of the hippocampal purkinje cells (Figure 7). When the response to carbachol was almost completely inhibited, perfusion buffers were changed and the cholesterol was washed out of the slice by perfusion with buffer containing albumin alone (Figure 8). Removal of cholesterol restored the carbachol response to near control levels. Characteristic action potentials were used to establish the identity of the cell, i.e., that the return of firing occurred in the same cell. It is possible that cholesterol incorporation disrupts the binding and/or stimulus transduction of acetylcholine like agents in neuronal membranes.

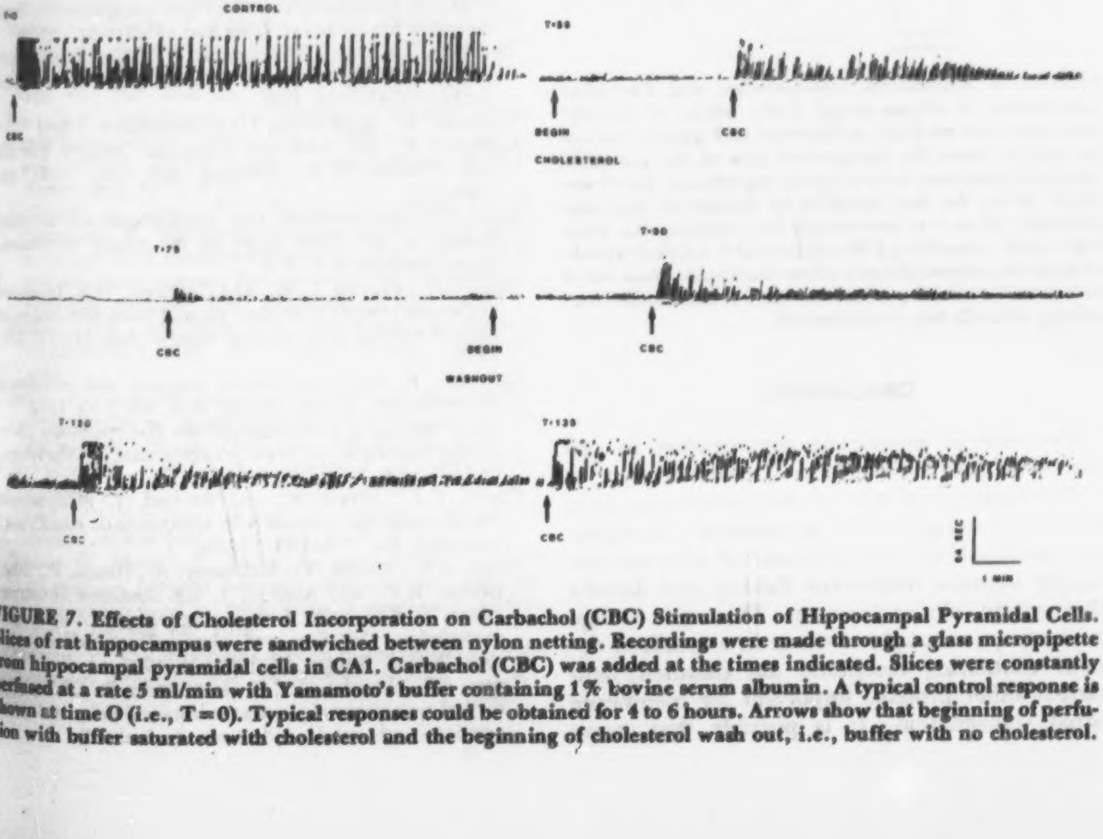


FIGURE 7. Effects of Cholesterol Incorporation on Carbachol (CBC) Stimulation of Hippocampal Pyramidal Cells. Slices of rat hippocampus were sandwiched between nylon netting. Recordings were made through a glass micropipette from hippocampal pyramidal cells in CA1. Carbachol (CBC) was added at the times indicated. Slices were constantly perfused at a rate 5 ml/min with Yamamoto's buffer containing 1% bovine serum albumin. A typical control response is shown at time O (i.e., T = 0). Typical responses could be obtained for 4 to 6 hours. Arrows show that beginning of perfusion with buffer saturated with cholesterol and the beginning of cholesterol wash out, i.e., buffer with no cholesterol.

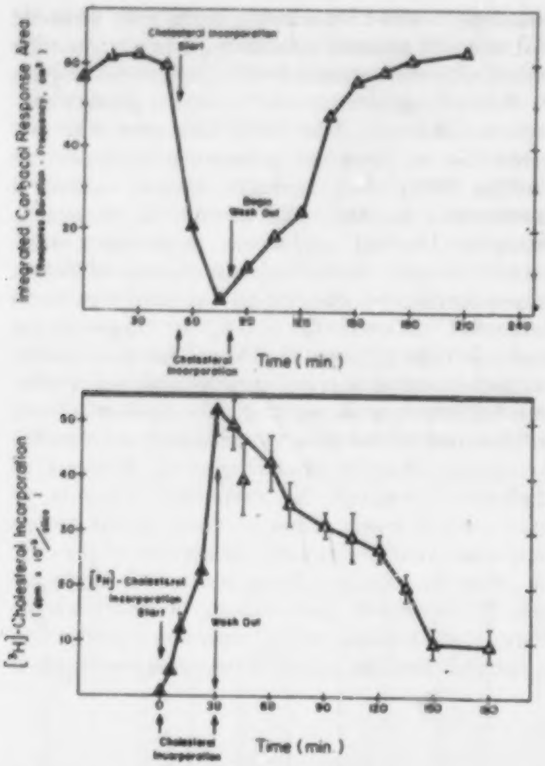


FIGURE 8. Cholesterol Incorporation and Carbachol Stimulation of Hippocampal Cells. Slices of rat hippocampus were perfused as described in Figure 8. The upper graph shows the intergraded area of the carbachol stimulated response from a typical experiment. The lower graph shows the incorporation of cholesterol into hippocampal slices was determined by perfusing the slices with media containing [³H]-cholesterol (1 uCi/ml) attached to bovine serum albumin where indicated. Wash out of cholesterol involved perfussion with the same buffer containing albumin but no cholesterol.

Conclusions

The role of membrane organization in cell function is just beginning to be understood.

The fluid properties of the membrane lipid matrix has a major effect on membrane function. The phospholipid methyltransferase enzymes can rapidly increase membrane fluidity and thereby alter certain cellular processes. This rapid change in viscosity is thought to occur in a localized domain containing receptors, ion channels, and various other proteins important for membrane signal transduction. It is possible that many transmitters and hormones transmit their sig by rapidly changing membrane fluidity.

The physiological and pharmacological facto that alter membrane fluidity by changing the C ratio are much slower than the rapid changes wi phospholipid methylation. In addition, it is n clear whether changes in bulk fluidity, the forma tion of distinct lipid domains, or some other effe of cholesterol on membrane structure, is responsi ble for the physiological changes that occur i cholesterol enriched membranes. However, it i clear that the regulation of cholesterol an phospholipid content provides the cell with ma potential ways to alter cell membrane functio Further studies on the regulation as well as th localization of the various membrane fluid do mains are likely to be exciting and physiologicall important studies on the functions of cell mem branes.

References

Blusztajn, J.K., Zeisel, S.H., and Wurtman, R.J. Synthe of lecithin (phosphatidylcholine) from phosphatidyletha lamine in bovine brain. *Brain Res.*, 179:319-327, 1979.

Blusztajn, J.K., and Wurtman, R.J. Choline biosynthe by a preparation enriched in synaptosomes from rat bra *Nature,* 290:417-418, 1981.

Camacho, A., and Phillips, I. (In preparation, 1981)

Cantor, C.R., and Schimmel. *Biophysical Chemistry, Part II,* San Francisco:W.H. Freeman and Co., 1980, p 1350-1351.

Chin, J.H., and Goldstein, D.B. Drug tolerance in biome branes: A spin label study of the effects of ethan *Science, changes34-685, 1977.*

Chin, J.H., Parsons, L.M., and Goldstein, D.B. Increas cholesterol content of erythrocyte and brain membranes i ethanol-tolerant mice. *Biochim. Biophys. Acta,* 513:358-36 1978.

Coleman, R. Membrane-bound enzymes and membra ultrastructure. *Biochim. Biophys. Acta,* 300:1-30, 1973.
and properties of methyltransferases that synthesize pho phatidylcholine in rat brain synaptosomes. *J. Neuroche* 34:1491-1498, 1980a.

Crews, F.T., Hirata, F., and Axelrod, J. Phospholip methyltransferase assymetry in synaptosomal membra *Neurochem. Res.*, 5:983-991, 1980c.

Crews, F.T., Morita, Y., McGivney, A., Hirata, F., Si ganian, R.P., and Axelrod, J. IgE mediated histami release in RBL cells: Receptor activation, phospholip methylation, Ca²⁺ flux, and release of arachidonic aci *Arch. Biochem. Biophys.*, 212:561-571, 1981.

Crews, F.T., Majchrowicz, E., and Meeks, R. Changes i cortical synaptosomal plasma membrane fluidity and co position in ethanol dependent rats. (submitted)

DeRobertis, E., and Vaz Ferreira, A. Electron microscope study of the secretion of catechol-containing droplets in the adrenal medulla. *Exp. Cell Res.*, 12:568-574, 1957.

Douglas, W.W. Stimulus-secretion coupling: Variations on the theme of calcum-activated exocytosis involving cellular and extracellular sources of calcium. *Ciba Found. Symp.*, 54:61-87, 1978.

Foreman, J.C., Hallett, M.B., and Mongar, J.L. The relationship between histamine secretion and ^{45}calcium uptake by mast cells. *J. Physiol.*, 271:193-205, 1977.

Higgins, J.A. Translocation of intermediates across the membrane bilayer during methylation of phosphatidylethanolamine. *Biochim. Biophys. Acta*, 640:1-5, 1981.

Hirata, F., and Axelrod, J. Enzymatic synthesis and rapid translocation of phosphatidylcholine by two methyltransferases in erythrocyte membranes. *Proc. Natl. Acad. Sci. USA*, 75:2348-2352, 1978a.

Hirata, F., and Axelrod, J. Enzymatic methylation of phosphatidylethanolamine increases erythrocyte membrane fluidity. *Nature*, 275:219-220, 1978b.

Hirata, F., Axelrod, J., and Crews, F.T. Concanavalin A stimulates phospholipid methylation and phosphatidylserine decarboxylation in rat mast cells. *Proc. Natl. Acad. Sci. USA*, 76:4813-4816, 1979a.

Hirata, F., Strittmatter, W.J., and Axelrod, J. β-Adrenergic receptor agonists increase phospholipid methylation, membrane fluidity, and β-adrenergic receptors-adenylate cyclase coupling. *Proc. Natl. Acad. Sci., USA*, 76:386-390, 1979b.

Hirata, F., and Axelrod, J. Phospholipid methylation and biological signal tranmission. *Science*, 209:1082-1090, 1980.

Ishizaka, T., Hirata, F., Ishizaka, K., and Axelrod, J. Stimulation of phospholipid methylation, calcium influx, and histamine release by bridging of IgE receptors on rat mast cells. *Proc. Natl. Acad. Sci., USA*, 77:862-865, 1980.

Jones, D.H., and Matus, A.I. Isolation of synaptic plasma membrane from brain by combined flotation-sedimentation density gradient centrifugation. *Biochim. Biophys. Acta*, 356:276-287, 1974.

McGivney, A., Crews, F.T., Hirata, F., Axelrod, J., and Siraganian, R., Rat basophilic leukemia cell lines defective in phospholipid methyltransferase enzymes, Ca^{2+} influx, and histamine release: Reconstitution by hybridization. *Proc. Natl. Acad. Sci. USA*, 78:6176-6180, 1981.

Melchoir, D.L., and Steim, J.M. Thermotropic transitions in biomembranes. *Ann. Rev. Biophys. Bioeng.*, 5:205-238, 1976.

Mozzi, R., and Porcellati, G. Conversion of phosphatidylethanolamine to phosphatidylcholine in rat brain by the methylation pathway. *FEBS Lett.*, 100:363-366, 1979.

Nakajima, M., Tamura, E., Irimura, T., Tovoskima, S., Hirano, H., and Osawa, T. Mechanisms of the concanavalin A-induced change of membrane fluidity of chicken erythrocytes. *J. Biochem.*, 89:665-675, 1981.

Rimon, G., Hanski, E., Brown, S., and Levitzki, A. Mode of coupling between hormone receptors and adenylate cyclase elucidated by modulation of membrane fluidity. *Nature*, 276:394-396, 1978.

Seeman, P. The membrane actions of anesthetics of tranquilizers. *Pharmacol. Rev.*, 24:583-655, 1972.

Shinitzky, M., and Inbar, M. Microviscosity parameters and protein mobility in biological membranes. *Biochim. Biophys. Acta*, 433:133-149, 1976.

Singer, S.J., and Nicolson, G.L. The fluid mosaic model of the structure of cell membranes. *Science*, 175:720-731, 1972.

Siraganian, R.P. Basophil Activation by concanavalin A. In: Oppenheim, J.J. and Rosenstreich, D.L. (eds.), *Mitogens in Immunology*, New York:Academic Press, 1976, pp. 69-84.

Strittmatter, W.J., Hirata, F., Axelrod, J., Mallorga, P., Tallman, F., and Hennenberry, R.C. Benzodiazepine and β-adrenergic receptor ligands independently stimulate phospholipid methylation. *Nature*, 282:857-859, 1979.

A Study of the Metabolism of Des-Tyrosine-γ-Endorphin Using an Improved HPLC System[1]

Hans Schoemaker, Ph.D.,[2] Andrew Chen, B.S.,[2] Thomas P. Davis, Ph.D.,[2] and Henry I. Yamamura, Ph.D.[2]

Introduction

In vitro proteolytic processing of β-endorphin (βE) by rat brain enzymes results in the formation of α-endorphin (αE, βE 1-16), γ-endorphin (γE, βE 1-17), and their non-opiate analogs des-tyrosine^1-α-endorphin (DTαE, βE 2-16) and des-tyrosine^1-γ-endorphin (DTγE, βE 2-17) (Austen et al. 1977; Burbach et al. 1980a). These peptide fragments, the presence of which has recently been confirmed in the rat (Verhoef et al. 1982) and human brain (Van Ree & De Wied 1981), differentially affect central mechanisms of adaptive behavior (Bohus 1981; De Wied et al. 1978). Consequently, βE homeostasis has been implicated in various aspects of behavioral adaptation (De Wied et al. 1978; Van Ree & De Wied 1981). Furthermore, it has been proposed that disturbances in βE homeostasis could be of etiological significance in psychopathological disorders (Berger & Barchas 1981; Bloom et al. 1976; De Wied 1979).

Several γE related peptides, and most notably DTγE, have shown neuroleptic-like activity in a variety of behavioral paradigms (Davis et al. 1981; De Wied et al. 1978; Dorsa et al. 1979). Clinical studies also indicate that DTγE may be of therapeutic value in the treatment of schizophrenia (Verhoeven et al. 1978, 1981). Like classical neuroleptics, DTγE decreases in ^{3}H-spiperone binding in the rat striatum nucleus accumbens (Pedigo et al. 1979b), which indicative of an inhibitory effect on the postsynaptic dopamine receptor. Since DTγE fails to af the *in vitro* binding of radiolabeled agonists an antagonists to the dopamine receptor (Pedigo e al. 1979a; Van Ree et al. 1978), it was suggeste that DTγE may exert its selective neuroleptic-li effect *in vivo* through an active metabolite (D Wied et al. 1980; Pedigo et al. 1979b). In the present study, the *in vitro* metabolism of DTγE wa examined with the use of a sensitive and selectiv high performance liquid chromatograph (HPLC) system that allows for a rapid and efficient separation of βE peptide fragments (Davis e al. 1982).

Method

The *in vitro* metabolism of DTγE was studie by incubating DTγE in a final concentration o 1-2 mg/ml with whole rat brain homogenates (5 mg tissue/ml), rat striatal slices (0.5 × 0.5 × 0. mm, approximately 25 mg tissue/ml), an homogenates of the human caudate nucle Postmortem human brain samples were obtaine at autopsy from subjects with no know neurological or mental disease. Autopsy too place within 3.5-16 hours after death, and tissue were stored at -80°C for 4-6 months before use After incubation at 37°C in 50 mM sodium potassium phosphate buffer (81 mM Na$^+$, 9 m K$^+$), pH 7.4, samples were boiled for 10 minute at 100°C and centrifuged at 15,000 × g for 15 minutes. The clear supernatant was stored a -20°C until HPLC analysis (Davis et al. 198 Schoemaker et al. 1982).

The HPLC analysis was performed using tw Model 6000A pumps and a Model 600 Solve Programmer (Waters Associates, Milford Mass.). Eluting peptides were detected using a Perkin-Elmer LC-65T variable wavelength UV detector (Perkin-Elmer, Norwalk, Conn.) set a 210 nm. Baseline drift due to mobile phase refractive index changes was corrected for using an Axxiom Model 301-99 Data Saver (Cole Scientific, Calabasas, Cal.). Recording and peak quantification was accomplished using a Hewlett-Packard 3390A integrator and strip chart recorder. Peptides were separated using a Beckman Ultraspher

---

[1] This study was supported in part by USPHS Grants MH-27257 and MH-30626 to H.I.Y., a BRSG College of Medicine grant, a Pharmaceutical Manufacturers Association Program Starter grant to T.P.D., and a USPHS Research Scientist Development Award (MH-00095) from the NIMH to H.I.Y.,

[2] Departments of Pharmacology, Biochemistry, and Psychiatry and the Arizona Research Laboratories, University of Arizona Health Sciences Center, Tucson AZ 85724.

Correspondence may be addressed to: Dr. Henry I. Yamamura, Department of Pharmacology, University of Arizona Health Sciences Center, Tucson, AZ 85724.

ODS 5μ column maintained at 40°C, and a curve-linear gradient of acetonitrile against 0.1 M NaH_2PO_4 (pH 2.1) from 18 to 30 percent over 40 minutes at a flow rate of 2.0 ml/minute. Peptide quantification was based on the external standard method of analysis using reference peptides which had previously been tested for purity by chromatographic methods.

Endorphin fragments were generously donated by Drs. N.C. Ling (The Salk Institute), and H.M. Greven and J.W. van Nispen (Organon Int.).

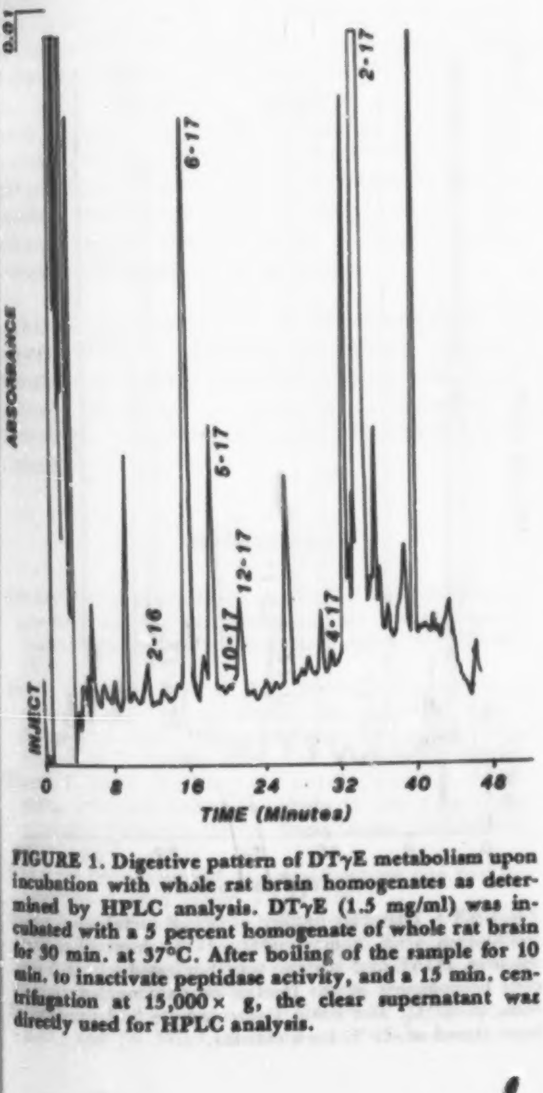


FIGURE 1. Digestive pattern of DTγE metabolism upon incubation with whole rat brain homogenates as determined by HPLC analysis. DTγE (1.5 mg/ml) was incubated with a 5 percent homogenate of whole rat brain for 30 min. at 37°C. After boiling of the sample for 10 min. to inactivate peptidase activity, and a 15 min. centrifugation at 15,000 × g, the clear supernatant was directly used for HPLC analysis.

Results

The HPLC method employed in the present experiments results in a rapid and efficient separation of βE related peptide fragments. The detection limit under these conditions is 10 ng for each peptide (Davis et al. 1982).

A representative fragmentation pattern of the metabolism of DTγE upon incubation with rat brain homogenates for 30 minutes is shown in Figure 1. The major metabolite was identified as βE 6-17, whereas minor metabolites could be identified as βE 4-17, βE 5-17, βE 10-17, βE 12-17, and βE 2-16 (DTαE). After a 30-minute incubation, approximately 33 percent of the parent DTγE could be recovered. After incubation of DTγE with boiled homogenates for 30 minutes DTγE was recovered unchanged, indicating that breakdown is indeed enzymatic. Conversely, no peptide peaks could be detected in extracts of tissue incubated in the absence of exogenously added DTγE. Time-course experiments (Schoemaker et al. 1982) indicated that the decline in residual DTγE levels was monoexponential with a half life of 14-15 minutes. The major metabolite, βE 6-17, reaches a maximal level of about 30 percent of that of the parent peptide, DTγE, after 30 minutes of incubation. Maximal levels of βE 5-17 were observed after 15 minutes of incubation, and represented about 5 percent of the residual amount of DTγE at this time.

A qualitatively similar pattern of metabolism was found upon incubation of DTγE with rat striatal slices. Prior to incubation, the slices were thoroughly rinsed with 2 × 10 ml buffer in order to remove intracellular enzymes from those cells damaged during the preparation of the tissue. Figure 2 illustrates the metabolic pattern observed after incubation at 37°C for 120 minutes. Major metabolites were identified as βE 5-17 and βE 6-17, whereas minor amounts of βE 2-16, βE 4-17, βE 10-17, and βE 12-17 were also present.

In addition, *in vitro* DTγE metabolism was studied using homogenates of the human caudate nucleus. Metabolism was qualitatively similar to that observed in whole rat brain homogenates and rat striatal slices (Figure 3). Also in this case βE 6-17 emerged as the major metabolite. Moreover, the fragmentation pattern was virtually identical between the different subjects studied.

Discussion

The metabolism of DTγE upon incubation with whole rat brain homogenates, rat striatal slices, and homogenates of the human caudate nucleus was examined using a newly developed, sensitive and selective HPLC chromatographic system for βE fragments. In each tissue preparation studied, the enzymatic breakdown of DTγE proceeded in a qualitatively similar manner, and βE 6-17 constantly emerged as the major metabolite. The βE sequences 2-16, 4-17, 5-17, 10-17, and 12-17 were also present but in minor amounts. βE 6-17 was previously reported to be among the major metabolites associated with DTγE digestion by peptidase activity in synaptosomal plasma membranes (Burbach et al. 1980b). Interestingly, the major DTγE metabolite identified in this study, βE 6-17, is the shortest γE related peptide to retain the full spectrum of behavioral effects of DTγE (De Wied et al. 1980), including its putative antipsychotic activity (Verhoeven et al. 1981). Like DTγE, βE 6-17 fails to affect the ^{3}H-spiperone labeled dopamine receptor *in vitro* (Pedigo et al. 19 Schoemaker et al. 1982). Similarly, no inhibition of ^{3}H-spiperone binding to rat striatal membranes could be demonstrated for C-terminal fragments of DTγE up to βE 14-17 in concentrations of 1 μM (unpublished observations). It therefore seems unlikely that the inhibitory effect of DTγE on *in vivo* ^{3}H-spiperone binding in the rat striatum and nucleus accumbens (Pedigo et al. 1979b) arises from a direct interaction of the γ-type endorphins with the postsynaptic dopamine recep

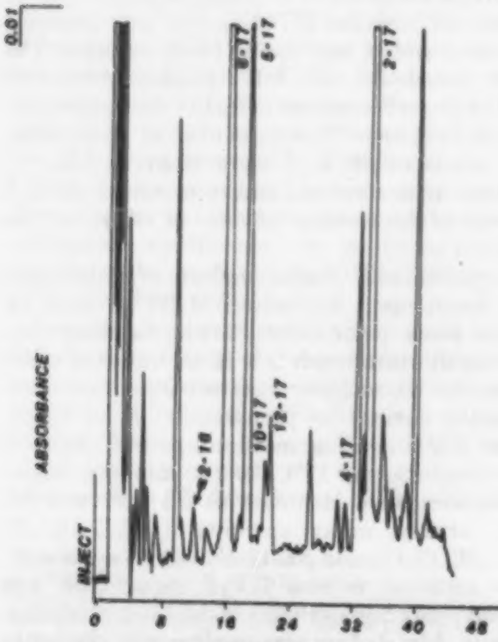


FIGURE 2. Digestive pattern of DTγE metabolism upon incubation with rat striatal slices. DTγE (1.5 mg/ml) was incubated with rat striatal slices (0.5 × 0.5 × 0.5 mm) for 120 min. at 37°C. Samples were prepared for HPLC analysis as described in Figure 1.

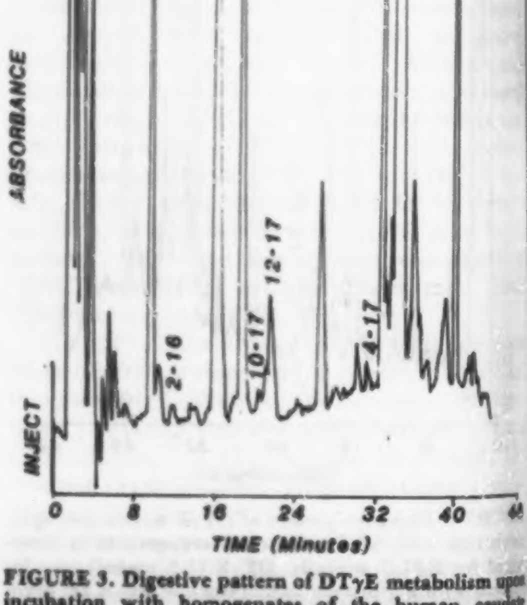


FIGURE 3. Digestive pattern of DTγE metabolism upon incubation with homogenates of the human caudate nucleus. DTγE (1.5 mg/ml) was incubated with a 5 percent homogenate of the human caudate nucleus for 30 min. at 37°C. The brain tissue sample had previously been stored at -80°C for 6 months.

tor. The possibility remains that DTγE alters dopaminergic activity in the mesolimbic and triatal pathways by an indirect effect on the postsynaptic dopamine receptor or through a presynaptic mechanism, as suggested by *in vitro* (Schoemaker & Nickolson 1980) and *in vivo* experiments (Davis et al. 1981; Nickolson 1981; Nickolson & Berendsen 1980; Van Ree & De Wied 1981).

Derangements in the balance of α-, β-, and γ-type endorphins in the human brain have been suggested to underly the etiology of schizophrenia (De Wied 1979). Thus, a relative excess of βE was hypothesized to result in the catatonic aspects of this disease, whereas an imbalance towards the α-type endorphins that show amphetamine-like behavioral activity (De Wied et al. 1978; Dorsa et al. 1979), would be prevalent in paranoid schizophrenia. The present findings that DTγE metabolism upon incubation with homogenates of the previously frozen human caudate nucleus proceeds similarly to that found using fresh rat brain tissues, suggest the feasibility of future studies directly addressing this hypothesis.

Acknowledgment. The authors acknowledge the expert technical assistance of Alison Culling. Postmortem human tissue samples were obtained through Dr. Peter C. Johnson (Department of Pathology, University of Arizona Health Sciences Center).

References

Austen, B.M., Smyth, D.G., and Snell, C.R. γ-Endorphin, α-endorphin, and met-enkephalin are formed extracellularly from lipotropin C fragment. *Nature*, 269:619-621, 1977.

Berger, P.A., and Barchas, J.D. Studies of β-endorphin in patients with mental illness. In: Li, C.H. (ed.), *β-Endorphin (Series: Hormonal Proteins and Peptides.)* New York, N.Y.: Academic Press, Vol. X, 1981, pp. 293-310.

Bloom, F, Segal, D., Ling, N., and Guillemin, R. Endorphins: Profound behavioral effects in rats suggest new etiological factors in mental illness. *Science*, 194:630-632, 1976.

Bohus, B. Neuropeptides in brain functions and dysfunctions. *Int. J. Ment. Health*, 9:6-44, 1981.

Burbach, J.P.H., Loeber, J.G., Verhoef, J., Wiegant, V.M., De Kloet, E.D., and De Wied, D. Selective conversion of β-endorphin into peptides related to γ- and α-endorphin. *Nature*, 283: 96-97, 1980a.

Burbach, J.P.H., Schotman, P., Verhoef, J., De Kloet, E.D., and De Wied, D. Conversion of des-tyrosine-γ-endorphin by brain synaptic membrane associated peptidases: Identification of generated peptide fragments. *Biochem. Biophys. Res. Comm.*, 97:995-1007, 1980b.

Davis, K.L., Samuel, A., Mathe, A.A., and Mohs, R.C. Intracerebral des-tyrosine-γ-endorphin inhibits methylphenidate induced locomotor activity. *Life Sci.*, 28:2421-2424, 1981.

Davis, T.P., Schoemaker, H., Chen, A., and Yamamura, H.I. High performance liquid chromatography of pharmacologically active amines and peptides in biological materials. *Life Sci.*, 30:971-987, 1982.

De Wied, D. Schizophrenia as an inborn error in the degradation of β-endorphin—A hypothesis. *Trends Neurosci.*, 2:79-82, 1979.

De Wied, D., Kovacs, G.L., Bohus, B., Van Ree, J.M., and Greven, H.M. Neuroleptic activity of the neuropeptide β-LPH 62-77 ((des-tyr¹)-γ-endorphin: DTγE). *Eur. J. Pharmacol.*, 49:427-436, 1978.

De Wied, D., Van Ree, J.M., and Greven, H.M. Neuroleptic-like activity of peptides related to des-tyr¹-γ-endorphin: Structure activity studies. *Life Sci.*, 26:1575-1579, 1980.

Dorsa, D.M. Van Ree, J.M., and De Wied, D. Effects of (des-tyr¹)-γ-endorphin and α-endorphin on substantia nigra self-stimulation. *Pharmacol. Biochem. Behav.*, 10:899-905, 1979.

Nickolson, V.J., and Berendsen, H.H.G. Effects of the potential neuroleptic peptide des-tyrosine¹-γ-endorphin and haloperidol on apomorphine-induced behavioral syndromes in rats and mice. *Life Sci.*, 27:1377-1385, 1980.

Nickolson, V.J. Potentiation by des-tyr-γ-endorphin of apomorphine-induced changes in rat open field behavior. *Eur. J. Pharmacol.*, 72:77-81, 1981.

Pedigo, N.W., Ling, N.C., Reisine, T.D., and Yamamura, H.I. Examination of des-tyrosine¹-γ-endorphin activity on ³H-spiroperidol binding sites in rat brain. *Life Sci.*, 24:1645-1650, 1979a.

Pedigo, N.W., Schallert, T., Overstreet, D.H., Ling, N.C., Ragan, P., Reisine, T.D., and Yamamura, H.I. Inhibition of *in vivo* ³H-spiperone binding by the proposed antipsychotic des-tyr¹-γ-endorphin. *Eur. J. Pharmacol.*, 60:359-364, 1979b.

Pedigo, N.W., Schoemaker, H., Ragan, P., Berens, E.S., Ling, N.C., and Yamamura, H.I. Neuroleptic-like activity of des-tyrosine-γ-endorphin (β-LPH 62-77): Possible mediation by an active metabolite, β-LPH 66-77. *Psychopharmacol. Bull.*, 17:147-151, 1981.

Schoemaker, H., Davis, T.P., Pedigo, N.W., Chen, A., Berens, E.S., Ragan, P., Ling, N.C., and Yamamura, H.I., Identification of β-endorphin 6-17 as the principal metabolite of des-tyrosine-γ-endorphine (DTγE) *in vitro* and assessment of its activity in neurotransmitter receptor binding assays. *Eur. J. Pharmacol.*, 81:459-468, 1982.

Schoemaker, H., and Nickolson, V.J. Effects of des-tyr¹-γ-endorphin on dopamine release from various rat brain region *in vitro*. *Life Sci.*, 27:1371-1376, 1980.

Van Ree, J.M., and De Wied, D. Endorphins in schizophrenia. *Neuropharmacology*, 20:1271-1277, 1981.

Van Ree, J.M., Witter, A., and Leysen, J.E. Interaction of des-tyrosine-γ-endorphin (DTγE, β-LPH 62-77) with neuroleptic binding sites in various areas of rat brain. *Eur. J. Pharmacol.*, 52:411-413, 1978.

Verhoef, J., Wiegant, V.M., and De Wied, D. Regional distribution of α- and γ-type endorphins in rat brain. *Brain Res.*, 231:454-460, 1982.
Verhoeven, W.M.A., Van Praag, H.M., Botter, P.A., Sunier, A., Van Ree, J.M., and De Wied, D. (Des-tyr¹)-γ-endorphin in schizophrenia. *Lancet*, I:1046-1047, 1978.
Verhoeven, W.M.A., Van Ree, J.M., De Wied, D., and Van Praag, H.M. γ-Type endorphins and schizophrenia. *Arch. Gen. Psychiatry*, 38:1182, 1981.

The Central Nervous System Control of the Immune System—Enkephalins: Antitumor Activities

Nicholas P. Plotnikoff, Ph.D.[1]

In 1979, Wybran, et al. reported that human blood T lymphocytes bear surface receptor-like structures for methionine-enkephalin. The present study explores the relationships between the central nervous system and the immune system.

The effects of leucine-enkephalin as well as the effects of methionine-enkephalin were studied in BDF mice inoculated with 1 × 10^4, 1 × 10^3, and 1 × 10^2, L1210 leukemia cells. An increase in survival time of the leucine-enkephalin treated mice was seen in mice inoculated with 1 × 10^2 L 1210 cells. Furthermore, the survivors managed to rechallenge to 1 × 10^4 cells. Higher doses of the enkephalins (30 mg/kg) were found to prolong survival of mice inoculated with 1 × 10^4 cells.

In addition, methionine enkephalin, in the presence of PHA, was found to stimulate lymphocyte blastogenesis at high molarities while diminishing (slightly) at low concentrations. The reverse appeared to be the case with leucine enkephalin; that is, high concentrations diminished blastogenesis and low conentrations stimulated blastogenesis.

It is proposed that the enkephalins play neuroendocrine role between the central nervous system and the pituitary-adrenal axis. In addition, it is proposed that the enkephalins released from the adrenals, in time of stress, stimulate the immune system.

Reference

Wybran, J., Appelboom, T., Famaly, J.P., and Govaer A. Suggestive evidence for receptors for morphine methionine-enkaphlin on normal human blood T lymphocytes. *J. Immunology*, 123(3):1068-1070, 1979.

---

[1] Department of Pharmacology, Oral Roberts University School of Medicine, Tulsa, OK 74171.

A Behavioral Study of the Changes in the CNS of Mice After Subchronic Treatment With the Dopamine Autoreceptor Agonist 3-PPP

Stephan Hjorth, B.Sc.[1], David Jackson, Ph.D.,[2] Arvid Carlsson, M.D.,[1] and Per Lindberg, Ph.D.[3]

Introduction

It is becoming increasingly evident that changes in receptor sensitivity contribute to the long-term homeostasis of synaptic function in the dopamine (DA) systems of the central nervous system. This property of receptors to change their sensitivity may be of key importance in the clinical efficacy of a number of drugs and in the development of side effects.

We have recently described the properties of a new DA receptor agonist, 3-(3-hydroxyphenyl)-N-n-propylpiperidine (3-PPP) (Hjorth et al. 1981). This compound exhibits a considerable selectivity for DA autoreceptors and, except in very high doses, is essentially devoid of other psychopharmacological properties. This unique profile makes 3-PPP of considerable theoretical interest, both in its own right and as a tool for use in psychopharmacological research. Some preliminary behavioral studies of the effects of 3-PPP administered subchronically to mice are reported here.

Method

Animals and Equipment

Male mice (18-24 g at the beginning of experimentation) of the N.M.R.I. strain (Anticimex, Stockholm) were kept at 25 ± 1° on a 12-hour light-dark cycle, with food and water *ad libitum*. The locomotor activity of groups of three mice was assessed in four "M/P" 40 Fc electronic motility meters (Motron Products, Stockholm). In all activity studies, except where otherwise stated, recordings were commenced 5 minutes after drug challenge.

Chronic Pretreatment

Each mouse was injected twice daily, between 7:45 and 9:30 a.m., and between 4:00 and 5:45, with 23.5 mg/kg of 3-PPP expressed as the base, but given as the hydrochloride salt. The pretreatment dose was chosen with reference to the depressant potency of 3-PPP, and after several preliminary experiments. The subchronic pretreatment schedule lasted for 5 days (10 injections) and behavioral assessments were made 15 to 25 hours after the last subchronic dose. Control animals received an injection of saline (0.2 ml) at the appropriate times each day. All injections were intraperitoneal (i.p.), with an injection volume of 10 ml/kg. In the text, the doses of drugs are expressed in terms of the salt forms, except 3-PPP which is expressed in terms of the base.

Statistical Methods

Statistical comparisons were made with a two-tailed Student's *t*-test, in some cases preceded by an analysis of variance.

Results

Acute Experiments

In naive mice, the selective dopamine (DA) autoreceptor agonist 3-PPP (3-(3-hydroxyphenyl)-N-n-propylpiperidine) produced a dose-dependent depression of locomotor activity (Figure 1).

The duration of action of the depression was short, with no significant depression being noted 1 or more hours after a dose of 23.5 mg/kg i.p. (Table 1).

---

[1] Department of Pharmacology, University of Göteborg, Sweden.
[2] Department of Pharmacology, University of Sydney, Australia.
[3] Org. Chem. Unit, Department of Pharmacology, University of Göteborg, Sweden.

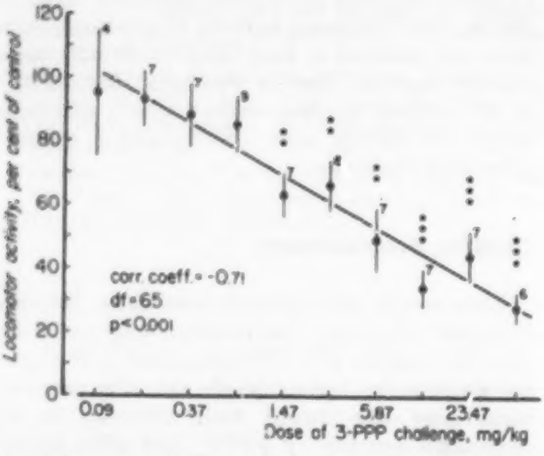


FIGURE 1. The effect of various doses of 3-PPP on the locomotor activity of groups of three mice. The data represent the means and standard errors of the activity in the 30 minutes beginning 5 minutes after injection, and each mean consists of 4 to 8 replicates. The line of best fit was calculated by regression analysis. $^{**}p<0.01$, $^{***}p<0.001$.

Subchronic Experiments

Mice, administered the drug twice daily (23.5 mg/kg i.p., in the morning and in the evening) for 5 days, were 15 to 25 hours after the last dose subsensitive to the locomotor depressant effects of a challenge with the same drug (Figure 2).

Table 1

The Effect of Different Treatment Times on the Locomotor Response of Mice to 23.5 mg/kg of 3-PPP

Treatment Time (h)	Treatment	Locomotor Activity	(*N*)
0	Saline	248 ± 8	(6)
	3-PPP	58 ± 14	(8)[a]
1	Saline	221 ± 21	(8)
	3-PPP	174 ± 10	(8)[b]
2	Saline	229 ± 13	(8)
	3-PPP	196 ± 12	(8)

[a] $p < 0.001$.
[b] $p = 0.056$ from the corresponding saline control.

Note: Locomotor activity was measured for 15 minutes either 0, 1, or 2 hours after injection of saline or 3-PPP. The locomotor activity is expressed as the counts per 15 minutes with standard error of the mean.

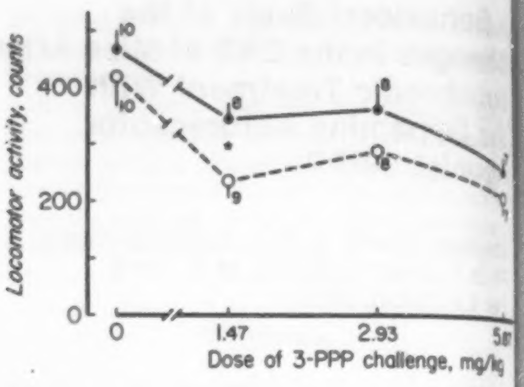


FIGURE 2. The effect of pretreatment of mice wi 3-PPP (•—•) or vehicle (○—○) on the response t challenge dose of 3-PPP. The data represent the mea and standard errors of the activity from 5 to 50 minu after beginning of the measurements. $^{*}p<0.05$ (for detai see the text).

Table 2

The Effect of Challenge with Apomorphine (0.5 or 1.0 mg/k on the Locomotor Response of 3-PPP or Vehicle-Pretreat Mice Treated with Reserpine (10 mg/kg) and α-M (250 mg/kg)

Dose of Apomorphine (mg/kg)	Locomotor Activity ± S.E.M. (*N*) 3-PPP-Pretreated	Vehicle-Pretreated
0	2 ± 1 (3)	3 ± 1 (3)
0.5	273 ± 38 (9)	262 ± 25 (9)
1.0	542 ± 34 (9)	563 ± 34 (9)

Note: The data represent the mean activities in the hour beginning 5 minu after challenge together with the standard errors of the means.

There was no change in the sensitivity of postsynaptic DA- and α-adrenergic receptors, as assessed by the locomotor stimulant effects of apomorphine and apomorphine plus clonidine, respectively, in reserpine- and α-methyltyrosine-treated animals (Table 2 and Figure 3).

However, 3-PPP-pretreated mice were supersensitive to the activating effects of *d*-amphetamine, and this supersensitivity was blocked by reserpine pretreatment (Figure 4 and Table 3).

In naive mice, a low, DA-autoreceptor selective dose of haloperidol (25 μg/kg) potentiated the locomotor stimulant effects of *d*-amphetamine (Figure 5).

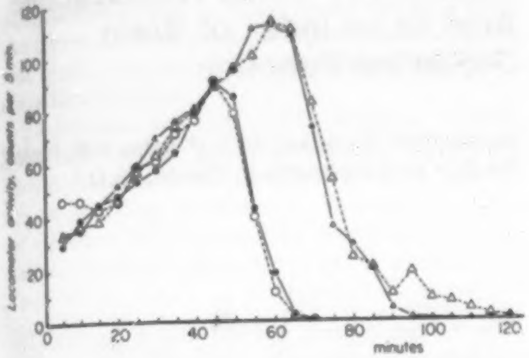


FIGURE 3. The effect of challenge with apomorphine (2 mg/kg) (circles) or apomorphine plus clonidine (2 mg/kg) (triangles) on the locomotor response of 3-PPP-pretreated (closed symbols) and vehicle-pretreated (open symbols) animals. Locomotor activity was assessed each 5 minutes, and the data represent the means of seven replicates. The standard errors of the means have been omitted for clarity, but in no case was there a significant difference in the response of the two groups to apomorphine challenge or to apomorphine plus clonidine challenge. The locomotor activities of animals challenged with saline or clonidine alone were essentially zero and have been omitted for clarity.

Table 3

Effect of Vehicle or Reserpine (10 mg/kg, 5 hv treatment) on the Response of 3-PPP- or Vehicle-Pretreated Mice to *d*-amphetamine (1.5 mg/kg) Challenge

Treatment	Challenge	Pretreatment Group Vehicle	3-PPP
Vehicle	Saline	388 ± 56 (6)	376 ± 29 (6)[a]
	d-Amphetamine	737 ± 90 (8)	1277 ± 166 (9)[b]
Reserpine	Saline	12.3 (2)	8.5 (2)
	d-Amphetamine	223 ± 17 (9)	285 ± 44 (9)[a]

[a] Not significant ($p > 0.05$)
[b] $p < 0.05$ from the corresponding vehicle-pretreatment group.

Note: The data represent the mean locomotor activities in the two groups during the 90 minutes immediately following *d*-amphetamine or saline challenge. The standard error of the means are given, and the numbers in parentheses represent the number of replicates.

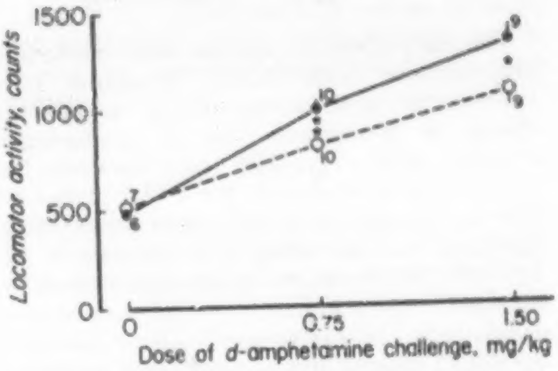


FIGURE 4. The effect of subchronic treatment with 3-PPP (or vehicle) on the locomotor response to *d*-amphetamine or saline challenge. The data represent the means and standard errors of the activity counts during the first hour of 6-10 replicates. ●—●, 3-PPP-pretreated: ○—○ vehicle-pretreated. $^*p < 0.05$, $^{**}p < 0.01$.

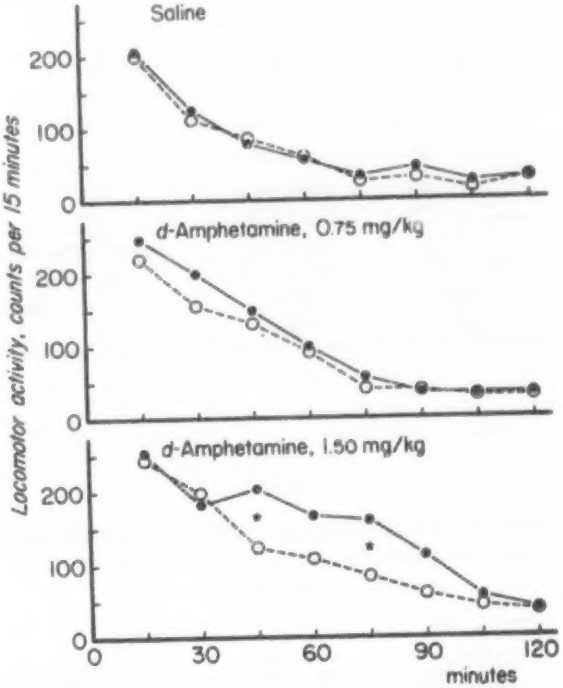


FIGURE 5. The effect of pretreatment of mice with haloperidol (25 μg/kg, 20 minutes ●—●) or acid vehicle (○—○) on their response to challenge with saline or *d*-amphetamine. Locomotor activity was monitored each 15 minutes for 2 hours. The data represent the means of 7-22 replicates with the standard errors omitted for clarity. $^*p < 0.05$.

Summary and Conclusions

The data obtained indicate that subchronic pretreatment with 3-PPP procuded DA-autoreceptor subsensitivity with no concomitant change in postsynpatic DA- or α-adrenergic receptor sensitivity. The supersensitivity to *d*-amphetamine evident in the 3-PPP pretreated mice may be due to the DA autoreceptors being subsensitive, thus leading to a reduction in the feedback control exerted by the DA released by the *d*-amphetamine.

Reference

Hjorth, S., Carlsson, A., Wikström, H., Lindberg, P., Sanchez, D., Hacksell, U., Arvidsson, L.-E., Svensson, U., and Nilsson, J.L.G. 3-PPP, a new centrally acting DA-receptor agonist with selectivity for autoreceptors. *Life Sci.*, 28:1225-1228, 1981.

Studies of Plasma Homovanillic Acid as an Index of Brain Dopamine Function[1]

Kenneth S. Kendler, M.D.,[2] John Y-K. Hsieh, Ph.D.,[2] and Kenneth L. Davis, M.D.[2]

In the rat, plasma levels of the dopamine (DA) metabolite homovanillic acid (HVA) change in parallel with brain levels of HVA after electrical stimulation, ablation of the brain DA system (Bacopoulos et al. 1979), and after administration of DA receptor-blocking neuroleptics (Bacopoulos et al. 1979; Kendler et al. 1981), and DA agonist drugs (Kendler et al. 1982). By selective inhibition of peripheral production of HVA by the drug debrisoquin, Kendler et al. (1981, 1982) showed that the alterations in plasma levels of HVA (pHVA) after DA blocking and agonist drugs were due largely or exclusively to the effect of the drugs on the brain. Based on these results and more limited studies in monkeys and man, pHVA has been proposed as a useful index of central DA function in human neuropsychiatric conditions. To further clarify the circumstances under which pHVA reflects brain DA function, the investigators examined the effects of a relevant behavioral stimulus, stress, and a relevant pharmacologic stimulus, probenecid, on central and plasma levels of HVA.

Approximately half of pHVA originates from sources other than the brain (Bacopoulos et al. 1979; Hoeldtke et al. 1974; Maas et al. 1979) probably from the sympathetic nervous system and the adrenal medulla. Stress increases plasma levels of catecholamines, including DA, several fold (Jindra et al. 1980; Van Loon et al. 1979). If appreciable amounts of these catecholamines were

---

[1] This study was supported in part by a program project grant from the National Institute on Aging (AG-02219) and research funds from the Veterans Administration.

[2] Department of Psychiatry, Veterans Administration Medical Center, Bronx, NY 10468 and Mt. Sinai School of Medicine, New York, NY 10029.

Address correspondence to: Kenneth S. Kendler, M.D., VA Medical Center, 130 West Kingsbridge Road, Bronx, NY 10468.

metabolized to HVA, stress could induce a selective increase in the peripheral production of HVA that could obscure the relationship of pHVA to brain DA function.

To measure the rate of DA turnover in man, levels of HVA in the cerebrospinal fluid (CSF) have been measured before and after administration of the drug probenecid. Probenecid blocks the egress of HVA from CSF and brain and also inhibits the renal clearance of HVA from plasma (Faull et al. 1981). It is therefore of interest to determine whether plasma levels of HVA continue to correlate well with central HVA levels after administration of probenecid. Could a low dose of probenecid selectively block renal excretion of HVA without altering clearance of HVA from CSF and brain thereby permitting measurement of whole body production of HVA by measuring the rate of rise of pHVA?

Method

Stress Studies

Male, Sprague-Dawley rats, weighing 250-350 g, and food-deprived for 24 hours prior to sacrifice, were subject to one of three forms of stress: brief (4 minutes) ether stress, one 90-minute period of restraint stress, and five daily 150 minutes periods of restraint stress. Blood was obtained by open-chest cardiac puncture after which the brains were immediately removed and frozen on dry ice. Immediate decapitation with blood collected from the carotid arteries was used as a control for the brief ether stress. Since no difference was found between these two groups, open-chest cardiac puncture after brief ether anesthesia was used for both control and experimental animals in further studies.

Probenecid Studies

Fasted, male Sprague-Dawley rats were administered vehicle or probenecid (20,40,60, and 80 mg/kg) 4 hours prior to sacrifice. Plasma for HVA levels was obtained just prior to lumbar puncture in seven psychiatric patients after no pretreatment and again after the administration orally of probenecid 100 mg/kg over 24 hours.

Free HVA in brain and CSF was measured by high-performance liquid chromatography and in plasma by gas chromatography/mass spectrometry.

Results

Brief ether stress compared to controls sacrificed by immediate decapitation had no significant effect on either plasma or whole brain HVA concentrations (Table 1). Similarly, one episode of restraint stress did not significantly alter plasma or whole brain HVA concentrations (Table 2). However, repeated restraint stress produced a small but significant 22 percent increase in pHVA and only a nonsignificant 7 percent increase in whole brain HVA (Table 3).

Table 1

The Response of Plasma and Whole Brain HVA in the Rat to Brief Ether Stress vs. Immediate Decapitation (*N* = 7 per Group)

Treatment	Plasma HVA (ng/cc ± SEM)	Whole Brain HVA (ng/g ± SEM)
Brief ether stress	3.1 ± 0.3	83.0 ± 5.8
Decapitation	3.1 ± 0.3	90.5 ± 7.2
t-test	0.13	0.80
p	NS	NS

Table 2

The Response of Plasma and Whole Brain HVA in the Rat to Acute Restraint Stress (90 min) vs. Control (*N* = 8 per Group)

Treatment	Plasma HVA (ng/cc ± SEM)	Whole Brain HVA (ng/g ± SEM)
Control	3.9 ± 0.4	83.3 ± 16.3
Acute restraint stress	4.4 ± 0.3	79.3 ± 16.1
t-test	1.08	0.17
p	NS	NS

Table 3

The Response of Plasma and Whole Brain HVA in the Rat to Chronic Restraint Stress ($N=6$ per Group)

Treatment	Plasma HVA (ng/cc ± SEM)	Whole Brain HVA (ng/g ± SEM)
Control	2.9 ± 0.1	120.9 ± 3.7
Chronic restraint stress	3.6 ± 0.2	129.0 ± 3.8
t-test	2.88	1.57
p	<.05	NS

Table 4

The Response of Plasma and Whole Brain HVA in the Rat to Varying Doses of Probenecid ($N=6$ per Group)

Treatment	Plasma HVA (ng/cc ± SEM)	Whole Brain HVA (ng/cc ± SEM)
Vehicle	3.5 ± 0.2	79.5 ± 4.4
Probenecid 20 mg/kg	3.2 ± 0.2	78.6 ± 5.5
Percent change	−8.6	−1.1
Probenecid 40 mg/kg	3.6 ± 0.3	84.8 ± 5.1
Percent change	+2.9	+6.7
Probenecid 60 mg/kg	4.4 ± 0.1[a]	109.8 ± 6.2[a]
Percent change	+25.7	+38.1
Probenecid 80 mg/kg	5.9 ± 0.4[a]	127.1 ± 11.4[a]
Percent change	+68.6	+59.9

[a] Significant at .01 level (two-tailed), by *t*-test, vs. vehicle.

Table 5

Plasma and CSF HVA in Humans With and Without Probenecid Treatment ($N=7$ per Group)

Treatment	Plasma HVA (ng/cc ± SEM)	CSF HVA (ng/cc ± SEM)
None	15.7 ± 1.4	67.7 ± 4.0
Probenecid	53.3 ± 5.1	249.5 ± 32.5
Percent increase	239.5	268.5
t-test (paired)	9.43	6.19
p	<.001	<.001

In the rat, neither 20 nor 40 mg/kg of probenecid produced a significant alteration in the concentrations of HVA in plasma or brain (Table 4). However, both 60 and 80 mg/kg produced significant and parallel increases in plasma and whole brain HVA (Table 4, Figure 1). The correlation of plasma and whole brain in this experiment was + .078 ($N = 30$) ($p < 0.001$). In psychiatric patients, probenecid (100 mg/kg over 24 hours) produced a highly significant increase in plasma and CSF HVA of approximately equal magnitude (Table 5, Figure 2). The correlation of plasma and CSF HVA in these patients was +0.86.

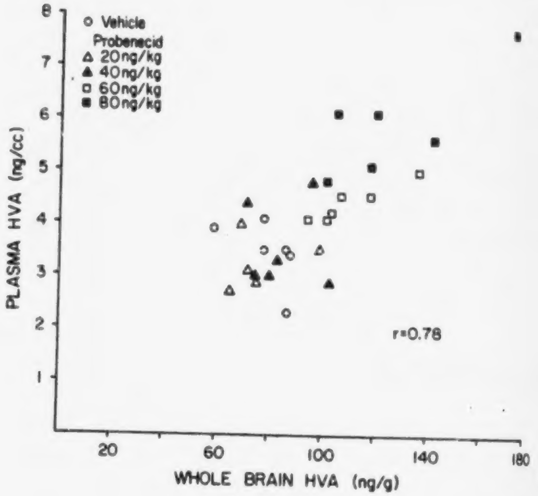


FIGURE 1

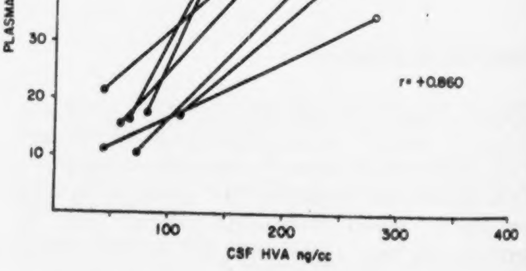


FIGURE 2

Discussion

Acute ether and immobilization stress produced no significant increase in pHVA concentrations in the rat. However, chronic restraint stress, which has been shown to increase levels of catecholamine synthetic enzymes (Kvetnansky 1980), produced a small but significant increase in pHVA. Although these results suggest that chronic, but not acute, stress may selectively increase peripheral production of HVA, two methodologic issues remain to be addressed. First, since even immediate decapitation produces a significant elevation in plasma levels of catecholamines, this method of sacrifice may not produce true "controls" for the examination of the effects of stress on pHVA. The investigators are currently using animals with chronic indwelling arterial cannula for "controls" in studies of the effects of stress on pHVA. Second, chronic stress could elevate pHVA concentrations in ways other than increasing peripheral HVA production. Hemoconcentration and decreased HVA clearance caused by the prolonged struggling and physical exhaustion may be the mechanism for the elevation of pHVA by chronic stress. The investigators are conducting experiments to examine this possibility. Despite these methodologic difficulties, these results suggest that compared to the effects of neuroleptic drugs (Kendler et al. 1981), stress probably has a relatively small effect on pHVA concentrations.

After probenecid administration in both rat and man, plasma concentrations correlate highly with central levels of HVA. In the rat, the threshold dose of probenecid necessary to produce a significant increase in plasma and brain concentrations of HVA was the same (60 mg/kg). These results suggest that selective inhibition of renal excretion of HVA by probenecid without altering transport of HVA from brain may be difficult to achieve. However, since after probenecid, pHVA correlates highly with central measures of HVA, measurement of pHVA levels in man after probenecid may be a useful measure of brain DA turnover.

References

Bacopoulos, N.G., Hattox, S.E., and Roth R.H. 3,4-Dihydroxyphenylacetic acid and homovanillic acid in rat plasma: Possible indicators of central dopaminergic activity. *Eur. J. Pharmacol.*, 56:225, 1979.

Faull, K.F., Kraemer, H.C., Barchas, J.D., and Berger, P.A. Clinical application of the probenecid test for measurement of monoamine turnover in the CNS. *Biol. Psychiatry*, 16:879-899, 1981.

Hoeldtke, R., Rogawski, M., and Wurtman, R.J. Effect of selective destruction of central and peripheral catecholamine-containing neurones with 6-hydroxydopamine on catecholamine excretion in the rat. *Br. J. Pharmacol.*, 50:265, 1974.

Jindra, A., Kvetnansky, R., Belova, T.I., and Sudakov, K.V. Effect of acute and repeated immobilization stress on plasma renin activity, catecholamines, and corticosteroids in wistar and august rats. In: Usdin, E., Kvetnansky, R., and Kopin, I.J. (eds.), *Catecholamines and Stress: Recent Advances.* New York: Elsevier, 1980, pp. 249-254.

Kendler, K.S., Heninger, G.R., and Roth, R.H. Influence of dopamine agonists on plasma and brain concentrations of homovanillic acid. *Life Sci.*, 30:2063-2069, 1982.

Kendler, K.S., Heninger, G.R., and Roth, R.H. Brain contribution to the haloperidol-induced increase in plasma homovanillic acid. *Eur. J. Pharmacol.*, 71:321-326, 1981.

Kvetnansky, R. Recent progress in catecholamines under stress. In: Usdin, E., Kvetnansky, R., and Kopin, I.J. (eds.), *Catecholamines and Stress: Recent Advances.* New York: Elsevier, 1980, pp. 7-18.

Maas, J.W., Hattox, S.E., and Landis, D.H. Differential effects on brain catecholamines by debrisoquin. *Biochem. Pharmacol.*, 3153, 1979.

Van Loon, G.R., Schwartz., L., and Sole, M.J. Plasma dopamine responses to standing and exercise in man. *Life Sci.*, 24:2273-2278, 1979.

Plasma Haloperidol Levels and Clinical Response in Acute Schizophrenia

Irl Extein, M.D.,[1] K.A. Augusthy, M.D.,[1] Mark S. Gold, M.D.,[2] A.L.C. Pottash, M.D.,[2] David Martin, B.S.,[2] and William Z. Potter M.D., Ph.D.[3]

Over the past three decades, neuroleptic medications have become the treatment of choice for schizophrenia, particularly for acute (Casey et al. 1960; Extein 1980) and prophylactic (Davis 1975) treatment of psychosis. However, a significant proportion of schizophrenic patients have an inadequate antipsychotic response to neuroleptics (Ayd 1975). One source of the variability in clinical antipsychotic response may be variability in plasma levels of medication. Several investigators have studied the relationship of neuroleptic levels and response to treatment (Calil et al. 1979; Forsman & Ohmen 1976; Magliozzi et al. 1981; Smith et al. 1979; Tune et al. 1980). Some of these investigators have suggested "therapeutic windows" for plasma levels of neuroleptics, including haloperidol (Forsman & Ohmen 1976; Magliozzi et al. 1981; Tune et al. 1980).

Haloperidol is a potent neuroleptic with a relatively low profile of sedation and cardiovascular effects that is extremely useful in the treatment of acute psychosis (Extein 1980). Steady-state plasma levels are achieved in about 6 days (Forsman & Ohmen 1976). Because haloperidol has no significant active metabolites, it is an ideal medication to use to study the relationship between clinical efficacy and neuroleptic levels. Most other neuroleptics have active metabolites, and studies of plasma levels and clinical response to these medications must involve assays of multiple compounds or dopamine-receptor binding assays (Calil et al. 1979). Magliozzi et al. (1981) have recently reported a therapeutic window for haloperidol levels in schizophrenic outpatients. In order to study the relationship of clinical responses and haloperidol levels in acute treatment, we measured steady-state plasma haloperidol levels and rated clinical response in 18 newly admitted, acutely psychotic schizophrenic inpatients.

Method

Eighteen actively psychotic patients newly admitted to the Fair Oaks Hospital Neuropsychiatric Evaluation Unit and diagnosed by Research Diagnostic Criteria (Spitzer et al. 1978) were included in this study. Fourteen had schizophrenia, undifferentiated or paranoid subtype, and four had schizoaffective disorder. All were treated with haloperidol. Mean age of these patients ± s.e.m. was 26 ± 1 years. The Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham 1962) was done by a research psychiatrist at the time of admission and at regular intervals thereafter. Haloperidol dosage was adjusted by the treating psychiatrist based on standard clinical criteria. Dosage ranged from 7-60 mg daily. Anticholinergic medications were used as needed for extrapyramidal symptoms (EPS). Some patients received some of their haloperidol by intramuscular injection during the first week, but thereafter the medication was administered orally. Blood samples for assay of steady-state plasma haloperidol levels were obtained by venipuncture at regular intervals while patients were receiving haloperidol. Steady-state levels (Forsman & Ohmen 1976), were defined as those obtained at 8 a.m. in the morning 10 hours after the previous dosage of haloperidol in a patient who had been on the same dosage for at least 1 week. Plasma haloperidol levels were determined by gas-liquid chromatography (GLC) with nitrogen-phosphorus selective detection using a modification of the method of Bianchetti and Morselli (1978). The absolute sensitivity of the method was 1 ng/ml with a mean day-to-day coefficient of variation of less than 10 percent. Haloperidol responders were defined as patients showing a decrease of 10 points or more on the BPRS at a given time point. Data are expressed as mean ± s.e.m.

Results

The mean BPRS score on admission was 60 ± 2. Nine patients were responders to haloperidol at the end of 4 weeks. Mean decrease in BPRS at 4 weeks in these nine patients was 17 ± 3. Of these nine responders, seven had steady-state haloperidol in the therapeutic range suggested by the literature (Forsman & Ohmen 1976; Magliozzi et al. 1981) of 5-15 ng/ml, and two had higher levels. Mean plasma level in the nine patients identified as responders at 4 weeks was 15.6 ± 4.0 ng/ml. Dosage in these nine patients ranged from 10-60 mg daily, with a mean of 27 ± 5 mg daily. Three responders were dropped from the study before 4 weeks, because of severe extrapyramidal syndrome (EPS). All three of these responders had haloperidol levels in the 5-15 ng/ml range. Six patients were nonresponders. Four of these six were dropped from the study before 4 weeks because of poor response Three of these six nonresponders had haloperidol levels outside the 5-15 ng/ml range — two higher and one lower. Mean plasma level in the six nonresponders was 14.4 ± 4.1 ng/ml. Dosage in these six patients ranged from 7-60 mg daily, with a mean of 25 ± 9 mg daily. In summary, 10 of 12 responders but only 3 of 6 nonresponders had haloperidol levels in the 5-15 ng/ml range (*see* Table and Figure).

---

[1] Fair Oaks Hospital, Summit, NJ 07901.

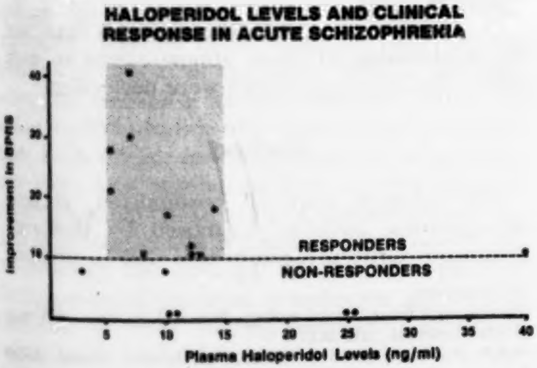
[2] Psychiatric Diagnostic Laboratories of America, Summit NJ 07901.

[3] Clinical Psychobiology Branch, National Institute of Mental Health, Bethesda, MD 20205.

Table

Plasma Haloperidol Levels and Clinical Response in Acute Schizophrenia

	Plasma Haloperidol Levels	
	5-15 ng/ml	> 15 < 5 ng/ml
Responders	10	2
Nonresponders	3	3



FIGURE

There was a significant positive correlation between steady-state plasma haloperidol levels and dosage ($r = .68$, $p < .01$). There was no significant correlation between haloperidol levels and change in BPRS.

Discussion

These results suggest that a high proportion of acutely psychotic schizophrenic inpatients who respond to treatment with haloperidol do so at plasma levels in the range of 5-15 ng/ml. This is in basic agreement with a previous study showing outpatients to respond within this approximate range (Magliozzi et al. 1981). There are certain methodological limitations inherent in attempting to define a therapeutic window of plasma levels in an open clinical trial of a therapeutic agent. Dosage adjustments are partially dependent on clinical response, unlike a fixed-dose trial. Also, it is not certain that patients who respond within a given range of plasma levels would not respond at levels above or below this range. Nor is it certain that nonresponding patients would not respond at higher or lower levels. However, this study does identify a range of plasma levels within which most acute schizophrenic patients who respond to haloperidol will fall. There is certainly no linear relationship between haloperidol levels and clinical response. The results here are consistent with either a "therapeutic window" or a "threshold" for effective plasma levels of haloperidol in acute schizophrenia. Individual patient data suggest that nonresponders continue not to respond when haloperidol levels are increased above 15 ng/ml. For example, a 33-year-old woman was unimproved after 2 weeks on haloperidol 15-20 mg daily with plasma levels of 6.7-12.2 ng/ml. She showed no improvement when her haloperidol was raised to 60 mg daily with a plasma level of 25.0 ng/ml.

There are certain practical advantages to measuring plasma haloperidol levels. First, because haloperidol has no known significant active metabolites (Magliozzi et al. 1981), assay of haloperidol alone measures the pharmacologically active compound. Second, the GLC assay (Bianchetti & Morselli 1978) is adaptable to a large volume of clinical samples.

The results presented here, along with previous results from other investigations, suggest that measurement of plasma haloperidol levels may provide useful guidelines for adjusting medication dosage in schizophrenic patients. Most of the acutely psychotic schizophrenic patients reported here responded with plasma levels in the range of 5-15 ng/ml. Further research needs to be focused on better defining a possible "therapeutic window" or "threshold" for effective haloperidol levels in schizophrenic patients.

References

Ayd, F.J., Jr. Treatment-resistant patients: A moral, legal, and therapeutic challenge. In: Ayd, F.J., Jr. (ed.), *Rational Psychopharmacotherapy and the Right to Treatment.* Baltimore: Ayd Medical Communications, 1975.

Bianchetti, G., and Morselli, P.L. Rapid and sensitive method for determination of haloperidol in human samples using nitrogen-phosphorus selective detection. *J. Chromatogr.,* 153:203, 1978.

Calil, H.M., Avery, D.H., Hollister, L.E., Creese, I., and Snyder, S.H. Serum levels of neuroleptics measured by dopamine radioreceptor assay and some clinical observations. *Psychiatry Res.,* 1:39-44, 1979.

Casey, J.F., Bennett, I.F., Lindley, C.J., Hollister, L.E., Gordon, M.H., and Springer, N.N. Drug therapy in schizophrenia. *Arch. Gen. Psychiatry,* 2:100-110, 1960.

Davis, J.M. Overview: Maintenance therapy in psychiatry. I. Schizophrenia. *Am. J. Psychiatry,* 132:1237-1245, 1975.

Extein, I. Psychopharmacology in psychiatric emergencies. *Int. J. Psychiatr. Med.,* 10:189-204, 1980.

Forsman, A., and Ohmen, R. Pharmacokinetic studies on haloperidol in man. *Curr. Ther. Res.,* 20:319-336, 1976.

Magliozzi, J.R., Hollister, L.E., Arnold, K.V., and Earle, G.M. Relationship of serum haloperidol levels to clinical response in schizophrenic patients. *Am. J. Psychiatry,* 138:365-367, 1981.

Overall, J.E., and Gorham, D.R. The Brief Psychiatric Rating Scale. *Psychol. Rep.,* 10:799-812, 1962.

Smith, R.C., Crayton, J., Dekirmenjian, H., Klass, D., and Davis, J.M. Blood levels of neuroleptic drugs in nonresponding chronic schizophrenic patients. *Arch. Gen. Psychiatry,* 36:579-584, 1979.

Spitzer, R.L., Endicott, J., and Robins, E. Research diagnostic criteria: Rationale and reliability. *Arch. Gen. Psychiatry,* 35:773-782, 1978.

Tune, L.E., Creese, I., De Paulo, Jr., Slavney, P.R., Coyle, J.T., and Snyder, S.H. Clinical state and serum neuroleptic levels measured by radioreceptor assay in schizophrenia. *Am. J. Psychiatry,* 137:187-190, 1980.

Abnormal Immune Regulation in Schizophrenic Patients

Lynn E. DeLisi, M.D.,[1] and Richard Jed Wyatt, M.D.[2]

Introduction

Associations between psychological states, disease susceptibility and immunity are well known (Stein et al. 1981). In addition, several published reports suggest that schizophrenic patients may have abnormal immune responsiveness and laboratory signs of altered immunity (reviewed by Wyatt et al. 1982) Lymphocyte populations from schizophrenic patients have been shown to contain histologically and functionally abnormal cells as well as abnormal proportions of lymphocyte subtypes (Fessel & Hirata-Hibi 1963; Hirata-Hibi et al. 1982; Kamp 1962; Vartanian et al. 1978). Alterations in plasma and cerebral spinal fluid (CSF) gamma globulin concentrations have also been found (Bock et al. 1970; Domino et al. 1975; Solomon et al. 1969; Strahelivitz et al. 1976; Torrey et al. 1978), as well as evidence of increased antinuclear antibody titres (Gallien et al. 1975; Johnson & Whaley 1975; Zarrabi et al. 1979). Furthermore, the incidence of various diseases known to be associated with immune abnormalities such as rheumatoid arthritis, cancer, asthma, and allergic reactions have been reported to be lower in schizophrenic patients compared with general populations (Baldwin 1979).

In a further attempt to examine this issue and the relationship of these abnormalities to each other, the following studies were performed.

Method

The subjects were all hospitalized, chronic schizophrenic patients diagnosed by Research Diagnostic Criteria (Spitzer et al. 1977), who had

---

[1] Section on Clinical Pharmacology, National Institute on Mental Health, Bethesda, MD 20205.

[2] Adult Psychiatry Branch, Division of Special Mental Health Research, Intramural Research Program, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, D.C. 20032.

little or no response to conventional treatment, and were residing on the research units of the National Institute of Mental Health, Saint Elizabeths Hospital, Washington, D.C.

Thirty-eight patients (mean age ± S.D. 35.0 ± 10.5) had blood drawn into heparinized plastic syringes on serial occasions for determination of the proportion of lymphocyte subpopulations (*see* Thaler et al. 1977, for review of the immune system). Seven patients were free of medication for at least 1 month; the remaining 31 were medicated on stabilized doses of neuroleptic medication. Forty-seven healthy volunteers (mean age ± S.D. 27.7 + 6.7) from nearby universities and the research laboratory served as controls. Monoclonal antibodies specific to antigens on the surface of T lymphocytes (Leu-1), B lymphocytes (HLA-DR), Suppressor T cells (Leu-2), and Helper T cells (Leu-3) and tagged with fluorescence (Becton-Dickinson Monoclonal Antibody source book), were employed in the following procedure: Lymphocytes were separated from whole blood by the method of Boyum (1968) on a ficoll gradient and centrifuged at 400 g for 50 minutes. The lymphocyte containing band was removed, washed with a buffer consisting of balanced salt solution (Hank's), 2 percent Bovine Serum Albumin (BSA), and .2 percent NaN_3 and spun at 200 g for 10 minutes, then resuspended in 10 ml of buffer and counted in a coulter counter. Cells were then resuspended at a concentration of 1×10^7 cells per cc. Five μl of either Leu-1, Leu-2, Leu-3, or HLA-DR (Becton-Dickinson) was added to 100 μl of cells and vortexed. The suspensions were incubated in the dark on ice for 45 minutes, then pelleted by spinning in an Eppendorf Centrifuge for 15 minutes. The supernatant was aspirated, washed once, and the pellet resuspended in 100 μl of the above buffer. Samples were run through a Becton-Dickinson FACS III using the 488 nM line of an argon laser for excitation. Each sample run (approximately 12 samples per day) was standardized to known chicken erythrocyte light scatter and fluorescence curves. The fluid stream was adjusted to a flow rate of approximately 200 cells per second. The percent fluroescence of the total lymphocyte population (percent of cells having receptors for each monoclonal antibody) was determined on the FACS. Split samples in the same day run had a 2 percent mean variation.

Twenty patients who had HLA-DR binding measured had concurrent plasma immunoglobulins (IgG, IgA, IgM) quantified using an immunofluorescent assay (Clinical Immunology Laboratories, Inc., Los Angeles, Cal.).

Additionally, a total of 51 chronic schizophrenic patients, including 26 of the patients who had lymphocyte subpopulation determinations plus 24 first-episode Diagnostic and Statistical Manual-III (DSM-III) schizophreniform-disordered patients, had serum antinuclear antibody titres determined by an indirect immunofluorescent technique at Clinical Immunology Laboratories. All patients with positive antinuclear antibody titres also had antinative DNA antibody and Histone reactive ANA titres determined (specific tests to diagnose Idiopathic Systemic Lupus Erythematosis and drug-induced Lupus, respectively; Fritzler & Tan 1978).

The schizophreniform patients were sampled prior to neuroleptic treatment over a 2-year period from acute psychiatric admission facilities in the Washington, D.C. area.

Results

Percentages of Leu-1 (total T cells), Leu-2 (Suppressor T cells), Leu-3 (Helper T cells), and HLA-DR (total B cells) are summarized in the Table. The patient group had significantly higher total T cell, as well as B cell, percentages than controls, although an in inverse relationship was suggested for B and T cell percentages for subjects in each group (for patients: Pearson $r = .61$, $p < .003$; for controls: $r = -.51$, $p < .07$). No significant differences were found when comparing the means of the medicated patients with the means of the nonmedicated patients.

B-cell percentages were significantly correlated with IgG plasma concentrations (Pearson $r = .52$, $p = .015$) while not correlated with IgA or IgM concentrations (Pearson $r = .33$; $p = .15$ and $r = -.01$; $p = .97$, respectively). Five of the 20 patients had IgG concentrations higher than the normal range; three of these five had additional elevations in IgA concentrations. One patient had an elevated IgM concentration and normal IgG and IgA, and one patient had an IgG concentration below the normal range. All normal ranges were those established by the Clinical Immunology Laboratories.

Table

Mean (± S.D.) Percent of Total Lymphocytes of Each Lymphocyte Subtype in Schizophrenic Patients vs. Controls

	Percent Leu-1 (Total T's)	Percent Leu-2 (Suppressor T's)	Percent Leu-3 (Helper T's)	Percent HLA-DR (Total B Cells)
Schizophrenic Patients	62.4 ± 10.0	24.1 ± 6.0	34.7 ± 8.6	28.0 ± 9.7
(*N*)	(37)	(25)	(25)	(25)
Controls	56.7 ± 12.6	20.9 ± 5.0	32.9 ± 11.4	21.3 ± 4.2
(*N*)	(47)	(32)	(32)	(19)
t	2.2	2.2	.68	2.8
p	.03	.03	.50	.008

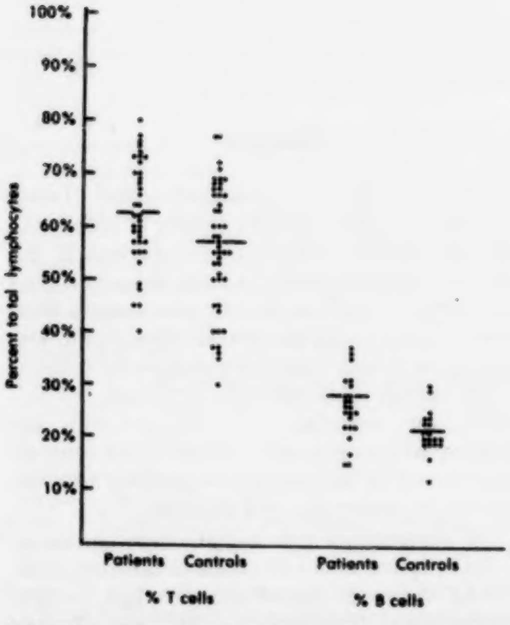


FIGURE 1. Scattergram of the percent HLA-DR binding (B cells) and Leu-1 binding (T-cells) to total lymphocytes in the schizophrenic patients compared with controls.

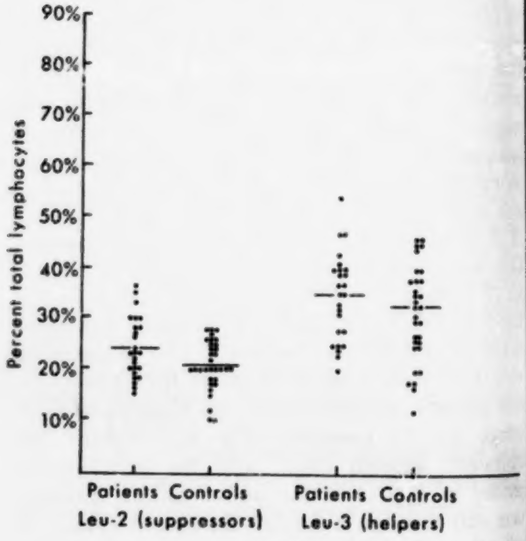


FIGURE 2. Scattergram of the percent Leu-2 (Suppres T cell) and Leu-3 (Helper T cell) binding to total lymphocytes in the schizophrenic patients compared wit controls.

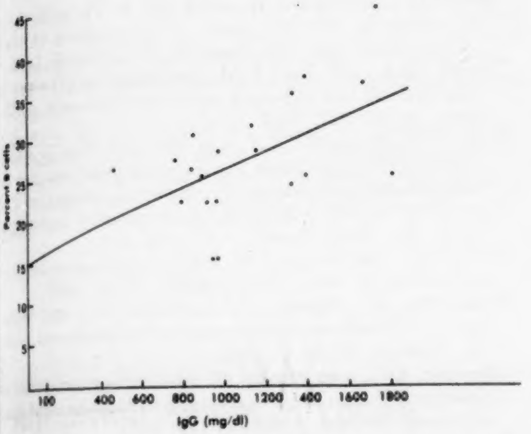


FIGURE 3. IgA concentration vs. percent B cells. Pearson $r = .53$. Mean percent B cells = 27.2 ± 7.2; mean IgG concentration = 1113.7 ± 356.

Antinuclear antibody titres were determined to be positive (> 1/10) of 21.7 percent of the chronic schizophrenic patients and 20.8 percent of the first-episode schizophrenic patients. It is known to be positive in 1-5 percent in the general population (Panush 1979). Positive antinuclear antibody titres did not correlate with elevated immunoglobulin concentrations or elevated proportions of B or T cells. None of the patients with positive antinuclear antibody titres had evidence of either antinative DNA antibodies or anti-Histone reactive DNA antibodies.

Discussion

The data presented here show small differences between schizophrenic and control populations in both the cellular and humoral immune systems. While a generalized decrease in the production of immunoglobulins among chronic schizophrenic patients had been previously found, (DeLisi et al. 1981), a subgroup of patients in the present study had elevated IgG concentrations that were correlated with elevated proportions of the lymphocyte subtype (B cells) that produces them.

These changes may be consistent with the notion that neuroleptic medications alter the immune response. All chronic schizophrenic patients studied had previously been under neuroleptic treatment for several years. That neuroleptics affect the immune system is supported by several lines of evidence. Chlorpromazine has been linked to the presence of abnormal lymphocytes in the blood of schizophrenic patients (Fieve et al. 1966) and the development of systemic lupus erythematosis (Ananth & Minn 1973; Dubois et al. 1972; Fessel & Solomon 1960), an immune complex disorder. Antinuclear antibodies have also been associated with long-term neuroleptic treatment (Gallien 1975; Johnstone & Whaley 1975; Zarrabi et al. 1979). Lovett et al. (1978) have reported a decrease in antibody production *in vitro* by B cells associated with chlorpromazine and Ferguson et al. (1978) reported a suppressive effect of chlorpromazine on several *in vitro* measures of T lymphocyte responsiveness. In addition, *in vivo* proportions of B and T lymphocytes have been shown to return to normal after discontinuation of neuroleptic medication (Ferguson et al. 1978; Liedeman & Prilipko 1978).

The increased proportions of B and T lymphocytes found in our studies, however, may not solely be a result of neuroleptic medication. The few medication-free patients in our studies did not have proportions of B and T cells different from the medicated patients and contrary to the Lovett et al. (1978) study, the increases in B cell percentages were associated with increased antibody production. Furthermore, a recently published report of histological abnormalities in lymphocytes of schizophrenic patients defines distinct abnormalities present in unmedicated chronic schizophrenic patients as well as first-episode acute schizophrenics (Hirata-Hibi et al. 1982).

Heath and Krupp (1966) have hypothesized that abnormal immunity in schizophrenic patients may be the result of an autoimmune disorder and reported the presence of antibrain antibodies in postmortem brain specimens from schizophrenic patients. The present study supports previous findings of a 20-25 percent incidence of positive antinuclear antibody titres that are not specific for lupus erythematosis in chronic schizophrenic patients (Gallien et al. 1975; Johnstone & Whaley 1975; Zarrabi et al. 1979). The increased antinuclear antibody titres in first-episode schizophrenic patients never medicated with neuroleptics, and the negative titres of antibodies characteristic of drug-induced lupus, suggest that this finding in chronic schizophrenic patients is not simply an effect of long-term medication. Further studies are necessary to determine if an autoimmune phenomena is related to the etiology of schizophrenia.

Torrey et al. (1978) have proposed a viral etiology to schizophrenia subsequent to their findings of specific increases in viral antibody titres. Chronic viral infection, in turn, may cause multiple alterations in immune response. We have not determined in the present studies whether increased viral antibody titres are associated with these abnormalities. Even if found, it would not be clear whether the increased viral antibody titres were associated with the pathology of the illness itself or a consequence of altered immunity.

Finally, the differences reported here are small. It is uncertain if these alterations in immune functioning are related to reported altered incidences of various autoimmune, infectious, and neoplastic disorders in schizophrenic populations.

References

Ananth, J.V., and Minn, K. Chlorpromazine-induced systemic lupus erythematosis. *Can. Med. Assoc. J.*, 108:680, 1973.

Baldwin, J.A. Editorial: Schizophrenia and physical disease. *Psychol. Med.*, 9:611-618, 1979.

Bock, E., Week, B., and Rafaelson, O.J. Immunoglobulins in schizophrenic patients. *Lancet*, II:523, 1970.

Bøyum, A. Isolation of mononuclear cells and granulocytes from human blood. *Scand. J. Clin. Lab. Invest.*, 21(Suppl.):77-89, 1968.

DeLisi, L.E., Weinberger, D.R., Potkin, S.G., Neckers, L.M., Shiling, D.J., and Wyatt, R.J. Quantitative determination of immunoglobulins in CSF and plasma of chronic schizophrenic patients. *Br. J. Psychiatry*, 139:513-518, 1981.

Domino, E.F., Krause, R.R., Thiessen, M.M., and Batsakis, J.G. Blood protein fraction comparisons of normal and schizophrenic patients. *Arch. Gen. Psychiatry*, 32:717-721, 1975.

Dubois, E.L., Tallman, E., and Wonka, R.A. Chlorpromazine-induced systemic lupus erythematosis. *JAMA*, 221:595-596, 1972.

Ferguson, R.M., Schmidtke, J.R., and Simmons, R.L. Effects of psychoactive drugs on *in vitro* lymphocyte activation. In: Bergsma, D., and Goldstein, A.L. (eds.), *Neurochemical and Immunologic Components in Schizophrenia. (Original Articles Series: Birth Defects)*. Vol. 18. New York:Alan R. Liss Co., 1978, pp. 379-405.

Fessel, W.J., and Hirata-Hibi, M. Abnormal leukocytes in schizophrenia. *Arch. Gen. Psychiatry*, 9:601-613, 1963.

Fessel, W.J., and Solomon, G.F. Psychosis and systemic lupus erythematosis: A review of the literature and case reports. *Calif. Med.*, 92:266-270, 1960.

Fieve, R.R., Blumenthal, B., and Little, B. The relationship of atypical lymphocytes, phenothiazines and schizophrenia. *Arch. Gen. Psychiatry*, 115:529-534, 1966.

Fritzler, M.J., and Tan, E.M. Antibodies to Histones in drug-induced and idiopathic lupus erythematosis. *J. Clin. Invest.*, 62:560-567, 1978.

Gallien, M., Schnetzler, J.P., and Morin, J. Anticorps antinuculeaire's et lupus induits par les phenothiazines chez six cents malades hospitalises. (Antinuclear antibodies and lupus cells in 600 hospitalized phenothiazine treated patients.) *Ann. Med., Psychol.*, 1:237-248, 1975.

Heath, R.G., and Krupp, I.M. Schizophrenia as an immunologic disorder. *Arch. Gen. Psychiatry*, 16:1-9, 1966.

Hirata-Hibi, M., Higashi, S., Tachibana, T., and Watanabe, N. Stimulated lymphocytes in schizophrenia. *Arch. Gen. Psychiatry*, 39:82-87, 1982.

Johnstone, E.C., and Whaley, K. Antinuclear antibodies in psychiatric illness: Their relationship to diagnosis and drug treatment. *Br. Med. J.*, 28:724-725, 1975.

Kamp, V.H. Nuclear changes in the white blood cells of patients with schizophrenic reactions. *J. Neuropsychiatry*, 4:1-3, 1962.

Liedeman, R.R., and Prilipko, L.L. The behavior of T lymphocytes in schizophrenia. In: Bergsma, D., and Goldstein, A.L. (eds.,) *Neurochemical and Immunologic Components in Schiozophrenia. (Original Article Series: Birth Defects)*. Vol. 18. New York:Alan R. Liss, Co., 1978, pp. 365-377.

Lovett, C.L., Ulrich, J.T., Simms, B.G., and Goldstein, A.L. Effects of chlorpromazine on antibody production in *vitro*. In: Bergsma, D. and Goldstein, A. L. (eds.), *Neurochemical and Immunologic Components in Schizophrenia. (Original Article Series: Birth Defects)*. Vol. 18. New York Alan R. Liss Co., 1978, pp. 407-422.

Panush, R.S. Autoantibodies and human disease. In: Waldman, R.H. (ed.), *Clinical Concepts of Immunology*. Baltimore:Williams and Wilkins, Co., 1979, pp. 134-152.

Solomon, G.F., Allansmith, M., McClellan, B., and Amkraut, A. Immunoglobulins in psychiatric patients. *Arch. Gen. Psychiatry*, 20:272-277, 1969.

Spitzer, R.L., Endicott, J.E., and Robins, E. *Research Diagnostic Criteria (RDC) for a Selected Group of Functional Disorders*. Third Ed. New York:New York State Psychiatric Institute, Biometrics Research, 1977.

Stein, M., Keller, S., and Schleifer, S. The hypothalamus and the immune response. In: Weiner, H., Hofer, M.A. and Stunkard, A.J. (eds.), *Brain, Behavior, and Bodily Disease*. New York:Raven Press, 1981, pp. 45-65.

Strahilevitz, M., Fleishman, J.B., Fischer, G.W., Harris, R., and Narasimhachari, N. Immunoglobulin levels in psychiatric patients. *Am. J. Psychiatry*, 133:772-776, 1976.

Thaler, M.S., Klausner, R.D., and Cohen, H.J. *Medical Immunology*. Philadelphia:J.B. Lippincott Co., 1977.

Torrey, F.E., Peterson, M.R., Brannon, W.L., Carpenter, W., Post. R.L., and van Kammen, D.P. Immunoglobulins and viral antibodies in psychiatric patients. *Br. J. Psychiatry*, 132:342-348, 1978.

Vartanian, M.E., Kolyaskina, G.I., Lozovsky, D.V., Burbaeva, and Ignatov. Aspects of humoral and cellular immunity in schizophrenia. In: Bergsma, D., and Goldstein, A.L. (eds.), *Neurochemical and Immunological Components of Schizophrenia. (Original Article Series: Birth Defects)*. Vol. 18. New York:Alan R. Liss Co., 1978, pp. 339-364.

Wyatt, R.J., Cutler, N., DeLisi, L.E., Jeste, D., Luchins, M., Potkin, S.G., and Weinberger, D.R. Biochemical and morphological factors in schizophrenia. In: Grinspoon, L. (ed.), *American Psychiatric Association Annual Reveiw 1982.* (In press)

Zarrabi, M.H., Zucker, S., Miller, F., Derman, R.M., Romano, G.S., Hartnett, J.A., and Varma, A.O. Immunologic and coagulation disorders in chlorpromazine-treated patients. *Ann. Int. Med.*, 91:194-199, 1979.

Abnormal Scans in Young Schizophrenics

S. Charles Schulz, M.D.,[1] Miriam Koller, M.D.,[1] Pulla R. Kishore, M.D.,[1] Robert M. Hamer, Ph.D.,[1] and Robert O. Friedel, M.D.[1]

Introduction

Although brain abnormalities have been reported for years in the psychiatric literature, the use of the computed tomography (CT) scanner allowed investigators to assess the brain in some new ways. Johnstone et al. (1976) and Weinberger et al. (1979a) reported a difference in ventricular size between schizophrenic patients and control subjects. Since these reports have been published, a significant amount of research has appeared which has bolstered their significance. Correlations of neuropsychological tests such as the Halstead-Reitan Battery (Donnelly et al. 1980) and Luria-Nebraska Test (Golden et al. 1980) and CT scale abnormalities have been demonstrated. In addition, enlarged lateral ventricles in schizophrenic patients has been associated with poor response to antipsychotic agents when compared to schizophrenic patients with normal-sized ventricles (Weinberger et al. 1980). Increased sulcal size of the cerebral cortex (Weinberger et al. 1979b) and atrophy of the cerebellar vermis (Weinberger et al. 1979c) have also been noted.

In studies reported to date, the patients have usually been ill and have received treatment for some time. The investigators of the early reports hypothesized that the CT scan changes would probably be present early in the course of the illness because there was no correlation with increased ventricular brain ratio (VBR) or lenth of time since onset of symptoms (Weinberger et al. 1979a). The purpose of this investigation was to examine the CT scans of young schizophrenics, many of whom had not received neuroleptics.

Methods

The patients studied included all consecutive admissions diagnosed as schizophrenic (or schizophreniform) who were 22 years old or younger and had not been ill or treated with medication for more than 24 months. They included 10 males and 5 females (total $N = 15$) with average age of 17.1 years (range 15 to 22). They had been ill 13.7 (± 2.1 S.E.) months and treated for an average of 5.2 months. Ten had never received neuroleptics. No patients had significant medical illness or mental retardation.

The control group were selected at random by the neuroradiologist from CT scans read as normal. There average age was 16 (13 to 19).

The ventricular brain ratio (VBR) was obtained by planimetric measurement performed as described by Weinberger et al. (1979a). Results were analyzed by application to *t*-test after log transformation of the VBR measures to equalize the variances.

Results

The schizophrenic patients had a mean VBR of 8.3 ± 4.9 S.D. which was significantly larger than the control population whose mean VBR was 2.7 ± 2.35 S.D. ($p < .0001$).(Figure 1)

There was no correlation with the length of time since the onset of symptoms and VBR. (Figure 2)

When a standard of "normality" was constructed by adding two standard deviations to the mean of the control group, it was noted that 8/15 (53%) patients had "abnormal" VBRs. Even when compared to adult standards of abnormality (VBR > 10), 7/15 were judged to be large.

---

[1] Medical College of Virginia, Richmond, VA 23298.

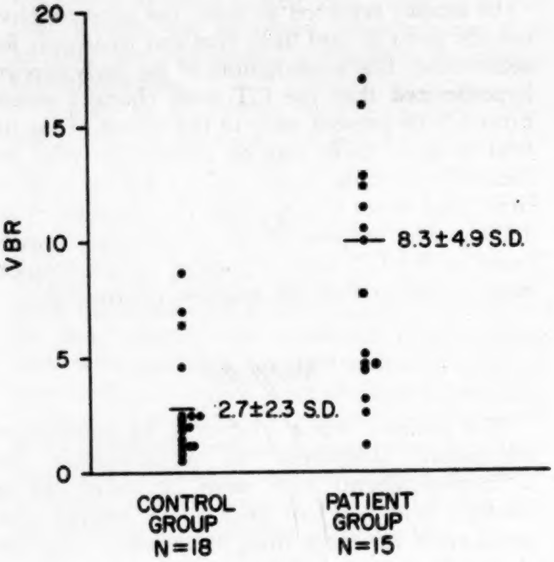


FIGURE 1.

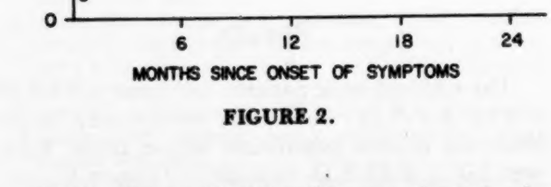


FIGURE 2.

Of the three schizophreniform patients in the study, one had an abnormal scan (VBR = 10). No tumors were seen in this series.

Conclusion

These results corroborate the finding of increased VBR in schizophrenic patients and are comparable in magnitude to Weinberger's initial report. This finding is consistent with the hypothesis that the CT scan abnormality is present early in the illness and is not a result of treatment with medication or institutionalization.

Although the prevalance of the increased VBR was about 50 percent in the authors' group of patients, this may not be an accurate assessment of the rate of abnormality in all young schizophrenics, as the Medical College of Virginia is a tertiary referral center.

There are other parameters concerning these patients that are currently being evaluated.

References

Donnelly, E.F., Weinberger, D.R., Waldman, I.N., and Wyatt, R.J. Cognitive impairment associated with morphological brain abnormalities on computed tomography in chronic schizophrenic patients. *J. Nerv. Ment. Dis.*, 168:305-308, 1980.

Golden, C.J., Moses, J.A., Zelazowski, R., Graber, B., Zatz, L.M., Horvath, T.B., and Berger, P.A. The relationship of cerebral ventricular size and neuropsychological impairment as measured by the standardized Luria Neuropsychological Battery in young chronic schizophrenics. *Arch. Gen. Psychiatry*, 37:619-623, 1980.

Johnstone, E.C., Crow, T.J., Frith, C.D., Husband, J., and Kreel, L. Cerebral ventricular size and cognitive impairment in chronic schizophrenia. *Lancet*, ii:924-926, 1976.

Weinberger, D.R., Torrey, E.F., Neophytides, A.N., and Wyatt, R.J. Lateral cerebral ventricular enlargement in chronic schizophrenia. *Arch. Gen. Psychiatry*, 36:735-739, 1979a.

Weinberger, D.R., Torrey, E.F., Neophytides, A.N., and Wyatt, R.J. Structural abnormalities of the cerebral cortex in chronic schizophrenia. *Arch. Gen. Psychiatry*, 36:935-939, 1979b.

Weinberger, D.R., Torrey, E.F., and Wyatt, R.J. Cerebellar atrophy in chronic schizophrenia. *Lancet*, i:718-719, 1979c.

Weinberger, D.R., Bigelow, L.B., Kleinman, J.E., Klein, S.T., Rosenblatt, J.E., and Wyatt, R.J. Cerebral ventricular enlargement in chronic schizophrenia: An assessment with poor response to treatment. *Arch. Gen. Psychiatry*, 37:11-13, 1980.

Computer EEG Drug Data Base in Psychopharmacology and in Drug Development

Turan M. Itil, M.D.,[1] Gopi N. Menon, M.D.,[2] and Kurt Z. Itil, B.A.[3]

The quantification of human electroencephalogram (EEG) with a digital computer, called computer-analyzed EEG (CEEG™) (Itil 1974), is the only objective method in the development of new psychotropic drugs in humans. The method was developed based on a series of observations and hypotheses.

One of these observations has been that all drugs that are effective on human behavior (psychotropic drugs) also produce changes in human brain function, which can be established by scalp recorded EEG. Some of the psychotropic drug-induced changes in EEG are relatively minimal and therefore difficult to evaluate visually. Thus, it is imperative that the EEG be quantified. The most advanced quantifications of EEG are via specific-purpose computers. Although it is recorded with similar equipment, and the recorded activities on paper are the same, the computer-analyzed EEG for psychotropic drug development is distinctly different from neurologically used "conventional" EEGs for clinical diagnosis. Whereas a "conventional" EEG is primarily concerned with very slow waves (less than 7 cps) and "abnormal" waveforms such as sharp waves, spikes, spikes and waves, focal abnormalities, and paroxysmal activities, the CEEG™ for psychopharmacology is primarily concerned with "normal" waveforms, and normal frequency (alpha, beta, and faster activities) and amplitude distributions. Only 3 of the 22 measurements of a CEEG™ (period analysis) are used in a conventional "clinical" EEG. The remainder of the 19 measurements are not considered in the conventional electroencephalography for the purpose of clinical diagnosis, although they are important in psychopharmacology. Therefore, in order to differentiate from the conventional EEG, the computer-analyzed EEG was termed "computer-analyzed bio-electrical potentials" (CABP) or "computerized EEG" (CEEG™) by Itil (1974) or cerebral electrometry by Fink (1974).

CEEG™ is most successfully applied during Phase I "safety" clinical pharmacology trials and Phase II psychotropic drug studies using the methods of quantitative pharmaco-EEG (QPEEG™) (Itil 1974; Itil et al. 1971). QPEEG™ is the method involving the use of digital computer-analyzed EEG and a series of statistical procedures for the establishment of the mode of action of a new compound in humans after an orally administered single dose. More specifically, this method can help to:

A. Determine the potency (quantity) of *central nervous system (CNS)* effects;

B. Estimate the *onset and duration* of the CNS effects;

C. Predict clinical usefulness *(psychotropic properties)* of new drugs.

Until recently, the CEEG™ drug classification system was subjective. Classification was made based on "visual inspection" of CEEG™ profiles of a compound. More recently, the technique has become automated and objective. In the past ten years, the CEEG™ profiles of a variety of marketed psychotropic drugs were obtained in standard trials using the QPEEG™ method. These data have recently been reanalyzed using both period analysis and EEG power spectral density analysis programs, and stored in a data base format in a minicomputer. The HZI Research Center computer data base includes the CEEG™ effects of 105 clinically well-known psychotropic compounds in 810 male and female volunteer subjects in the age range of 21 to 35, collected in 92 QPEEG™ studies. When a new drug is studied, first its CEEG™ profile is obtained based on a QPEEG™ trial. Subsequently, the CEEG™ profiles of this compound are compared with the CEEG™ profiles of data base psychotropic drugs using correlation statistics to classify the new drug.

Replicability, reliability, and validity of the HZI computer data base to classify psychotropic drugs were tested in a series of studies (Itil et al. 1981). It was established that the computer data base is able to classify the marketed anxiolytics, psychostimulants, and antidepressants statistically significantly better than chance ($p < .00001$ for anxiolytics, $p < .00001$ for psychostimulants, and $p < .0001$ for antidepressants; binomial statistics). Classification of marketed neuroleptics was not better than chance, in part because the doses of neuroleptics administered in these studies were less than those used for therapeutic purposes in clinical practice.

---

[1] Division of Biological Psychiatry, New York Medical College, Valhalla, NY 10591.
[2] HZI-Europe, Amsterdam, The Netherlands.
[3] HZI Research Center, Tarrytown, NY 10591.

Investigations in recent years have demonstrated (Itil et al. 1977, 1979, 1980) that application of the CEEG™ and a computer EEG drug data base are helpful not only in *quantitatively determining* the central nervous system (CNS) effects of drugs as well as the lowest CNS effective dose and *predicting psychotropic properties* of compounds, but also in predicting *psychotropic potency* and the *lowest psychotropic effective single dose* of a new compound using QPEEG™ methodology.

In this paper the use of CEEG™ will be presented in a series of Phase I single-dose tolerance and safety studies.

QPEEG™ Studies

Etizolam*

ETIZOLAM (Y-7131) [6-(o-Chlorophenyl)-8-ethyl-1-methyl-4H-s-triazolo (3,4-c) thierno(2,3-e) (1,4)diazepine] is a new derivative of the thienodiazepines and has biochemical profiles similar to diazepam, but differs from it in exhibiting an inhibitory effect on the NE turnover and its uptake; thus, antidepressant effects of etizolam were also predicted.

A double-blind crossover QPEEG™ study with latin-square design was conducted in 10 healthy male and female volunteers. Etizolam was orally administered in single doses of 0.5 mg, 1 mg, and 2 mg. Control compounds were 5 mg diazepam, and placebo. CEEG™ recordings were done pre, 1,3, and 6 hours after drug. The results were as follows:

1 - CNS effects of all dosages of etizolam and 5 mg diazepam could be discriminated (multivariate randomized T^2) from placebo at the statistical level ($p = .05 - .002$). Therefore, the lowest CNS effective dose of etizolam was established as 0.5 mg. Etizolam also produced statistically significant dose- and time-related CNS effects.

2 - The mode of action of etizolam resembled that of benzodiazepine anxiolytics. The HZI Research Center computer drug data base classified all doses of etizolam as anxiolytic (Figure 1). The similarity coefficient with data base anxiolytics was for 0.5 mg etizolam = .7 (mean), for 1 mg = .79, for 2 mg = .90. The control compound (5 mg diazepam) was also classified as anxiolytic, which indicated that the data collection and analysis systems were accurate and the subjects adequately responded to an anxiolytic. Based on a two-dimensional drug classification system, it was demonstrated that the CNS effects of etizolam, next to anxiolytics, showed greater similarity to tricyclic antidepressants than those of diazepam (similarity coefficient was .82).

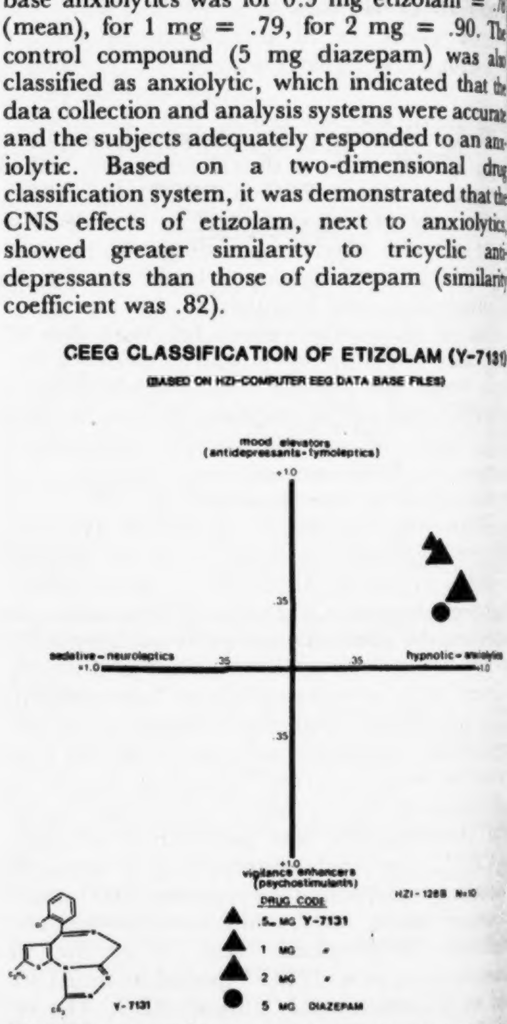


FIGURE 1. According to a two-dimensional classificati system (based on the two highest similarity coeffici with computer data base drug groups), all doses etizolam and diazepam were classified primarily hypnotic-anxiolytic and secondarily as antidepres (mood elevator). The highest hypnotic-anxiolytic prop ty was seen with 2 mg etizolam and the lowest with 0.5 etizolam; particularly the lower doses showed more elevator effects than that of diazepam.

---

*Yoshitomi Pharmaceutical Industries Ltd., Osaka 540-91, Japan.

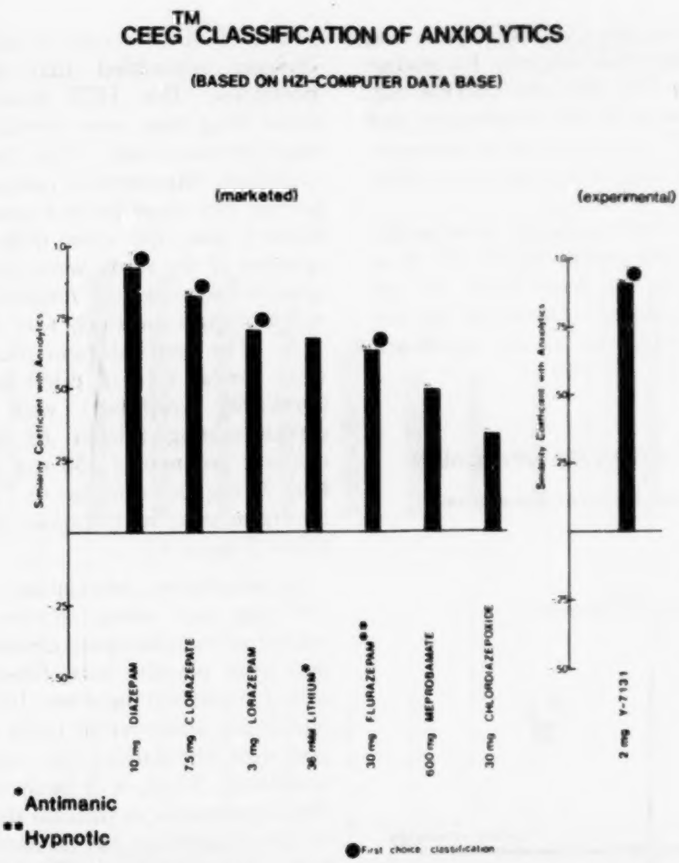


FIGURE 2. Among the marketed anxiolytics, diazepam showed the highest similarity coefficient with data base anxiolytics, and chlordiazepoxide the lowest; etizolam's (2 mg) similarity coefficient was slightly less than that of 10 mg diazepam.

3 - The anxiolytic potency of etizolam with 2 mg was slightly less than 10 mg diazepam but more than 7.5 clorazepate and 3 mg lorazepam (Figure 2).

4 - The minimum psychotropic effective single dose of etizolam probably starts lower than the minimum dose (0.5 mg) administered in this study.

In conclusion, it was established that etizolam is a very potent CNS effective compound with a significant effect on the CNS system at 0.5 mg or even lower. Its mode of action is similar to those of benzodiazepine hypnotic-anxiolytics. Thus, it is predicted to be effective in anxiety patients. The hypnotic-anxiolytic potency of 2 mg etizolam was found to be just slightly less than 10 mg diazepam. In clinical trials, the use of a 0.5 mg single dose is recommended.

Binodaline

BINODALINE (Sgd - Scha 1059)*. (1-[W-dimethylaminoethyl-methyl]-amino-3-phenyl-indole hydrochloride) is a compound with mood elevating properties similar to imipramine but stronger than amitriptyline, dibenzepin, and dimethacrine. It has neither monoamine oxidase-inhibiting properties nor anticholinergic activity. It has been shown to be devoid of serious toxic effects in animal toxicological studies.

---

*Siegfried AG, Zofingen, Switzerland.

pages tightly bound

A double-blind crossover QPEEG™ study was conducted in 10 healthy male subjects. Binodaline was used in four doses 150, 300, 450, and 600 mg. Control compounds were 50 mg imipramine, and placebo. The CEEG™ recordings were done pre, 1,3, and 6 hours after drug or placebo administration. The results were as follows:

1 - The CNS effects of binodaline could be discriminated (multivariate randomized T^2) from placebo in 300 and 600 mg doses (p = .01 and .05, respectively). However, binodaline did not produce any appreciable statistically significant dose- and time-related CNS effects.

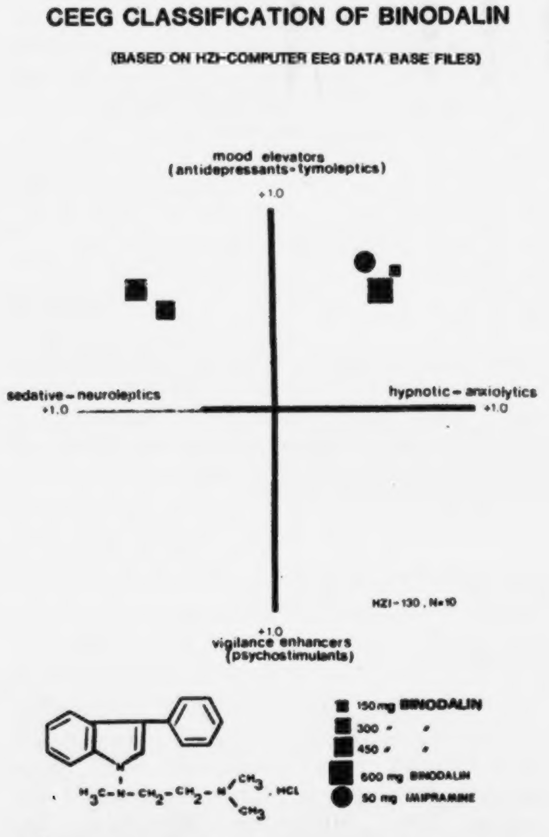


FIGURE 3. Based on the two-dimensional classification system, all dosages of binodaline were classified primarily as mood elevator, whereas 150 and 600 mg also showed hypnotic-anxiolytic properties, and 300 and 450 mg showed secondary sedative-neuroleptic effects. Imipramine was classified primarily as mood elevator and secondarily as hypnotic-anxiolytic.

2 - Mode of action of binodaline in all four dosages resembled that of tricyclic antidepressants. The HZI Research Center computer drug data base classified all dosages as a mood elevator with a first choice (Figure 3). Imipramine, the control compound, was, as expected, also classified as a mood elevator. This indicated that the data collection and analysis systems of the study were reliable, subjects adequately and accurately responded to a known mood elevator, and the study was therefore valid.

3 - The mood elevator potencies of binodaline were similar to each other in all dosages tested (similarity coefficient with data base mood elevators ranged from .64 to .77). The mood elevator potency of 150 mg binodaline was less than 75 mg amitriptyline or 75 mg imipramine or 30 mg mianserin, but more than 75 mg nortriptyline (Figure 4).

In conclusion, binodaline, in doses as low as 150 mg, has mood elevator-like CNS effects similar to tricyclic mood elevators. Its discrimination from placebo was, however, possible only with 300 and 600 mg doses. It did not produce any significant dose-related CNS effects. These suggest that binodaline may have high biological variability. Thus, it is likely to have therapeutic effects primarily in selected depressed patients.

Oxiracetam*

OXIRACETAM (ISF-2522)(4-hydroxy-2-oxo-1-pyrrolidinacestamide) is a gaba-gabob derivative similar to piracetam, and was found to be active on both some behavioral tests and brain biochemical parameters indicative for improvement of learning and memory (Pifferi et al. 1976). Based on animal toxicological data, it was predicted that oxiracetam can be administered in humans up to 2400 mg single dose without any serious side effects.

A single rising dose tolerance and efficacy study was conducted with oxiracetam in seven healthy subjects using a QPEEG™ study design. Five dosages of oxiracetam (200, 400, 800, 1200, and 2400 mg) were administered with randomized control compounds (15 mg dextroamphetamine, 1200 mg piracetam, placebo). The results were as follows:

---

*ISF S.p.A.-Milano, Italy.

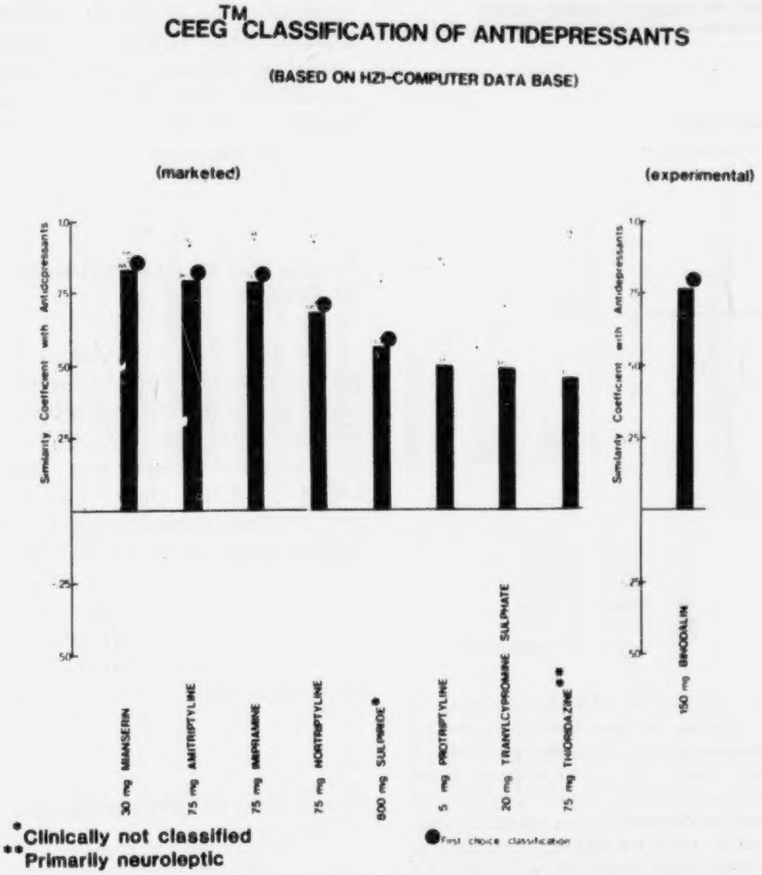


FIGURE 4. Among the marketed mood elevators, mianserin showed the highest, and thioridazine the lowest similarity coefficient with data base mood elevators. In this dose the mood-elevating properties of binodaline were less than mianserin (30 mg), amitriptyline (75 mg), and imipramine (75 mg), but more than nortriptyline (75 mg).

1 - The CNS effects of oxiracetam could be discriminated (univariate statistics) from placebo in dosages of 1200 and 2400 mg. Certain CEEG™ measurements indicated dose and time-related CNS effects of oxiracetam (regression analysis).

2 - The mode of action of oxiracetam on brain function is similar to that of vigilance-enhancing ("psychostimulant") compounds. The HZI Research Center computer drug data base classified oxiracetam in doses of 1200 mg (third choice) and 2400 mg (first choice) as a vigilance enhancing compound similar to 1200 mg piracetam and 15 mg dextroamphetamine (Figure 5).

3 - Based on the comparison of the similarity coefficients of oxiracetam with those of marketed vigilance enhancing compounds, it was predicted that 2400 mg oxiracetam would have vigilance enhancing effects which are less than 20 mg dextroamphetamine but more than 200 mg caffeine or 1200 mg piracetam (Figure 6).

4 - The lowest clinically therapeutic single dose of oxiracetam, which is safe and CNS effective, was predicted to be 1200 mg.

A double-blind clinical trial confirmed the CEEG™ prediction. Oxiracetam is effective in the improvement of memory, similar to piracetam, in daily doses of 2400 mg (Itil et al. in press).

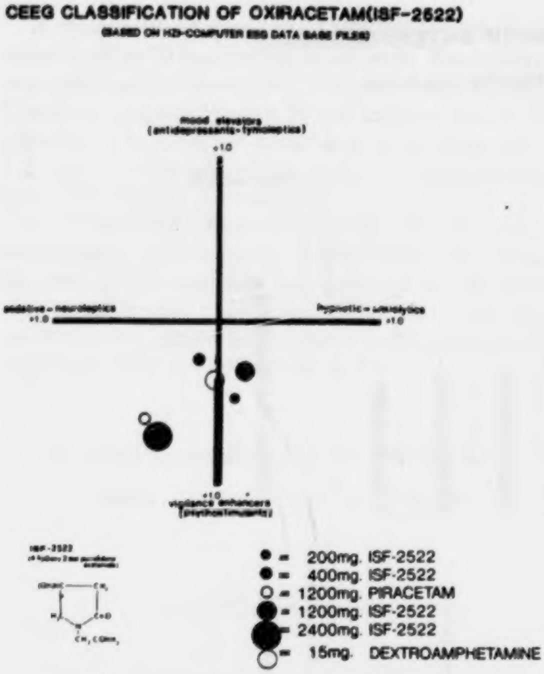


FIGURE 5. CEEG™ profiles of different dosages of ISF-2522 and control compounds were classified based on the HZI Research Center computer drug data base using a two-dimensional model. Correlation coefficients are based on the four recording conditions (1 hr and 3 hr RR and RT recordings), Dextroamphetamine was classified only as a vigilance enhancer, with no positive correlations with other drug groups. Four hundred and 2400 mg ISF-2522 and piracetam were classified between vigilance enhancers and sedative-neuroleptics, whereas 200 mg ISF-2522 and 1200 mg ISF-2522 were classified between vigilance enhancers and hypnotic-anxiolytics.

Conclusion

The use of CEEG™ in early drug screening (Phase 1) in man using QPEEG™ methodology and a computer EEG data base of established drugs is useful for the following:

Establishment of CNS Efficacy of Drugs

All clinically useful psychotropic drugs possess significant effects on human brain function, as established by computer analyzed scalp recorde human EEG (CEEG™). Accordingly, to be useful psychotropic, a new compound must ha significant CNS effects. This can be determine by discrimination of the CEEG™ effects of a dru from placebo, and by establishing dose and tim related CNS effects.

Prediction of Psychotropic Properties of Drugs

The HZI Research Center drug data base ca predict psychotropic properties of drugs afte single oral dose administration. The validity and reliability of the HZI data base to classify psychotropic drugs was successfully tested. CEEG™ drug data base classification of psychotropic properties can be independent of the animal pharmacology and biochemical properties or chemical structures of drugs. This was demonstrated through the discovery of psychotropic properties of drugs via CEEG™, which did not possess the "typical" pharmacological action of marketed psychotropics (It 1981).

Prediction of "Psychotropic Potency" of Drugs

It was established that the clinically most poten drugs also produce the most "typical" CEEG™ profiles, which show the highest similarity coefficient with the data base drugs.

Prediction of "Psychotropic Effective" Dos

The classification of the CEEG™ profiles of different doses of well-known drugs demonstrated that the minimum single dose, tolerable in man, and can be discriminated from placebo, and i classified by the HZI data base as psychotropic, i also similar to the clinically therapeutically effective single three times a day (t.i.d.) or four times a day (q.i.d.) dose (Figure 7).

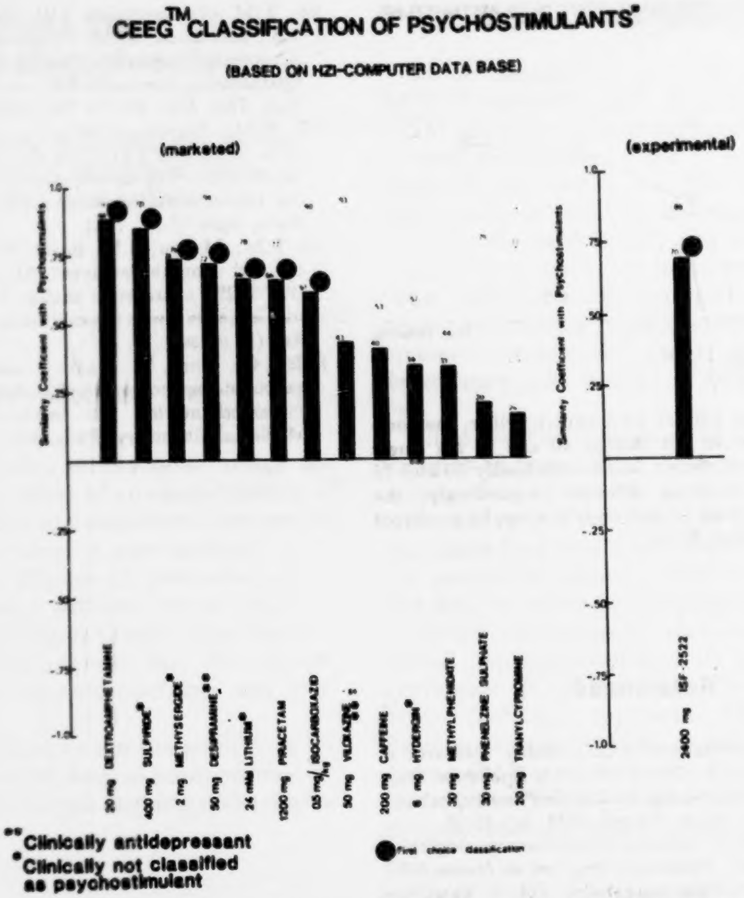


FIGURE 6. Of the marketed compounds which have some vigilance-enhancing properties, dextroamphetamine showed the highest, and tranylcypromine the lowest similarity coefficient with data base vigilance enhancers. Oxiracetam (2400) mg) has less vigilance-enhancing properties than 20 mg dextroamphetamine but more than 200 mg caffeine.

If a drug has significant CNS effects (discrimination from placebo) but cannot be classified by the data base, it is hypothesized that this compound has a different mode of action from existing major psychotropic drug groups (hypnotic-anxiolytics, mood elevators, sedative-neuroleptics, and vigilance enhancers); thus, it will have a new type of psychotropic property. On the other hand, if a drug is classified by the computer data base but cannot be discriminated from placebo, it is assumed either the dose studied is low, or sample size too small, or biological variability of this compound is too high; thus, this compound will not be a broad spectrum, effective psychotropic.

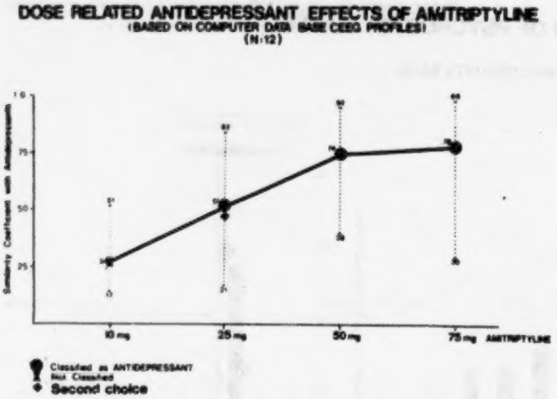


FIGURE 7. In our studies with amitriptyline, the computer data base could not classify 10 and 25 mg single dosages, with a first choice, but could classify 50 and 75 mg dosages as a mood elevator. Accordingly, the therapeutic single dose of amitriptyline can be predicted to be between 25 and 50 mg.

References

Fink, M. EEG profiles and bioavailability measures of psychoactive drugs. In: Itil, T.M. (ed.), *Psychotropic Drugs and the Human EEG, Modern Problems in Pharmacopsychiatry,* Vol. 8. Basel/New York: Karger, 1974, pp. 76-98.

Itil, T.M. Quantitative pharmaco-electroencephalography. In: Itil, T.M. (ed.), *Psychotropic Drugs and the Human EEG, Modern Problems in Pharmacopsychiatry,* Vol. 8. Basel/New York: Karger, 1974, pp. 43-75.

Itil, T.M. The discovery of psychotropic drugs by computer-analyzed cerebral bioelectrical potentials (CEEG). *Drug Develop. Res.*, 1:373-407, 1981.

Itil, T.M., Guven, F., Cora, R., Hsu, W., Polvan, N., Ucok, A., Sanseigne, A., and Ulett, G.A. Quantitative pharmaco-electroencephalography using frequency analyzer and digital computer methods in early drug evaluations. In: Smith, W.L. (ed.), *Drugs, Development, and Brain Functions.* Springfield, Ill.: Charles C Thomas, 1971, pp. 145-166.

Itil, T.M., Polvan, N., Engin, L., Guthrie, M.B., and Huque, M. Fluotracen (SKF-28175), a new thymo-neuroleptic with rapid action and long-acting properties (Quantitative pharmaco-EEG and clinical trials in the development of fluotracen [SKF-28175]). *Curr. Ther. Res.*, 21(3):343-360, 1977.

Itil, T.M., Soldatos, C., Bozak, M., Ramadanoglu, E., Dayican, G., Morgan, V., and Menon, G.N. CNS effects of ISF-2522, a new nootropic (a Phase I safety and CNS efficacy study with quantitative pharmaco-EEG and pharmaco-psychology). *Curr. Ther. Res.*, 26(5):525-538, 1979.

Itil, T.M., Frederickson, J.W., Schneider, S.J., Francis, I.B., and Khan, M.M. Clopipazan (SKF-69634), a new neuroleptic essentially free of extrapyramidal liability: Quantitative pharmacol-EEG and open label clinical trial. *Curr. Ther. Res.*, 27:719-730, 1980.

Itil, T.M., Shapiro, D.M., Lucadamo, F., and Menon, G.N. Computer EEG drug data base, a new method for psychotropic drug development in man. Proceedings of the 4th International Meeting of Pharmaceutical Physicians, Paris, April 27-30, 1981.

Itil, T.M., Menon, G.N., Bozak, M., and Songar, A. Clinical and computer-analyzed EEG effects of Oxiracetam (ISF-2522), a piracetam analog: A double-blind controlled trial in patients with organic brain syndrome. *Drug Develop. Res.* (In press)

Pifferi, C., Pinza, M., Banfi, S, and Tesa, E. Cyclic gaba-gabob analogs potentially active in learning and memory. Presented at the 4th International Symposium on Medicinal Chemistry, Paris, July 19-22, 1976.

The First Clinical Study of BW-234U in Schizophrenia

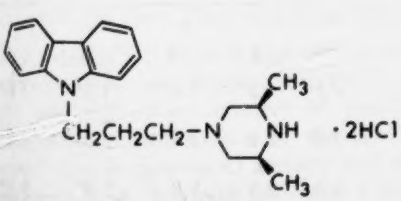
Jonathan Davidson, M.D.,[2] Robert Miller, M.D., Ph.D.,[1,2] Martha Wingfield, M.D.,[1,3] William Zung, M.D.,[2] and Anthony T. Dren, Ph.D.[4]

Introduction

Currently available antipsychotic drugs are associated with a number of unwanted effects, of which extrapyramidal and autonomic changes are particularly troublesome. A new carbazole compound, BW-234U, (Figure 1), promises to have antipsychotic activity without concomitant extrapyramidal or autonomic change. The results of testing BW-234U in animals, and the relevant underlying models, are presented elsewhere (Ferris et al. 1982).

This report describes an interim analysis in the first clinical study of the drug in schizophrenic inpatients; this study was still ongoing at the time of the report.

BW 234U



cis-9-[3-(3,5-Dimethyl-1-piperazinyl)propyl]carbazole dihydrochloride

FIGURE 1

Method

To be included in the study patients had to fulfill Diagnostic and Statistical Manual-III (DSM-III) criteria for schizophrenia, give informed consent, be between 18 and 55 years of age, be in good physical health, and have clinically acceptable values on SMA12, hematology, urinalysis, electrocardiograph (ECG), and electroencephalograph (EEG). Excluded from the study were patients with medically unstable illness, organic brain syndrome, mental retardation, blood pressure outside the range of 150/90, drug dependency, and women of childbearing potential.

All patients were assigned to receive BW-234U for up to 28 days. When the study was initiated, a starting dose of 100-200 mg/day was used, to be increased up to a maximum of 600 mg/day. This maximum limit was later reduced to 400 mg after one patient developed a seizure. Dosing, which was flexible, was administered on a b.i.d. basis.

Weekly assessments included the Clinical Global Impressions of Severity (CGI-S) and Improvement (CGI-I), Brief Psychiatric Rating Scale (BPRS), Inpatient Multidimensional Psychiatric Scale (IMPS), as well as the Simpson-Angus (SA) and Abnormal Involuntary Movement Scale (AIMS) scales which measured extrapyramidal and other movement disorder.

Results

Twelve patients entered the study, one dropping out within a week for family reasons unrelated to treatment. Eleven patients completed a minimum 3-week treatment and nine completed 4 weeks. One terminated treatment at 3 weeks because of a seizure, and the other recovered and was discharged. Baseline demographic data showed that all patients were male, eight were white and three black, mean age was 27.1 years (range 18 to 42). Ten patients were unmarried and one was separated. Using DSM-III subtypes, six patients had paranoid schizophrenia, four, chronic undifferentiated, and one, disorganized schizophrenia.

Mean doses at each weekly assessment were as follows: 295, 327, 363, and 344 mg/day. The median doses at each time were 300, 300, 400, and 300 mg.

---

[1] John Umstead Hospital, Butner, NC 27509.

[2] Duke University Medical Center, Department of Psychiatry, Durham, NC 27706.

[3] University of North Carolina, Department of Neurology, Chapel Hill, NC 27514,

[4] Wellcome Research Laboratories, Research Triangle Park, NC 27709.

CLINICAL GLOBAL IMPRESSION (CGI) SCALE

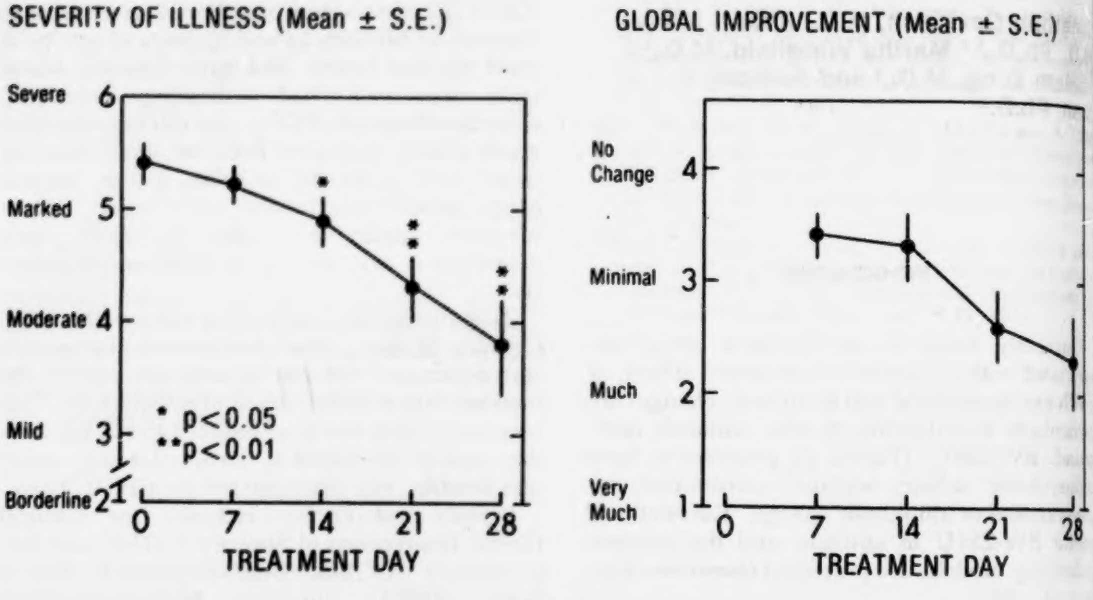
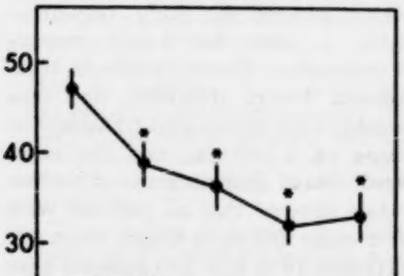


FIGURE 2

BRIEF PSYCHIATRIC RATING SCALE (BPRS)

TOTAL BPRS SCORES (Mean ± S.E.)



BPRS FACTOR SCORES (Means)

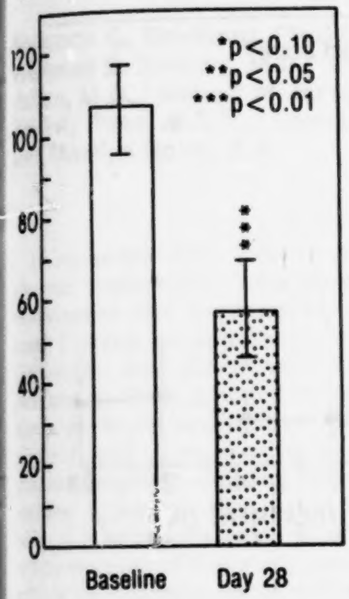
	Factor	Bo	1	2	3	4
I.	Anxiety/Depression	2.6	1.9*	1.8**	1.6**	1.6**
II.	Anergia	3.0	2.6	2.4**	2.0**	2.3*
III.	Thought Disturbance	3.1	2.8	2.6	2.3*	2.4*
IV.	Activation	1.4	1.4	1.3	1.3	1.2
V.	Hostile/Suspiciousness	2.1	1.8	1.8	1.6*	1.6*

*p<0.05; **p<0.01

FIGURE 3

INPATIENT MULTIDIMENSIONAL PSYCHIATRIC SCALE (IMPS)

TOTAL IMPS SCORES (Mean ± S.E.)



IMPS FACTOR SCORES (Means)

	Factor	Baseline	Day 28
I.	Excitement	4.0	1.0*
II.	Hostile/Belligerence	7.1	3.5*
III.	Paranoid Projection	6.1	3.5**
IV.	Grandiose Expansiveness	2.1	0.6*
V.	Perception Distortion	11.7	4.8***
VI.	Anxious/Intropunitiveness	16.1	6.5***
VII.	Retardation/Apathy	22.7	15.3*
VIII.	Disorientation	0.3	0.3
IX.	Motor Disturbances	3.6	1.7
X.	Conceptual Disorganization	2.8	1.5

FIGURE 4

Efficacy Scales

As shown in Figure 2, Global Severity of Illness decreased at each week from a baseline score of 5.3 to 3.8 by Week 4. This change was statistically significant at Weeks 2, 3, and 4. Overall improvement on the CGI-I was also noted.

The total BPRS score declined from 45.2 before treatment to 33.5 at Week 4 (Figure 3). Improvement was significant relative to baseline at all time points. Examination of the BPRS factors showed that symptoms of anxiety and depression responded first, followed at Week 2 by anergia, and at Week 3 by improvement on thought disorder, hostility, and suspiciousness.

Use of the IMPS (Figure 4) at pretreatment and termination showed a significant improvement on paranoid projection, perceptual distortion, anxious intropunitiveness, and on the total score.

Safety Data

No changes were noted on the SA and AIMS scales (Figure 5), consistent with the original expectation that this drug has few extrapyramidal side effects. The scores noted on the SA scale are similar to that found with placebo (Simpson & Angus 1971).

Clinical chemistry and hematology were performed weekly. Modest elevations of alkaline phosphatase (three patients), SGOT (four patients), and LDH (four patients) were noted. These gradually returned to normal after the drug was discontinued, or other neuroleptics substituted.

No significant changes were observed on blood pressure, pulse, weight, ECG, or EEG.

A number of adverse events noted in the study were judged to be drug related. These were as follows (number of patients in parentheses): seizure (1), fatigue (3), sleepiness (3), nausea (2), tremor (1), headache (1), insomnia (1), anorexia (1), diarrhea (1), gas (1).

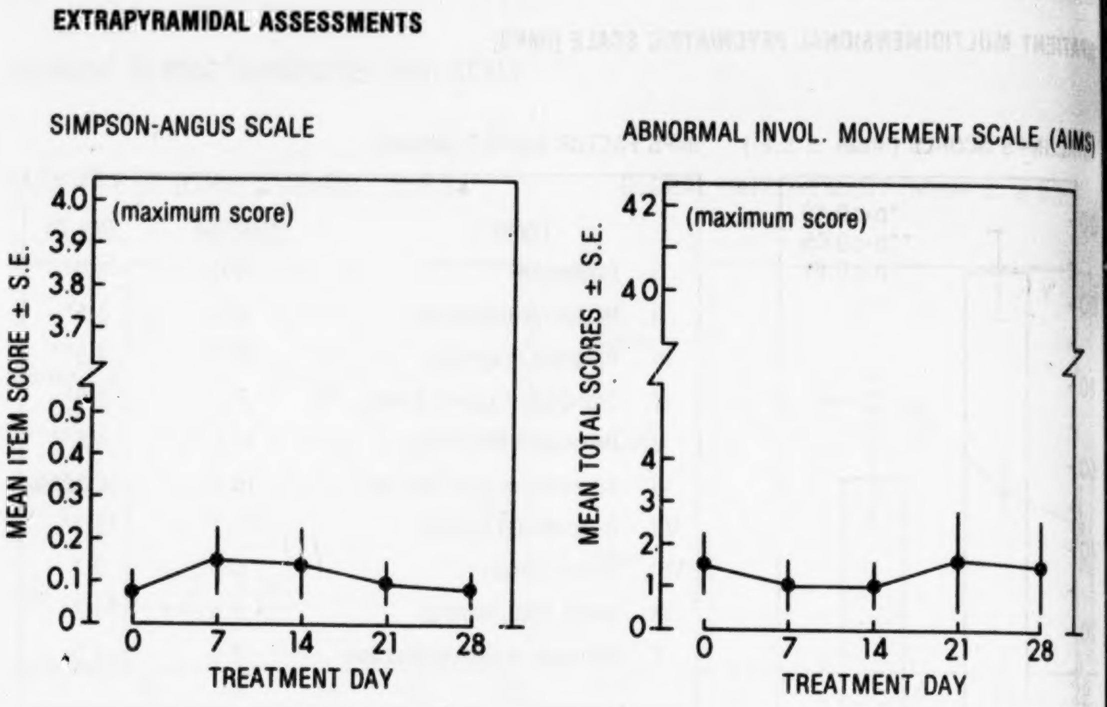


FIGURE 5

Summary

BW-234U is a well-tolerated antipsychotic agent in this acute schizophrenic population and has a low potential for inducing extrapyramidal or autonomic side effects. The efficacy which was seen needs to be confirmed by further controlled studies. The full dose range of this drug has yet to be determined.

References

Ferris, R.M., McKenzie, G., Cooper B., Soroko, F., an Maxwell, R.A. BW-234 U (*cis*-9 (3,5-Dimethyl-l-pipe azinyl) propyl carbazole ·2· HCL): A new anti psychotic agent. *J. Pharm. Pharmacol.*, 34:388-390, 1982.

Simpson, G.M., and Angus, J.W. A rating scale for extr pyramidal side effects. *Acta Psychiatr. Scand.*, (Suppl.) 212:11-19, 1970.

Does Long-Acting Injectable Neuroleptic Protect Against Tardive Dyskinesia?

Solomon C. Goldberg, Ph.D.[1] Ramakrishnan S. Shenoy, M.D.,[1] Demetrios Julius, M.D.,[1] Robert M. Hamer, Ph.D.,[1] Beverly Ross, M.S.N.,[1] Teena Minton, R.N.,[1] and Marilyn Spiro, B.A.[1]

In an earlier study (Shenoy et al. 1981) of 34 chronic ambulatory schizophrenics who were maintained with fluphenazine decanoate for at least 2 years, an unusually low level of tardive dyskinesia was discovered compared to comparable patients reported in the literature. If anybody should have tardive dyskinesia, these patients should. It occurred to the authors that the patients might be suffering from a form of covert tardive dyskinesia that would become manifest only if medications were withdrawn. Since one major purpose of that study was to determine the effects on symptom status and tardive dyskinesia of discontinuation of drug therapy, there was the opportunity to see whether patients who initially showed no tardive dyskinesia would manifest any after being withdrawn from medication. Half the patients were randomly discontinued for a period of 6 weeks. Within that period, there was essentially no change in the level of tardive dyskinesia, either in the group that continued on medication or the random group that was withdrawn. Tardive dyskinesia was assessed by means of the Abnormal Involuntary Movements Scale (AIMS), a commonly employed instrument for this purpose. Inter-rater reliability was shown to be substantial.

That group of chronic ambulatory patients maintained on fluphenazine decanoate is part of a larger group of like patients who are maintained on a variety of oral neuroleptics. The patients on the long-acting injectable medication had been assigned to it years earlier because there had been problems in medication compliance with oral medication.

The obvious next step was to determine the level of dyskinesia in the larger group of patients on oral medication. If they showed the same low level, the results would be consistent, but puzzling. If they showed a higher level of tardive dyskinesia, the results would imply a protective or ameliorative mechanism in the injectable form of the medication.

Patients

The patients were 76 primarily male chronic ambulatory schizphrenic patients who were maintained on a variety of oral neuroleptics for at least the past 2 years. Patients whose medications included antidepressants or lithium were not included in this sample. These patients lived in the community even though they occasionally manifested a moderate level of schizophrenic symptomatology. The patients had had multiple prior hospitalizations for schizophrenic episodes, even after being placed on maintenance medication.

Assessment of Tardive Dyskinesia

Symptoms of tardive dyskinesia were assessed by means of the Abnormal Involuntary Movements Scale (AIMS) developed for this purpose by the Psychopharmacology Research Branch of the National Institute of Mental Health (1975). Although the words "tardive dyskinesia" are not employed in the scale itself, the particular movements the observer has to record are those that have been identified in the literature pertaining to tardive dyskinesia in contrast to extrapyramidal side effects such as fine tremors, gross dystonic reactions, cogwheel rigidity, and akathisia. After a period of orientation and practice on nonstudy patients, the 76 patients were observed for tardive dyskinesia by one of three rating team pairs. Each rating team saw only a portion of the 76 patients.

Results

Reliability of Measurement

In observing the patients for tardive dyskinesia, one member of the rating team took the responsibility for conducting the procedure and asking questions, while both members of the team rated the patient simultaneously. Rating team members would alternate conducting the examination. Immediately after a patient was rated, there was a postmortem comparison of the ratings given, but no changes were allowed to be made even if there were differences. Discussion of rating differences served as continuing training in the procedure and would hopefully have a beneficial effect on greater reliability on the subsequent occasions. Under these conditions, the rater agreement reliability by means of an intraclass correlation was .83 for global severity of tardive dyskinesia; for the sum of the seven specific items, intraclass correlation was .91. These levels of rater agreement compare favorably with those obtained on ratings of psychopathology.

---

[1] Medical College of Virginia, Richmond, VA 23298.

Oral versus Depot Medication Maintenance on Tardive Dyskinesia

The Table shows the percent distribution of each item on the AIMS for the two medication groups. There is very obviously a greater prevalence of tardive dyskinesia in the group maintained on oral medications than in the group maintained on fluphenazine decanoate. The size of the significant differences in descending order are: a) tongue, b) face muscles, c) jaw, and d) eyes and perioral area. Nonsignificant differences were found for a) arms, wrists, hands, and fingers ($p = .089$) and b) legs, knees, ankles, and toes ($p = .26$).

Both age and duration of treatment were correlated with tardive dyskinesia. When entered as covarates, they reduced but did not eliminate the significant difference between medication groups. Measures of organicity in these patients were not available as another measure of risk for tardive dyskinesia.

Discussion

The results imply either that fluphenazine decanoate reduces the level of tardive dyskinesia if it is present, or protects against its development if not present.

If it is true that fluphenazine decanoate is le productive of tardive dyskinesia, what might the possible mechanism of action be? Baldessarin and Tarsy (1978) cite evidence supporting the interpretation that tardive dyskinesia "is associated with a state of relative dopaminergic overactivi or supersensitivity." This would account for worsening on withdrawal of dopamine-antagonistic neuroleptic drugs and worsening on administration of L-DOPA. Tune et al. (1980) found lower steady-state blood levels in patients who are maintained on long-acting injectable medication. It may then be that the oral medication is providing a higher steady-state blood level than is therapeutically required, bombards the post-synaptic receptors, and renders them "supersensitive." Tune et al. did not show a link between blood level and tardive dyskinesia, which now becomes a next obvious next step in research.

From a practical clinical point of view, the authors are not yet in a position to conclude that switching to the injectable form will reduce tardive dyskinesia. It is conceivable that the depot neuroleptic protects against the development of tardive dyskinesia if not present; but once tardive dyskinesia does become apparent, it may be persistent and hence may not be affected by switching to another form of medication. While the foregoing is possible, it is not a certainty, and the first and easier procedure to try on a patient with tardive dyskinesia would be a change to the long acting form. In the context of a formal study, this would be done by randomly assigning a group with tardive dyskinesia who are being maintained on oral medication to a) either continuing on the oral, or b) changing to the long-acting form However, for those practitioners who are not in position to undertake formal research, they have nothing to lose by trying on an open, informa basis a change to long-acting medication in those patients suffering from moderate to severe tardive dyskinesia.

References

Baldessarini, R.J., and Tarsey, D. Tardive dyskinesia. I Lipton, M.A., DiMascio, A., and Kilam, K.F. (eds *Psychopharmacology: A Generation of Progress*. New Yor Raven Press, 1978, pp. 993-1004.

Psychopharmacology Research Branch, NIMH. Abnorma Involuntary Movements Scale. *ECDEU Interco* 4(1):3-6, 1975.

Shenoy, R.S., Sadler, A.G., Goldberg, S.C., Hamer, R.M., and Ross, B. Effects of a 6-week drug holiday on symptom status, relapse, and tardive dyskinesia in chronic schizophrenics. *J. Clin. Psychopharm.*, 1:141-145, 1981.

Tune, L.E., Creese, I., Coyle, V.T., Pearlson, G., and Snyder, S.H. Low neuroleptic serum levels in patients receiving fluphenazine decanoate. *Am. J. Psychiatry*, 137:80-82, 1980.

Table

Percent Distributions of AIMS Items for Patients on Oral Neuroleptic (*N* = 76) vs. Fluphenazine Decanoate (*N* = 31)

	Percent (rounded)					
Item	Absent	Minimal	Mild	Moderate	Severe	*P*
1. Muscles of Facial Expression						
Oral neuroleptic	67	12	14	6	1	
Fluphenazine deconoate	98	2	0	0	0	.0004
2. Lips and Perioral Area						
Oral neuroleptic	50	16	11	13	2	
Fluphenazine decanoate	63	31	6	0	0	.0099
3. Jaw						
Oral neuroleptic	68	11	9	11	1	
Fluphenazine decanoate	92	6	2	0	0	.0041
4. Tongue						
Oral neuroleptic	38	22	26	10	5	
Fluphenazine decanoate	76	13	8	3	0	.0003
5. Upper extremities						
Oral neuroleptic	56	11	13	17	3	
Fluphenazine decanoate	66	13	18	3	0	.0898
6. Lower extremities						
Oral neuroleptic	72	9	11	7	1	
Fluphenazine decanoate	84	5	8	0	3	.2636
7. Neck, shoulders, hips						
Oral neuroleptic	86	5	3	3	3	
Fluphenazine decanoate	91	3	3	3	0	.5756
8. Global Severity						
Oral neuroleptic	22	37	22	16	3	
Fluphenazine decanoate	32	44	21	0	3	.0525
9. Incapacitation						
Oral neuroleptic	75	16	4	2	3	
Fluphenazine decanoate	81	16	0	3	0	.3634
10. Patients awareness of movements						
Oral neuroleptic	69	15	8	5	3	
Fluphenazine decanoate	53	29	15	3	0	—
Sum of items 1-7:						
Oral neuroleptic						.0005
Fluphenazine decanoate						

Combined MAOI-Tricylic Antidepressant Treatment: A Controlled Trial

Kerrin White, M.D.,[1] Javad Razani, M.D.,[1] George Simpson, M.D.,[1] Ronald Rebal, M.D.,[1] R. Bruce Sloane, M.D.,[1] Judith O'Leary, M.A.,[1] and Ruby Palmer, R.N., M.A.[1]

The practice of combining monoamine oxidase inhibitor (MAOI) and tricyclic (TCA) antidepressants in treatment has been a source of controversy for nearly two decades. Case reports of severe reactions such as hyperthermic crises, delirium, and seizures led to widespread warnings against concurrent use of MAOIs and TCAs. However, reviewers raised many questions about these case reports, and uncontrolled clinical series on these treatments suggested both reasonable safety and unusually potent antidepressant effects. Until the past few years, no controlled clinical trials had been reported on these questions. The present study represents only the second such trial to use both double-blind methodology and random assignment to treatments.

This study was designed to assess whether combined treatment with tranylcypromine (TCP) and amitriptyline (AMI) has any pronounced advantages or disadvantages compared with single drugs used alone on a relatively heterogeneous group of depressed patients. The combined treatment followed an approach recommended by many clinicians who have used MAOIs and TCAs together: 1) first allowing a drug-free interval of at least 1 week; 2) then starting both drugs together, within the same day, at low dosage; 3) then gradually increasing dosage of both drugs together, to a maximum of half the dosage used with each single drug. This approach was compared with treatments involving the single drugs used alone at full dosage, so that patients in each treatment group would receive about equivalent amounts of "total antidepressant drugs," to avoid confusing simple summation of side-effects with unusual toxic drug interactions.

Seventy-one inpatients and outpatients meeting Diagnostic and Statistical Manual-III (DSM-III) criteria for Major Depression were randomly assigned to a 4-week trial of double-blind treatment with either TCP, AMI, or the TCP-AMI combination. After a fixed starting dosage for the first week (either TCP 20 mg, q a.m., AMI 100 mg, q h.s., or TCP 10 mg, q a.m. plus AMI 50 mg, q h.s.), the treating psychiatrist could adjust dosage upwards on a weekly basis to maxima reached by the beginning of the third week (TCP 20 mg, t.i.d., AMI 300 mg, q h.s. or TCP 10 mg, t.i.d. plus AMI 150 mg, q h.s.).

Ratings of depressive symptoms by the patient and the treating psychiatrist were conducted weekly and included the Hamilton Depression and Anxiety Scales, the Clinial Global Impression, and the Zung Self-Rated Depression Scale. Monitoring for toxicity included a side-effect list completed weekly by the treating psychiatrist; frequent measurement of blood pressure, pulse rate, respiratory rate, temperature and weight; and repeated electrocardiograms, complete blood counts, serum electrolytes, liver function tests, and urinalyses.

Sixty patients completed the study; eleven dropped out prior to the end of the fourth week. Patients sometimes dropped out because of side-effects such as drowsiness or dizziness, but never because of life-threatening adverse reactions such as hyperthermic or hypertensive crises. The dropout rate was highest in the AMI-only group (24 percent) and lowest in the combined TCP-AMI group (5 percent).

There were no statistically significant differences between the three treatment groups at baseline on common demographic characteristics such as age, sex, or education; nor on clinical characteristics such as percentage of patients meeting RDC criteria for endogenicity or degree of symptom severity. Average maximum dosage was 40 mg/day TCP, 239 mg/day AMI, and in the combined treatment group 24 mg/day TCP and 128 mg/day AMI.

The psychiatrists, listing of side effects showed similar side-effect profiles for the three treatments. The most common side effects included dry mouth (72 percent of patients reported this), dizziness (61 percent), sedation (41 percent), and constipation (23 percent). Significant differences between the three treatments were confined to a more frequent association of AMI with dry mouth (90 percent) and tremor (40 percent), and a less frequent association of TCP with anticholinergic effects as a group ($p < .01$). Blood pressure measurements suggested both resting and postural hypotension as effects of TCP, but only postural hypotension with AMI. The combined TCP-AMI treatment showed intermediate effects. Pulse rate and weight increases both seemed more pronounced with AMI.

---

[1] Department of Psychiatry and the Behavioral Sciences, University of Southern California School of Medicine, Los Angeles, CA 90033.

On the four major outcome measures, patients on all three treatments improved to an equivalent degree at about the same rate. Improvement was moderate to marked for 76 percent on TCP, 75 percent on AMI, and 79 percent on TCP-AMI. Analyses of individual symptom items suggested superiority of TCP and TCP-AMI over AMI alone for hypochondriasis ($p < .01$ and $p < .03$, respectively), and superiority for AMI and TCP-AMI over TCP alone for insomnia ($p < .01$ and $p < .01$), as well as advantage for TCP over TCP-AMI on anxious mood ($p < .04$) and TCP over AMI on autonomic anxiety ($p < .05$).

These results indicate quite similar therapeutic and adverse effects for all three treatments. There is certainly no indication of either unusually severe toxicity or unusually potent efficacy for the MAOI-TCA combination as compared to the single drugs used alone. However, some differences in specific side effects and symptom improvement may have clinical relevance. For example, TCP may have an advantage in avoidance of anticholinergic side effects, while AMI or TCP-AMI may have an advantage for insomnia. As in prior research, there are suggestions of an MAOI advantage for "atypical" depressive symptoms such as hypochondriasis and anxiety.

These results support the relative safety of combined MAOI-TCA treatment when used according to specific guidelines such as were followed in this study. It should be emphasized that evidence for apparent safety does *not* extend to certain other ways of combining these drugs. For example, there is substantial case report evidence for hazards in the addition of a TCA to an established course of treatment with an MAOI.

Despite these indications of safety if the MAOI-TCA combination is used according to specific guidelines, there exists virtually no evidence from the few controlled studies to date for any major advantage to such combinations over rigorous treatment with single drugs or ECT. Nevertheless, there are suggestions from clinical experience that some patients refractory to adequate trials of the single drugs may still respond to their combination. This issue has yet to be addressed in controlled research.

For a complete review of the literature, see White and Simpson (1981).

Reference

White, K., and Simpson, G. Combined MAOI-tricyclic antidepressant treatment: A reevaluation. *J. Clin. Psychopharmacol.*, 1:264-282, 1981.

Differential Efficacy of L-Deprenyl, a Selective MAO Type-B Inhibitor, in Endogenous and Nonendogenous Depression

**J. John Mann, M.D.,[1] Allen Frances, M.D.[1]
Eric D. Peselow, M.D.,[2] and Samuel Gershon, M.D.[3]**

Introduction

Recent systematic studies have affirmed the value of classical nonselective monoamine oxidase (MAO) inhibitors as effective antidepressants. Overall these drugs appear effective in nonendogenous depression (Robinson et al. 1973) and perhaps some subgroup(s) of endogenous depression (Himmelhoch et al. 1972; Pare & Mack 1971). MAO inhibitors appear as effective as tricyclics for nonendogenous depression and perhaps superior for any associated anxiety symptoms (Ravaris et al. 1980). There is also evidence for a therapeutic effect in phobic disorders (Tyrer 1980). However, despite the usefulness of these agents, the risks of a hypertensive food or drug interraction, known colloquially as the "cheese" reaction, has remained as a deterrent to the use of MAO inhibitors.

The selective MAO type-A inhibitor clorgyline, although appearing to have antidepressant properties in unipolar patients (Wheatley 1970), also has a significant potential for the hypertensive "cheese" reaction comparable to classical MAO inhibitors (Lader et al. 1972). Therefore it is important to evaluate the MAO type-B inhibitors for safety and antidepressant potential. L-deprenyl is a potent selective MAO type-B inhibitor with a demonstrated safety advantage (Elsworth et al. 1978).

In this study, the effects of L-deprenyl were compared in endogenous and nonendogenous depression. We also monitored the degree of platelet MAO inhibition in order to evaluate whether the level of MAO inhibition would be a factor in determining clinical response in this study.

Methods

Twenty-five patients who met Research Diagnostic Criteria for a major depressive disorder completed the study. The patients were subdivided into endogenous and nonendogenous subgroups using the Newcastle scale.

All patients underwent a single-blind placebo washout for one week to screen out strong placebo responders. Patients who still scored 16 or higher on the first 17 items of the Hamilton Depression Scale (HDS) then underwent 4 weeks of treatment with L-deprenyl. Patients were treated with initial doses of 5-10 mg per day for the first week, building up to a maximum of 15-20 mg per day through weekly dose increments depending on clinical response.

Results

Thirteen patients with endogenous depression and 12 with nonendogenous depression were studied. The groups did not differ significantly on age, sex ratio, and baseline severity of illness as measured by the HDS.

As shown in the Figure, both groups showed a statistically significant amerlioration of depression, but the onset of improvement appeared sooner in the nonendogenous group. The rate of dropout was greater in the endogenous group with three patients dropping out because of lack of therapeutic response and one because of hypomania.

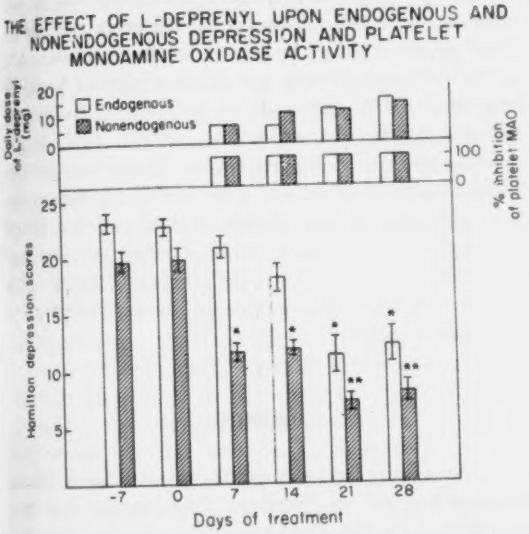
If responders were defined by a >50 percent reduction in Hamilton Score or an endpoint score of ≤ 10 in the HDS, then the endogenous group had 6/13 responders and the nonendogenous group had 10/12 responders. The difference in the rate of responders between the two groups approached significance ($p<0.10$ Fisher Exact Probability Test). Five of seven patients responded in the bipolar endogenous group compared to 1/6 unipolar patients, a non significant difference.

---

[1] Cornell University Medical College, Payne Whitney Clinic, New York, NY 10021.
[2] New York University Medical Center, New York, NY 10016.
[3] Wayne State University, Detroit, MI 48201.

Send reprint requests to: J. John Mann, M.D., Department of Psychiatry, Cornell University Medical College, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021.

All responders in the endogenous group and 9/10 of the nonendogenous responders had responded according to the above criteria by Day 21. There was a trend for the amelioration in the HDS score after only 1 week of active drug to be greater in the responder groups: (−4 ± 2.5 in the endogenous and −9.1 ± 2.3 in the nonendogenous) than in the nonresponders (−0.1 ± 1.4 and −3.5 ± 1.5), respectively, in endogenous and nonendogenous groups ($p<0.1$ and $p<0.05$, one-tailed t-test).



*p<.05 **p<.01 2-tail t test contrast with day 0 HD scores

FIGURE
(From: Mann et al. *J. Clin. Psychopharmacology,* 2: 54-57, 1982.)

The degree of endogenicity or nonendogenicity as indicated by the Newcastle scale, or the duration of the illness, showed no significant linear correlation with the amelioration in the HDS score in either the endogenous or nonendogenous groups.

The Figure shows the degree of platelet MAO inhibition and the mean daily dosages of L-deprenyl in both groups. Deprenyl was a potent rapid inhibitor of platelet MAO. A 10 mg dose of L-deprenyl almost totally inhibited platelet MAO within 2 hours.

Baseline MAO activity showed no significant linear correlation with amelioration in HDS scores. However, baseline MAO activity of responders in the endogenous and nonendogenous groups was respectively 32.0 ± 6.6 and 24.5 ± 5.4 nmol/hour/mg protein, which, although not statistically higher than nonresponders (22 ± 2.9 and 17.3 ± 7.9), may prove to be significant in a study with greater numbers of patients.

Deprenyl produced several of the typical side effects of classical MAO inhibitors including increased energy, initial insomnia, reduced appetite, increased aggressive feelings, and agitation. However, no changes were seen in blood pressure or electrocardiograph (ECG). In particular, no patient developed significant orthostatic hypotension (a drop in systolic blood pressure of >20 mmHg). When each group was subdivided into responders and nonresponders, there were still no significant changes in blood pressure. In contrast to classical nonselective MAOIs, no patients developed impotence or peripheral edema.

Discussion

There is a body of evidence in the literature suggesting that classical MAO inhibitors such as phenelzine are more effective in nonendogenous rather than endogenous depression as a whole. Although this study had design limitations by being an open study, and involved relatively small numbers of patients, L-deprenyl did appear to have an antidepressant effect in nonendogenous depression and perhaps the bipolar subgroup of endogenous depression (in contrast to unipolar endogenous depressives) in a dose range that is reported to preserve selective MAO inhibition (Ekstedt et al. 1979; Reiderer & Reynolds 1980).

The use of selective MAO inhibitors, apart from creating the possibility of safer, more specific drugs, also permits a valuable alternative approach to the biochemical subclassification of depressive disorders. We are initiating double-blind controlled studies to examine the therapeutic spectrum of action of L-deprenyl and its efficacy in order to evaluate the potential biochemical heterogeneity of depressive disorders. Mendlewicz (1982) has recently reported that L-deprenyl was an effective antidepressant in a group of patients with major depression in a placebo-controlled, double-blind study.

References

Ekstedt, B., Magyer, K., and Knoll, J. Does the B form selective monoamine oxidase inhibitor lose selectivity by long-term treatment? *Biochem. Pharmacol.*, 28:919-923, 1979.

Elsworth, J.D., Glover, V., Reynolds, G.P., Sandler, M., Lees A.J., Phuapradit, P., Shaw, K.M., Stern, G.M., and Kumar, P. Deprenyl administration in man: A selective monoamine oxidase B inhibitor without the "cheese effect." *Psychopharmacology (Berlin)*, 57:33-38, 1978.

Himmelhoch, J.M., Detre, T., Kupfer, D.J., Swartzburg, M., and Byck, R. Treatment of previously intractable depressions with tranylcypromine and lithium. *J. Nerv. Ment. Dis.*, 155:216-220, 1972.

Lader, M.H., Sakalis, G., and Tansella, M. Interaction between sympathetic amines and a new monoamine oxidase inhibitor. *Psychopharmacologia (Berlin)*, 18:118-123, 1972.

Mendlewicz, J. Paper presented at an International Symposium on Jumex. Szombately, Hungary, May 1982.

Pare, C.M.B., and Mack, J.W. Differentiation of two genetically specific types of depression by response to antidepressant drugs. *J. Med. Genet.*, 8:306-309, 1971.

Ravaris, C.L., Robinson, D.S., Ives, J.O., Nies, A., and Bartlett, D. Phenelzine and amitriptyline in the treatment of depression. *Arch. Gen. Psychiatry*, 37:1075-1080, 1980.

Reiderer, P., and Reynolds, G.P. Deprenyl is a selective inhibitor of brain MAO-B in the long-term treatment of Parkinson's disease. *Br. J. Clin. Pharmacol.*, 9:98-99, 1980.

Robinson, D.S., Nies, A., Ravaris, C.L., and Lamborn, K.R. The monoamine oxidase inhibitor, phenelzine, in the treatment of depressive-anxiety states. *Arch. Gen. Psychiatry*. 29:407-413, 1973.

Tyrer, P. Clinical use of monoamine oxidase inhibitors. In: Paykel, E.S., and Coppen, A. (eds.), *Psychopharmacology of Affective Disorders*. New York:Oxford University Press. 1978, pp. 159-178.

Wheatley, D. Comparative trial of a new monoamine oxidase inhibitor in depression. *Br. J. Psychiatry*, 117:547, 1970.

Pharmacological Treatment of Delusional Depressives[1]

Duane G. Spiker, M.D.,[2] Israel Hanin, Ph.D.,[2] James M. Perel, Ph.D.,[2] Jane E. Cofsky, M.S.W.,[2] Albert J. Rossi, M.D.,[2] and Denise Sorisio, B.S.[2]

Introduction

The optimal pharmacological treatment of patients with a delusional depression is not clear. Most of the studies reported in the literature are either retrospective or not double-blind (Avery & Winokur 1977; Moradi et al. 1979; Nelson & Bowers 1978). In addition, only a few of the studies measured plasma levels of the tricyclic antidepressant (Glassman et al. 1977). Consequently, a prospective double-blind study of delusional depressives, in which plasma levels of the antidepressant were measured, was initiated. This report describes the results of the first 2 years of the 3-year project.

Method

All subjects were inpatients on the Clinical Research Unit at Western Psychiatric Institute and Clinic (WPIC). At the time of admission, patients were given a traditional psychiatric interview and a complete physical examination. During the subsequent 7-day drug-free period, they underwent a variety of routine laboratory tests including thyroid function tests, an electroencephalogram, and any other tests indicated based on their history and physical examination. Any patient who was found to have a medical illness affecting his or her central nervous system was excluded from the study. All patients gave informed consent.

At the end of the 7-day drug-free period, the Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott & Spitzer 1978) was completed using information from the initial interview, case records, collateral information from relatives, observation on the unit, and a second interview with each patient. The SADS is a structured research interview that collects information necessary to make diagnoses using the Research Diagnostic Criteria (RDC) (Spitzer et al. 1978). For inclusion in the study the patients had to meet the RDC for major depressive disorder, primary subtype. In addition, they had to meet the criteria for psychotic subtype based on the presence of a clear-cut delusion. The severity of depression was measured by the Hamilton Rating Scale (HRS), using the sum of two raters on the 17-item HRS (Hamilton 1960). Patients entered the study if the combined HRS score for two raters was 30 or more. After the 7-day drug-free period, the patients were randomly assigned to perphenazine, amitriptyline, or perphenazine + amitriptyline in adequate doses for 35 days. Blood collection and measurement of plasma levels of amitriptyline and nortriptyline were measured as previously described (Kupfer et al. 1977).

---

[1] This study was supported in part by USPHS Grant MH-32707 from the National Institute of Mental Health.

[2] Department of Psychiatry, University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, Pittsburgh, PA 15213.

To date, 44 patients have entered the study and 36 have completed the 35-day project. Four patients left the hospital against medical advice for reasons unrelated to the protocol. Two patients developed an organic brain syndrome — one on perphenazine and one on amitriptyline + perphenazine. One patient became unmanageable on amitripyline. One patient was dropped because of medical problems unrelated to the study. The responses of the 36 patients who completed the study are shown in Table 1. Responders were defined as patients who no longer were delusional or depressed. Nonresponders were defined as patients who were either depressed, delusional, or both. The patients so far have been either clear-cut responders or clear-cut nonresponders.

Table 1

Response to Treatment

	Responders	Nonresponders
Amitriptyline	3	6
Perphenazine	2	11
Amitriptyline + Perphenazine	11	3

The role of amitriptyline and its metabolite nortriptyline in explaining why some delusionally depressed patients respond to amitriptyline and some do not is unclear. Of the nine patients on amitriptyline who completed the study, three were responders and six were nonresponders. Their plasma levels of amitriptyline and nortriptyline are shown in Table 2. The plasma level of 200 ng/ml of amitriptyline + nortriptyline was used because previous work at WPIC using the same methodology has shown that amitriptyline + nortriptyline ≥ 200 ng/ml is the effective level for treating nondelusional depressed patients (Kupfer et al. 1977).

Patients who were treated with amitriptyline + perphenazine had a mean plasma level of amitriptyline + nortriptyline of 297 ng/ml, while patients treated only with amitriptyline had a mean plasma level of 245 ng/ml.

Discussion

Although the sample size is still too small to make a definitive statement, some trends are apparent. The combination of the antidepressant and the antipsychotic appears to be the most efficacious with a 79 percent response rate. There are very clearly patients with a delusional depression who do respond to an antidepressant alone. There is also a suggestion that the response rate increases with increasing plasma levels of amitriptyline + nortriptyline. Interestingly, amitriptyline alone appears to be more effective than perphenazine alone. Whether the increased response rate of patients treated with amitriptyline + perphenazine can be explained by the increased amitriptyline + nortriptyline plasma levels, or whether the perphenazine has some additional effect, remains to be determined.

Table 2

Plasma Levels of Amitriptyline + Nortriptyline in Patients Treated with Amitriptyline

	Responders	Nonresponders
Amitriptyline + Nortriptyline ≤ 200 ng/ml	1	3
Amitriptyline + Nortriptyline ≥ 200 ng/ml	2	3

References

Avery, D., and Winokur, G. The efficacy of electroconvulsive therapy and antidepressants in depression. *Biol. Psychiatry,* 12:507-523, 1977.

Endicott, J., and Spitzer, R.L. A diagnostic interview: The Schedule for Affective Disorders and Schizophrenia. *Arch. Gen. Psychiatry,* 35:837-844, 1978.

Glassman, A.H., Perel, J.M., Shostak, M., Kantor, S.J., and Fleiss, J.L. Clinical implications of imipramine plasma levels for depressive illness. *Arch. Gen. Psychiatry,* 34:197-204, 1977.

Hamilton, M. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry,* 23:56-62, 1960.

Kupfer, D.J., Hanin, I., Spiker, D.G., Grau, T., and Coble, P. Amitriptyline plasma levels and clinical response in primary depression. *Clin. Pharmacol. Ther.,* 22:904-911, 1977.

Moradi, S.R., Muñiz, C.E., and Belar, C.D. Male delusional depressed patients: Response to treatment. *Br. J. Psychiatry,* 135:136-138, 1979.

Nelson, J.C., and Bowers, M.B., Jr. Delusional unipolar depression. *Arch. Gen. Psychiatry,* 35:1321-1328, 1978.

Spitzer, R.L., Endicott, J., and Robins, E. Research Diagnostic Criteria: Rationale and reliability. *Arch. Gen. Psychiatry,* 35:773-782, 1978.

Erythrocyte and Plasma Choline In Bipolar Psychiatric Patients: A Followup Study[1]

Israel Hanin, Ph.D.,[2] Bruce M. Cohen, M.D., Ph.D.,[3] Ursula Kopp,[2] and Joseph F. Lipinski, M.D.[3]

Introduction

Over the past four years there has been considerable interest in red blood cell (RBC) choline (Ch) as a potential cholinergic marker. Significantly elevated levels of RBC Ch have been reported in a subset of drug-free unipolar depressed patients (Hanin et al. 1980a); in drug-free bipolar manic patients (Jope et al. 1980); in patients with Gilles de la Tourette's Syndrome (Hanin et al. 1979); in a major portion of biological relatives of patients with Gilles de la Tourette's Syndrome (Comings et al. 1982); as well as in a segment of patients with Alzheimer's disease (Barclay et al. 1982, Friedman et al. 1981).

These elevated levels of RBC Ch are not drug induced; in fact, among the commonly used psychotherapeutic agents to date, only lithium has been shown to alter RBC Ch levels (Domino et al. 1981; Hanin et al. 1981; Jones & Kuchel 1980; Jope et al. 1978; Shea et al. 1981). This effect appears to be irreversible (Lee et al. 1974), and due to inhibition of efflux of Ch accumulated as a result of breakdown of membrane phospholipids on the inside of the RBC (Hanin et al. 1980b; Jenden et al. 1980).

The clinical significance of these elevated RBC Ch levels, whether endogenous or related to chronic lithium administration, is as yet not entirely understood. However, there still is a need for more well-controlled analyses to be conducted, and for reliable baseline data to be obtained (without any room for individual bias in interpreting the results), before one can move on to the

---

[1] This study was supported in part by USPHS Grants MH-26320 and MH-31154 from the National Institute of Mental Health.

[2] Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213.

[3] McLean Hospital Mailman Research Center, Clinical Biochemistry Laboratory, Belmont, MA 02178.

task of establishing any clinical relevance, or any potential biological marker role for RBC Ch *in vivo*. Hence the present studies, the results of which are reported in this paper.

Method

These results represent a collaborative effort between investigators from two institutions: Western Psychiatric Institute and Clinic Department of Psychiatry (WPIC), University of Pittsburgh School of Medicine (I.H. and U.K.); and the McLean Hospital Mailman Research Center, Laboratories for Psychiatric Research, in Belmont, Massachusetts (B.M.C. and J.F.L.). These studies were conducted for the purpose of establishing plasma and RBC Ch levels in a broad spectrum of manic-depressive patients, using a totally "blind" approach for data handling.

Patients were diagnosed and selected at McLean Hospital; blood samples were coded, processed, frozen, sent in dry ice packing to Pittsburgh, and stored at −20°C until preparation for analysis. Thawing, isolation, and analysis of Ch content in all samples was conducted in Pittsburgh. The results were then sent to McLean Hospital and decoded.

Patients selected for these studies were between 18 and 55 years old. They were admitted to the study on the condition that they had received no prior psychoactive medication for at least 1 month; no depot neuroleptic for at least 3 months; and no lithium for at least 6 months (except where specifically noted below). Patients were diagnosed by Diagnostic and Statistical Manual-III (DSM-III) criteria. They were excluded from the study if the presence of medical or neurological disease was noted.

On admission, patients were subjected to routine blood work (CBC, SMA-12, T4), urine analysis, ECG, EEG, chest X-ray, and a physical examination. This was followed by weekly determinations of complete blood count and SMA-12. Vital signs were taken daily. Subjects remained off all medications in the hospital for several days, during which blood was drawn for baseline Ch levels.

Blood (10 ml) was drawn in the morning after an overnight fast, into heparinized (green top) Venoject® tubes, and processed according to Hanin et al. (1980a). Subsequent analysis of plasma and RBC Ch was conducted using gas chromatography-mass spectrometry, according to Hanin and Skinner (1975).

In manic patients serial bloods were also drawn weekly for Ch determinations during treatment. Treatment with lithium alone, lecithin alone, or a combination of both are as noted in data shown below. Lithium carbonate was started at 300 mg b.i.d. Serum lithium levels were subsequently adjusted to 0.5-0.7 meq/l in the second week. Lecithin (Phospholipon 100, 30 g/day dissolved in ethanol) on ice cream was given to patients in three divided doses. Placebo for lecithin consisted of cod liver oil, castor oil, and ethanol.

Control subjects were drug-free, psychiatrically normal individuals, of the same age range as the patients.

Results

RBC and Plasma Ch levels: Drug-Free Manics vs. Controls

Table 1 shows values of plasma and RBC Ch levels measured in 18 drug-free bipolar disorder manic patients. Table 2 shows values of plasma and RBC Ch levels measured in 18 normal control subjects. While mean RBC Ch levels appeared to be higher in the manic patients, the values were not significantly different from RBC values in the control group ($t=1.04$; $N=34$). Also, the range of values was quite similar for both groups. Neither were plasma Ch levels significantly different between the two groups ($t=0.39$; $N=34$).

Effect of Lithium Treatment on RBC and Plasma Ch Levels

Results obtained with eight manic patients are shown in Table 3. Time of exposure of these patients to lithium varied between individuals. It is nevertheless clear that lithium treatment significantly elevated RBC Ch levels, while not affecting plasma Ch levels at all (Compare Tables 1 and 2).

Table 1

Plasma (P) and Erythrocyte (RBC) Choline (nmol/ml) in Bipolar Disorder Manic Patients Which Were Either Drug-Free or Treated With Neuroleptics, But Were Not Exposed to Lithium

Subject	Age	Sex	Meds	P Choline	RBC Choline
1	18	M		7.7	8.8
2	27	F		5.7	7.2
3	30	F		9.0	27.5
4	51	M		8.4	11.2
5	27	F		5.8	7.9
6	36	M	N	8.6	11.2
7	23	F		8.7	8.7
8	23	F	O	6.0	18.5
9	34	F		9.6	10.6
10	19	F	N	4.2	83.8
11	31	M		7.5	53.7
12	35	F	E	6.8	6.9
13	44	M		7.5	111.2
14	32	F		8.6	9.3
15	20	M		7.8	15.3
16	19	M		5.6	13.7
17	48	F		10.2	14.8
18	43	F		6.1	5.6

Mean ± SE: Plasma = 7.4 ± 1.1; RBC = 23.7 ± 6.9

Table 2

Plasma and Erythrocyte (RBC) Choline (nmol/ml) in Normal Control Subjects

Subject	Age	Sex	Meds	Plasma Choline	RBC Choline
1	18	M		8.8	21.2
2	25	F		7.5	9.2
3	27	F		7.5	9.7
4	29	M		6.8	8.6
5	28	F		5.1	7.6
6	24	M		7.8	7.5
7	23	F	N	7.9	7.8
8	24	M		6.2	7.4
9	29	M	O	8.9	12.3
10	23	F		7.9	8.5
11	26	F	N	7.0	32.0
12	39	F		5.6	5.2
13	22	M	E	10.5	12.8
14	18	M		7.1	75.5
15	30	M		7.3	23.2
16	25	F		6.9	9.2
17	26	M		7.2	8.3
18	34	M	Hydrochlorthiazine	11.4	10.1

Mean ± SE for Normal Controls: Plasma = 7.8 ± 0.4, RBC = 15.3 ± 3.6

Table 3

Plasma and Erythrocyte (RBC) Choline (nmol/ml) in Bipolar Disorder, Manic Patients, Treated with Lithium[a]

Subject	Age	Sex	Plasma Choline	RBC Choline
1	26	M	6.9	376.0
2	18	M	8.9	311.5
3	25	F	7.2	103.3
4	24	M	5.0	694.3
5	28	M	5.8	175.7
6	22	F	5.7	334.4
7	20	F	6.2	112.6
8	21	M	7.6	59.6

[a] Exposure to lithium varied within individual patients. Mean ± SE for above patients on lithium: Plasma = 6.6 ± 0.4; RBC = 258.2 ± 79.0.

Effect of Lecithin Alone, or Concurrent with Lithium and Other Drugs on Plasma and RBC Ch Levels

Table 4 demonstrates the effect of lecithin treatment on plasma and RBC Ch levels. Subjects were concurrently drug-free, or treated with another psychotropic agent, as specified in the Table.

Although variable, and shown only in the case of four individuals, the measured changes in plasma and Ch levels are important for purposes of interpreting the role of the RBC as a Ch carrier *in vivo*. (*See* Discussion)

Discussion and Summary

The data reported in this paper confirm some of our earlier findings; disagree with others reported in the literature; and also provide some new intriguing observations which will require further experimentation and analysis. Although preliminary, the authors believe that these findings were well worth reporting, particularly because of the "double-blind" circumstances inherent in the generation and analysis of the data.

The results reported in this paper allow for the following conclusions:

1. *In drug-free manics RBC Ch and plasma Ch levels are not statistically different from the respective values found in controls.* The authors' data thus are in contradiction to Jope et al. (1980), who reported

elevated levels of RBC Ch in patients diagnosed as manic, prior to lithium therapy. Shea et al. (1981) have also reported that there was no significant difference in RBC Ch between lithium-free patients with affective disorder and normal subjects. Unfortunately the number of drug-free bipolar manics in this group of patients was not identified.

At present there is no clear explanation for the discrepancy in these reported results. The differences could not be attributed to methodologic variances since both Hanin and co-investigators, and Jope and co-investigators used an essentially identical gas chromatograph-mass spectrometric technique for the analysis of RBC Ch levels, while Shea and co-investigators used a radioenzymatic assay. Conceivably, the differences could be due to the fact that, once lithium treatment is discontinued, drug-induced elevated RBC Ch levels require over 4 months (essentially the life-time of the RBC) to return to normal (Hanin et al. 1980b). Thus, any prior exposure to lithium within 4 to 5 months of the analysis in any of the five patients used by Jope and co-investigators could explain the elevation in RBC Ch levels as reported by these investigators. In the present studies extra precautions were taken to exclude from the protocol any patient who had been exposed to lithium within 6 months of the time of the analysis for RBC and plasma Ch levels. Further studies with a large number of patients may resolve this question.

2. *Lithium treatment significantly elevates RBC Ch levels.* This finding confirms earlier reports from the laboratories of Jope, Jones, Hanin, Domino, Shea, and others.

3. *Plasma Ch is not significantly affected by lithium treatment.* Shea et al. (1981) did however report significantly elevated levels of plasma Ch in samples obtained from lithium-treated patients. These investigators state that it is possible that the plasma was contaminated by RBC, although any plasma samples with a tinge of red were discarded. In any case, the elevation in plasma Ch levels observed by Shea and co-investigators was only twofold at best, while RBC Ch levels were elevated more than tenfold.

4. *Treatment of patients with lecithin elevates plasma Ch levels, irrespective of whether RBC Ch levels are concomitantly in the "normal" range, or abnormally elevated due to lithium therapy.*

This finding, in conjunction with data summarized above, suggests separate physiological roles for Ch in plasma and in RBCs. The findings suggest that both compartments in blood should be considered as separate, yet interdependent, entities in their function as carriers of Ch from blood to other tissues, *in vivo*.

Table 4

Plasma (P) and Erythrocyte (RBC) Choline (nmol/ml) in Patients Before and After Receiving Lecithin

Subject	Age	Sex	Lecithin	Other Medications	Plasma Choline	RBC Choline
A	18	M	None	Haldol, Artane	9.6	10.2
			On × 4 days	Haldol, Artane	13.5	16.3
			Off × 5 days	Haldol, Artane	5.9	7.1
			Off × 10 days	Haldol, Artane	9.3	7.2
			Off × 17 days	Lithium × 6 days	9.3	126.2
B	26	M	None	Tril, Artane, Lithium	6.9	376.0
			On × 10 days	Tril, Artane, Lithium	29.1	682.2
			Off × 8 days	Tril, Artane, Lithium	10.1	462.7
C	33	F	None	None, but on lithium	6.5	127.5
			On × 1 days	within a few months	23.8	127.8
			On × 10 days	of admission	25.1	203.6
D	22	F	None	Mellaril, Lithium	5.7	334.4
			On × 7 days	Mellaril, Lithium	19.3	259.4

It is anticipated that future studies will ascertain whether the extent of normal exchange of Ch between plasma and RBC in blood will, in turn, predicate the amount of free Ch available to key physiological sites *in vivo*; such as the cholinergic nerve terminal for the synthesis of acetylcholine. Previous studies by Hanin et al. (1980b) have clearly demonstrated that Ch exchange between plasma and RBC is inversely proportional to RBC Ch levels. In clinical situations where endogenous RBC Ch levels have been shown to be higher than normal, this could reflect deviations from normal in the extent of availability of Ch to central nerve terminals crucial for acetylcholine synthesis *in vivo*.

References

Barclay, L.L., Blass, J.P., Kopp, U., and Hanin, I. Red cell/plasma choline ratio in dementia. *New Engl. J. Med.* 307:500, 1982.

Comings, D.E., Gursey, B.T., Avelino, E., Kopp, U., and Hanin, I. Red blood cell choline in Gilles de la Tourette syndrome. In: Chase, T.N., and Friedhoff, A.J. (eds.), *Tourette Syndrome.* New York:Raven Press, 1982. (In press)

Domino, E.F., Mathews, B., Tait, S.K., Demetriou, S.K., and Fucek, F. Red blood cell/plasma choline ratio—A possible biological marker of lithium therapy-clinical correlations and limitations. In: Pepeu, G., and Ladinsky, H. (eds.), *Cholinergic Mechanisms.* New York: Plenum Publishing Corp., 1981, pp. 891-900.

Friedman, E., Sherman, K.A., Ferris, S.H., Reisberg, B., Bartus, R.T., and Schneck, M.K. Clinical response to choline plus piracetam in senile dementia: Relation to red cell choline levels. *New Engl. J. Med.*, 304:1490-1491, 1981.

Hanin, I., and Skinner, R.F. Analysis of microquantities of choline and its esters utilizing gas chromatography-chemical ionization mass spectrometry. *Anal. Biochem.*, 66:568-583, 1975.

Hanin, I., Merikangas, J.R., Merikangas, K.R., and Kopp, U. Red cell choline and Gilles de la Tourette syndrome. *New Engl. J. Med.*, 301:661-662, 1979.

Hanin, I., Kopp, U., Spiker, D.G., Neil, J.F., Shaw, R., and Kupfer, D. RBC and plasma choline levels in control and depressed individuals: A critical evaluation. *Psychiatry Res.*, 3:345-355, 1980a.

Hanin, I., Mallinger, A.G., Kopp, U., Himmelhoch, J.M., and Neil, J.F. Mechanism of lithium-induced elevation in red blood cell choline content: An in vitro analysis. *Commun. Psychopharmacol.*, 4:345-355, 1980b.

Hanin, I., Spiker, D.G., Mallinger, A.G., Kopp, U., Himmelhoch, J.M., Neil, J.F., and Kupfer, D. Blood choline and its meaning in psychiatric and neurologic disease states. In: Pepeu, G., and Ladinsky, H. (eds.), *Cholinergic Mechanisms.* New York:Plenum Publishing Corp., 1981, pp. 901-919.

Jenden, D.J., Jope R.S., and Fraser, S.L. A mechanism for the accumulation of choline in erythrocytes during treatment with lithium. *Commun. Psychopharmacol.*, 4:339-344, 1980.

Jones, A.J., and Kuchel, P.W. Measurement of choline concentration and transport in human erythrocytes by ^{1}H NMR: Comparison of normal blood and that from lithium-treated psychiatric patients. *Clin. Chim. Acta*, 104:77-85, 1980.

Jope, R.S., Jenden, D.J., Ehrlich, B.E., and Diamond, J.M. Choline accumulates in erythrocytes during lithium therapy. *New Engl. J. Med.*, 299:833-834, 1978.

Jope, R.S., Jenden, D.J., Ehrlich, B.E., Diamond, J.M., and Gosenfeld, L. Erythrocyte choline concentrations are elevated in manic patients. *Proc. Natl. Acad. Sci. USA*, 77:6144-6146, 1980.

Lee, G., Lingsch, C., Lyle, P.T., and Martin, K. Lithium treatment strongly inhibits choline transport in human erythrocyte. *Br. J. Clin. Pharmacol.*, 1:365-370, 1974.

Shea, P.A., Small, J.G., and Hendrie, H.C. Elevation of choline and glycine in red blood cells of psychiatric patients due to lithium treatment. *Biol. Psychiatry*, 16:825-830, 1981.

Relationship Between Cognition and Mood in Geriatric Depression

Barry Reisberg, M.D.,[1] Steven H. Ferris, Ph.D.,[1] Anastase Georgotas, M.D.,[1] Mony J. de Leon, Ed.D.,[1] and Michael K. Schneck, M.D.[1]

The interrelationship between cognition and affect among geriatric depressed patients is an area of major clinical and therapeutic importance. The clinical importance of this relationship derives from the need to differentiate geriatric depression and Primary Degenerative Dementia (PDD), the two major psychiatric disorders of the elderly. Current evidence indicates that depressed patients do not demonstrate marked global cognitive deficits (Friedman 1964; Neville & Folstein 1979; Sternberg & Jarvik 1976). However, depressed patients do rate themselves more negatively in cognitive and other areas (Friedman 1964), and may demonstrate deficits in circumscribed cognitive areas, notably on attention and immediate memory tasks (Neville & Folstein 1979; Sternberg & Jarvik 1976). Because of the potential importance and implications of the relationship between geriatric depression and cognition, we examined the correlation between magnitude of both self-rated and clinically rated depression and the magnitude of cognitive deficit in elderly outpatients.

Method

Twenty-two outpatient volunteers (mean age 64.8 ± 4.5 years) with subjective complaints of depression were accepted for the study. They met all of the following criteria after treatment with placebo for 7 days: 1) 60 to 85 years of age; 2) a score of 18 or more on the 17-item Hamilton Rating Scale (Hamilton 1960); 3) a Wechsler Adult Intelligence Scale Vocabulary Score ≥ 8 (Wechsler 1941); 4) at least five symptoms of Depressive Affective Disorder, Diagnostic and Statistical Manual-III (DSM-III) diagnoses 296.2, 296.3, 296.5, 296.6, or 300 (American Psychiatric Association 1980), including depressed mood; 5) clinical laboratory evaluations within ± 10 percent of the normal range. Patients were excluded if they had a history of, or active symptoms indicating: 1) central nervous system (CNS) infection, neoplasm, or evidence of progressive neurologic disease other than PDD; 2) epilepsy; 3) schizophrenia; 4) alcoholism or drug dependence; 5) other psychiatric conditions which prevented the subject's cooperation in the study; or 6) major medical illnesses including uncontrolled congestive heart failure, uncontrolled diabetes mellitis, chronic pulmonary insufficiency, or severe angina.

The patients were assessed with respect to clinical and psychometric parameters. The degree of memory impairment was assessed using the Guild Memory Scale (Gilbert et al. 1968; Gilbert & Levee 1971). Normative values are available for each of the five subtests of the Guild with respect to age and intelligence level as estimated by the Wechsler Adult Intelligence Scale (WAIS) vocabulary score of the subject (Crook et al. 1980). Additional cognitive measures included assessment of primary (short-term) memory, digit span forward and backward; secondary (long-term) memory; First and Last Names (French et al. 1974); Memory for Faces (Ferris et al. 1980); and perceptual-motor tasks: Perceptual Speed (Moran & Mefferd 1959), Simple and Disjunctive Reaction Time (Ferris et al. 1976), and Finger-Tapping Speed (Lehmann & Ban 1970).

The clinical assessments included two psychiatric ratings, the Hamilton Depression Scale, and the Inventory of Psychic and Somatic Complaints in the Elderly (IPSC-E) (Raskin & Crook 1977); and two self-ratings, the Beck Depression Inventory (Beck et al. 1961), and the Mood Scale for the Elderly (MS-E) (Raskin & Crook 1976). Pearson correlation coefficients were computed between the psychiatrist-rated or self-rated clinical assessments and the psychometric test performance scores.

Results

Based upon the norms for the Guild Memory Test, nine subjects were above average in memory, seven were below average, and six were one standard deviation or more below average.

---

[1] Geriatric Study and Treatment Program, Department of Psychiatry, New York University Medical Center, New York, NY 10016.

No subjects demonstrated more than mild global cognitive deterioration as defined on the Global Deterioration Scale (GDS) for PDD (GDS ≤ 3), an instrument for which Guild and clinical rating criteria are available (Reisberg et al. 1982). Hence, depressive affective disorder was not associated with marked cognitive impairment in these elderly outpatients.

There were no statistically significant correlations between total Hamilton scores and any of the psychometric test scores. For the IPSC-E, the total score on the depression cluster, (Items 8 through 14) correlated only with simple reaction time ($r = .51$, $p < .05$). When total IPSC-E Depression scores were combined with related assessments of Energy Loss (Items 1 through 7), Sleep Disturbance (Items 15 through 17), and Anxiety-Tension (Items 18 through 25), no significant correlations with performance on any of the psychometric tests were observed. Total self-assessment scores on the Beck Depression Scale also failed to correlate significantly with any of the psychometric test scores. Self-assessments of negative mood on the MS-E correlated with poor performance on four of the psychometric measures (*see* Table). The strongest relationship ($r = .68$, $p < .01$), was observed for slowing of simple reaction time.

Conclusions

Our findings with respect to the magnitude of cognitive impairment in geriatric depressed outpatients are consistent with the findings of previous investigators with respect to both adult depression (Friedman 1964; Sternberg & Jarvik 1976) and geriatric depression (Neville & Folstein 1979). Specifically, geriatric patients with clinically significant depression actually perform better than average (41 percent of our sample), or only slightly below average (32 percent), on assessments of memory. Hence, the overall magnitude of cognitive impairment associated with geriatric depression in most patients is not large.

However, sensitive clinical mood assessment instruments and cognitive tests are capable of demonstrating some significant relationships between magnitude of depression and psychometric performance. These relationships occurred only for measures such as reaction time, perceptual speed and motor speed, but not for measures of memory function. Since these tests are measures of attention or alertness, our results are consistent with earlier findings suggesting attentional, rather than memory deficits in geriatric depressed patients (Neville & Folstein 1979). Self-ratings of dysphoric mood on the MS-E were found to relate more strongly to impaired psychometric performance than psychiatrist's assessments of the magnitude of dysphoric symptomatology.

We have previously found that in patients with early symptoms of age associated cognitive decline or PDD, psychometric deficits of a global nature tend to accompany progression of the disorder (Reisberg et al. 1981). Hence, the patterns of psychometric impairments in geriatric depression and in PDD do appear to differ. Further work is needed to determine if these patterns are of differential diagnostic significance.

Table

Significant Pearson Correlations Between MS-E Self-Assessments and Psychometric Indices ($N = 22$)

Measure	Combined MS-E Global Score
Digit Span	
Forward	
Backward	.46[a]
Names	
Trial 1 - Correct	
Trial 2 - Correct	
Trial 3 - Correct	
Delay - Correct	
Faces	
Trial 1	
Trial 2	
Trial 3	
Perceptual Speed	
Correct	.43[a]
Errors	
Reduction Time	
Simple	.68[b]
Disjunctive	
Finger-Tapping Speed	
Dominant Hand	.48[a]
Non-Dominant Hand	

[a] Significant at .05 level (two-tailed)
[b] Significant at .01 level (two-tailed)

References

American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders (3rd ed.).* Washington, D.C.: American Psychiatric Association Printing Office, 1980.

Beck, A.T., Ward, C.H., Mendelson, M., Mock, J., and Erbaugh, J. An inventory for measuring depression. *Arch. Gen. Psychiatry,* 4:561-571, 1961.

Crook, T., Gilbert, J.G., and Ferris, S.H. Operationalizing memory impairment in elderly persons: The Guild Memory Test. *Psychol. Rep.,* 47:1315-1318, 1980.

Ferris, S.H., Crook, T., Clark, E., McCarthy, M., and Rae, D. Facial recognition memory deficits in normal aging and senile dementia. *J. Gerontol.,* 35:707-714, 1980.

Ferris, S.H., Crook, T., Sathananthan, G., and Gershon, S. Reaction time as a diagnostic measure in senility. *J. Am. Geriatr. Soc.,* 24:529-533, 1976.

French, J.W., Ekstrom, R.B., and Leighton, A. First and last names test. In: *Kit of Reference Tests for Cognitive Factors (Rev. Ed.).* Princeton, N.J.: Educational Testing Service, 1974.

Friedman, A.S. Minimal effects of severe depression on cognitive functioning. *Abnorm. Soc. Psychol.,* 69:237-243, 1964.

Gilbert, J.G., Levee, R.F., and Catalano, F.L. A preliminary report on a new memory scale. *Percept. Motor Skills,* 27:277-278, 1968.

Gilbert, J.G., and Levee, R.F. Patterns for declining memory. *J. Gerontol.,* 26:70-75, 1971.

Hamilton, M. A rating scale for depression. *J. Neurol. Neurosurg. Psychiatry,* 23:52-62, 1960.

Lehmann, H.E., and Ban, T.A. Psychometric tests in the evaluation of brain pathology responsive to drugs. *Geriatrics,* 25:142-147, 1970.

Moran, L.J., and Mefferd, R.B. Repetitive psychometric measures. *Psychol. Rep.,* 5:269-275, 1959.

Neville, H.J., and Folstein, M.F. Performance on three cognitive tasks by patients with dementia, depression or Korsakov's syndrome. *Gerontology,* 25:285-290, 1979.

Raskin, A., and Crook, T.H. NIMH Mood Scales—Elderly (MS-E), available from the Psychopharmacology Research Branch, NIMH, ADM-523-5, Rev. 9-76, 1976.

Raskin, A., and Crook, T.H. Inventory of Psychic and Somatic Complaints in the Elderly (IPSC-E), available from the Psychopharmacology Research Branch, NIMH, ADM-523-2, Rev. 2-77, 1977.

Reisberg, B., Ferris, S.H., and Crook, T. Signs, symptoms and course of age-associated cognitive decline. In: *Alzheimer's Disease: A Review of Progress (Aging, Vol. 19).* New York: Raven Press, 1982, pp. 177-181.

Reisberg, B., Ferris, S.H., Schneck, M.K., de Leon, M.J., Crook, T. and Gershon, S. The relationship between psychiatric assessments and cognitive test measures in mild to moderately cognitively impaired elderly. *Psychopharmacol. Bull.,* 17:99-101, 1981.

Sternberg, D.E. and Jarvik, M.E. Memory function in depression. *Arch. Gen. Psychiatry,* 33:219-224, 1976.

Wechsler, D. *Measure of Adult Intelligence (2nd ed.).* Baltimore: Williams & Williams Co., 1941.

Cerebrospinal Fluid Acetylcholine, Choline, and Senile Dementia of the Alzheimer's Type[1]

Kenneth L. Davis, M.D.,[2] John Y-K. Hsieh, Ph.D.,[2] Michael I. Levy, M.D.,[2] Thomas B. Horvath, M.D.,[2] Bonnie M. Davis, M.D.,[2] and Richard C. Mohs, Ph.D.[2]

Degeneration of cholinergic neurons and formation of neurofibrillary tangles and senile plaques are characteristic findings in postmortem studies of patients with senile dementia of the Alzheimer's type (SDAT). The extent of these changes corresponds with the degree of memory loss as measured by psychometric tests such as the Memory Information Test (MIT) (Blessed et al. 1968). Brain samples from patients with SDAT display a significant loss of choline acetyltransferase (CAT) activity (Davies 1979), indicating that SDAT can be characterized by a deficit in central cholinergic activity. However, diminished dopaminergic, noradrenergic, and serotoninergic activity have all been implicated in SDAT, (Bowen et al. 1979; Carlsson et al. 1980) though not with the consistency of the cholinergic abnormality. Improved memory test performance following the administration of cholinergic drugs to patients with SDAT suggests that the cholinergic deficit is involved in the cognitive abnormalities of this disease (Davis et al. 1981). The present study was undertaken to determine whether cerebrospinal fluid (CSF) acetylcholine (Ach) concentrations and/or the concentrations of the major CSF metabolites of dopamine, norepinephrine, and serotonin are related to the severity of dementia in patients with SDAT.

---

[1] This work was supported in part by a program project grant from the National Institute on Aging (AG-02219) and research funds from the Veterans Administration.

[2] Department of Psychiatry, Veterans Administration Medical Center Bronx, NY and Mount Sinai School of Medicine, New York, NY 10468.

Address correspondence to: Kenneth L. Davis, M.D., Chief of Psychiatry Service, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468.

Methods

Ten males and four females, ages 53-80, who met Research Diagnostic Criteria for primary dementia/SDAT were entered in the study (Spitzer et al. 1978). Prior to entry particular attention was given to ruling out multi-infarct dementia, depression, alcoholism, and other medical causes of dementia. The MIT was administered by a trained rater prior to the lumbar puncture. The lumbar puncture was performed at 9:00 a.m. with the patient in recumbent position after 10 hours of bedrest. No medications had been given except an occasional dose of chloral hydrate to some patients for 2 weeks prior to the lumbar puncture.

CSF was collected into a dry ice bath and immediately frozen at − 70°C for storage. The first through fifth milliliters of CSF were analyzed by gas chromatograph/mass spectrometry (GCMS) for acetlycholine and choline (Jenden et al. 1973). All reagents were distilled twice before conducting the assay. This assay has a minimum sensitivity of approximately .025 nanomoles/ml. The interassay variability is 16 percent for Ach, and 7 percent for choline. The intraassay variability is 16 percent for Ach, and 9 percent for choline. Values derived from this procedure are in agreement with previous published data (Welch et al. 1976). The sixth through twelfth milliliters were analyzed for homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) and 3-methoxy-5-hydroxyphenylethyleneglycol (MHPG) (Anderson et al. 1979; Karoum et al. 1975).

Results

The Pearson correlation coefficient of MIT scores with CSF acetylcholine levels was $r=0.76$ ($p<.005$). Thus, patients with the most impaired memory functioning tended to have low acetylcholine concentrations in the CSF (*see* Table). There was a nonsignificant trend for CSF choline to increase as the severity of the dementia increased. The ratio of choline/Ach was inversely correlated with the severity of the dementia to a significant degree ($r=-0.79$, $p<.001$). There was no significant correlation of CSF levels of HVA, 5-HIAA, or MHPG with the severity of dementia

Table

CSF Measures in AD/SDAT

Patient	Age	MIT[a]	Ach Nanomoles/ML	Choline Nanomoles/ ML	5-HIAA Nanograms/ ML	HVA Nonograms/ ML	Ratio of Choline/ Acetylcholine	MHPG NG/ML
1	64	0	.026	3.26	29.0	38.0	125.4	8.6
2	62	1	.035	4.43	33.0	37.0	126.6	9.9
3	57	3	.046	3.02	33.8	80.4	65.7	7.8
4	53	6	.037	2.65	36.2	71.6	71.6	6.9
5	63	13	.049	2.78	26.0	50.4	66.7	---
6	62	0	.028	3.60	25.5	52.6	128.6	14.4
7	72	13	.058	3.05	15.7	17.8	52.6	5.9
8	57	7	.068	3.34	22.2	37.3	49.1	8.9
9	70	0	.029	2.35	22.0	38.8	81.0	6.2
10	59	1	.026	3.50	34.6	47.5	134.6	12.8
11	80	0	.038	3.80	27.0	21.0	100.0	8.7
12	75	10	.047	3.40	---	---	72.3	10.5
13	54	7	.035	3.23	---	---	92.3	10.1
14	78	12	.071	3.23	---	---	45.5	---
$\bar{X}$			.042 ± .004	3.26 ± 0.14	27.7 ± 1.9	44.7 ± 5.7	85.9 ± 8.6	9.2 ± 0.7

[a] MIT = Memory Information Test

Discussion

The results provide further evidence of the importance of the cholinergic deficiency in SDAT. Postmortem studies of patients with SDAT have emphasized the highly selective degeneration of cholinergic neurons, citing normal levels of synthetic enzymes associated with other neurotransmitter systems (Davies & Maloney 1976; Perry et al. 1977). The absence of a correlation of dementia with HVA, 5-HIAA, and MHPG levels here corroborates those studies.

The correlation of CSF Ach concentrations with severity of dementia as assessed by a histopathologically validated instrument represents the first biological antemortem reflection (excluding surgical brain biopsy) of the extent of illness in patients with SDAT. The crucial role of cholinergic activity in the memory deficit of SDAT is supported by this finding. Future applications might include predicting response to potential cholinomimetic drug treatments based on CSF Ach level, and monitoring the progression of the illness longitudinally. Measurement of CSF Ach in other types of dementia may yield data useful clinically in differential diagnosis.

Summary

Concentrations of several neurotransmitters and metabolites were measured in the CSF of patients with SDAT. CSF Ach concentration correlated significantly with memory test scores in these patients. There was no correlation with several other neurotransmitter metabolites.

References

Anderson, G.M., Young, J.G., and Cohen, D.J. Rapid liquid chromatographic determination of tryptophan, tyrosine, 5-hydroxyindoleactic acid, and homovanillic acid in cerebrospinal fluid. *J. Chromatogr.*, 164:501-505, 1979.

Blessed, G., Tomlinson, B.E., and Roth, M. The association between quantitative measures of dementia and senile change in the cerebral gray matter of elderly subjects. *Br. J. Psychiatry*, 114:797-811, 1968.

Bowen, D.J.M., Spillane, J.A., Gurzon, G., Meir-Ruge, W., White, P., Goodhardt, M.J., Iwangoff, P., Davison, A.N. Accelerated aging or selective neuronal loss as an important cause of dementia. *Lancet*, 1:11-14, 1979.

Carlsson, A. Adolfsson, R., Aquilonius, S.M., Gottfries, C.G., Oreland, L., Swennerholm, L., Winblad, B. Biogenic amines in brain in normal aging, senile dementia, and chronic alcoholism. *Adv. Biochem. Psychopharmacol.*, 23:295-304, 1980.

Davies, P., and Maloney, A.J.F. Selective loss of central cholinergic neurons in Alzheimer's disease. *Lancet*, 2:1403, 1976.

Davies, P. Neurotransmitter related enzymes in SDAT. *Brain Res.*, 171:319-327, 1979.

Davis, K.L., Mohs, R.C., Davis, B.M., Levy, M.I., Rosenberg, G.S., Horvath, T.B., Ross, A., Rothpearl, A. Cholinomimetics and the treatment of memory disorders. *Psychopharmacol. Bull.*, 17(3):141-142, 1981.

Jenden, D.J., Roch, M., and Booth, R.A. Simultaneous measurement of endogenous and deuterium-labelled trace variants of choline and acetylcholine in sub-picomolar quantities by gas chromatography/mass spectrometry. *Anal. Biochem.*, 55:438-448, 1973.

Karoum, F., Gillin, J.C., Wyatt, R.J., and Costa, E. Massfragmentography of nanogram quantities of biogenic amine metabolites in human cerebrospinal fluid and whole rat brain. *Biomed. Mass Spectrom.*, 2:183-189, 1975.

Perry, E.K., Perry, R.H., Blessed, G., and Tomlinson, B.E. Necropsy evidence of central cholinergic deficits in senile dementia. *Lancet*, 1:189, 1977.

Spitzer, R., Endicott, J., and Robins, E. *Research Diagnostic Criteria for a Selected Group of Functional Disorders, 3d ed.* New York:Biometrics Research, New York State Psychiatric Institute, 1978.

Welch, M.J., Markham, C.H., and Jenden, D.J. Acetylcholine and choline in cerebrospinal fluid of patients with Parkinson's disease and Huntington's chorea. *J. Neurol. Neurosurg. Psychiatry*, 39:367-374, 1976.

Cognitive and Performance Deficits in Depression

Allen Raskin, Ph.D.,[1] Alfred S. Friedman, Ph.D.,[2] and Alberto DiMascio, Ph.D.[3]

Among the characteristics most often cited as behavioral correlates of depressive illnesses are (a) disturbed psychomotor activity involving retardation or agitation, (b) ideational disturbances such as limitations of span of attention, slowness of thought processes, and learning impairment, (c) self-depreciation which is reflected by a lowering of level of aspiration and feelings of inadequacy, and (d) energy diminution with loss of drive and motivation (Ayd 1961; Lehmann 1965).

Empirical studies have not been uniformly successful in documenting these behavioral correlates of depression. For example, with regard to psychomotor functioning such as simple reaction time, investigators have found both no difference among normals and depressed patients (Hall & Stride 1954), and depressed patients to be slower than normals (Huston & Senf 1952). A similar situation obtains with regard to learning and other cognitive functions. For example, one study reported short-term memory deficits in depression (Sternberg & Jarvik 1976) whereas another failed to find impairment in short-term memory (Henry et al. 1973).

These inconsistencies across studies have been attributed to differences in the types and severity of illness of depressed patients admitted to these studies as well as the differences in how certain functions, such as short-term memory, are defined and assessed.

The general aim of the present study was to determine what effects, if any, the presence of moderate to severe depression has on tests sampling the aforementioned behavioral correlates of depression. The differential effects of age and sex on these measures was also examined.

Method

Patients

The study sample consisted of 277 patients drawn from three State hospitals (Boston State Hospital, Boston, Mass., Rochester State Hospital, Rochester, New York, and Rochester State Hospital, Rochester, Minn.) and two private institutions (Hartford Hospital, Hartford, Conn., and Philadelphia Psychiatric Center, Philadelphia, Pa.).

For admission, patients had to be newly hospitalized, between 16 and 70 years of age, and with no evidence of mental deficiency, chronic alcoholism, liver damage, unequivocal brain damage, cardiovascular disease, or epilepsy. Project coordinators (a psychiatrist or psychologist) at each hospital also rated patients on amount of depression in verbal report, behavior, and secondary symptoms of depression. Each of these three items were rated on 5-point intensity scales. For admission to the study, a patient had to achieve a total score of at least nine, which would be the equivalent of a moderate amount of depression.

Normals

The 112 normal subjects were drawn from the same institutions as the patients and matched to the patient sample on age, sex, and years of schooling (*see* Table 1). Although not noted in Table 1, there was also no significant difference between normals and patients on the vocabulary subtest of the Wechsler-Bellevue Intelligence Scale II. The normal subjects were between 16 and 60 years of age and the same exclusion criteria previously cited for the patients were applied to normal subjects. In addition, a normal subject could not be receiving in- or outpatient treatment for a medical disability, be a discharged mental patient being followed in an aftercare clinic, or be undergoing psychiatric treatment. These subjects also had to meet Diagnostic and Statistical Manual-II (DSM-II) criteria for No Mental Disorder (DSM-II diagnosis 318).

---

[1] National Institute of Mental Health, Rockville, MD 20857.
[2] Philadelphia Psychiatric Center, Philadelphia, PA 19104.
[3] Boston State Hospital, Boston, MA 02124.

Send reprint requests to: Allen Raskin Ph.D., Pharmacologic and Somatic Treatments Research Branch, NIMH, Room 10C-14, 5600 Fishers Lane, Rockville, MD 20857.

Table 1

Identifying and Background Characteristics of Study Sample

	Patients	Normals
Number	277	112
Age (Median)	41	42[a]
Sex (% female)	68	66[a]
Years Schooling (median)	11	12[a]
Neurotic Depression (%)[b]	51	
Psychotic Depression (%)[b]	38	
Schizoaffoctive (%)[b]	11	
Anxious Depression (%)[c]	29	
Withdrawn-Retarded Depression (%)[c]	20	

[a] None of the differences between the two groups on these demographic variables were statistically significant.

[b] Based on diagnoses in the Diagnostic and Statistical Manual-II.

[c] Based on depressive subtypes developed by John E. Overall.

Measures

There were 13 separate tests in the test battery yielding a total of 33 scores. A brief description of each test follows:

Psychomotor Performance. (a) Tapping. The rate of a simple repetitive movement is determined under both a "free" or non-speed condition, and a maximum speed condition. For each condition the number of taps in a 30-second period is recorded. After each trial, the subject is asked to estimate how many taps she or he did. (b) The Area Tapping Test (Foulds 1961). On this test, Caine (1960) found depressives to be constricted and cover less area on the paper than nondepressed individuals. The subject is instructed to make dots with a pencil on a piece of 8½ × 11" paper for a period of 1 minute. An 8½ × 11" clear stencil divided into squares indicates the total number of squares containing dots. (c) Circle Tracing Test. The Circle Tracing Test (Siegman 1961) is considered to be a test of the subject's impulse control level (motor-inhibition capacity). The subject is instructed to "trace this circle. . . as slowly as possible." The score is the time taken to complete the tracing. (d) Aiming. This paper and pencil visual-motor coordination test from Moran and Mefferd's (1959) battery involves the placing of a dot in the center of a series of circles 2mm in diameter. The number of dots placed completely within the circles, in each of four 30-second consecutive testing periods, and the number of errors (dots touching the edges or outside the circle), are recorded. After the task has been completed, the patient is asked to estimate the percentage of the time he was completely within the circle.

Measures of Ideational, Perceptual, and Cognitive Functioning. (a) Nonsense-syllable learning task. This task requires both learning and immediate recall. A list of 10 three-letter consonant nonsense syllables to be learned are presented on a memory drum. The syllables are presented twice, each for 3 seconds, in two different orders. A 1-minute task is then interposed. At its completion, the subjects are instructed to recall and write down correctly as many of the syllables as possible. The number of syllables recalled or attempted are recorded; the number of those that are correct recalls are also recorded. (b) The Gorham Proverb Test (1956). This test is used to assess verbal comprehension and abstract conceptualization. The subject's task is to give the meanings of proverbs. Thirteen items from Gorham's 40-item multiple-choice form of the test were selected for this study. From among four possible interpretations, the patient is to choose the best answer. These answers are ordered on the answer sheet from most abstract to most concrete. Three scores are obtained: an "Abstract" score, a "Concrete" score, and the combined "Adjusted" score. No time limit is imposed. (c) Unpaced Digit-Symbol Substitution Test. This test is a measure of incidental memory and learning. The Wechsler-Bellevue Intelligence Scale-II 2-minute subtest was used. The number of digit symbol substitutions and the number of errors made, in each of four consecutive 30-second periods, was recorded. (d) Paced Digit-Symbol Substitution Test. The paced digit-symbol test is similar to the regular or unpaced test with the exception that the numbers, rather than being presented on the sheet on which the symbols are to be written, are presented by means of a memory drum. The numbers are presented at the rate of 40 per minute, i.e., at 1½-second intervals. Because of the added pressure to respond within a specified time, it was felt that depressed patients would have more difficulty with paced tasks than with unpaced tasks. Three scores are derived from this test, the number of correct symbols, the number of errors, and the number of omissions. (e) Estimating Dots. This is a technique developed by Fisher, Williams, and Lubin (1957) that is considered to be a measure of self-adequacy or, conversely, of uncertainty of judgment. Subjects are shown a series of 10 cards each containing a large number of dots. After each presentation of a card, for 10 seconds, the subject is asked to estimate the number of dots on the card shown and then to reevaluate his estimate and to indicate by how many dots he felt he was in error. (f) Time Estimation. This task taps the ability to experience perceptual phenomena in the absence of external cues. Two procedures are employed. First, the subject is asked to estimate how many seconds have elapsed between two signals (i.e., "start" and "stop"). A 15-second interval between the two signals is employed. Next, the subject is required to give a signal (i.e., "stop") when 15 seconds has elapsed after the signal to "start" has been given. The two times, in seconds, are recorded. (g) Shift Test (Friedman 1964). This task taps flexibility of mental set or maintenance of motivation to a boring routine task, and involves circling a specified digit whenever it occurs (irregularly) on a page of digits, and then shifting on command to circle a different digit and discontinue circling the previous digit. This is a 1 ½-minute task, requiring three shift commands, each of 30-second duration. The number of digits completed in each 30-second period is recorded. (h) The Stroop Color-Word Interference Test (1935). This test is used to assess conceptual set and flexibility. The subjects are presented a card containing 50 color-name words printed in a colored ink that is incongruous with the printed name. The subjects' task is to name the color of the ink in which the color-name words are printed. The score is the time taken to name the 50 colors on the card. The number of wrong responses is also recorded. (i) Clock Reversal Test. This is also a test of perceptual flexibility. The first two trials of this task merely require the subject to read the times on two cards (with hands but without numbers) indicated by the position of the hour and minute hands. In the third trial, the subject is not shown a card but told to imagine where the hour and minute hands would be if 12:30 were reversed. In the final trial, the subject is asked to reverse 3:20. Each of the four parts of this test are scored to indicate whether the subject gave the correct or incorrect response.

Testing was done soon after the patients' admission to the hospital and after patients had been off all psychoactive medication for a minimum of 4 days. In most instances, patients were kept off medication for at least a week prior to testing. The order of testing is indicated in Table 2. At the end of testing, test examiners completed a modified version of the Friedhoff Task Behavior Scale (Friedhoff & Alpert 1960). This test includes items sampling the patient's ability to cooperate and attend to the tasks. Patients who had considerable difficulty in attending or who were very uncooperative were dropped from the study. Total testing time was approximately 1 hour.

Statistical Analysis. A multivariate analysis of variance was used to test for group differences. Main effects in this model were group (patient vs. normal), sex, and age (under 40 vs. 40 and over). The score attained on the Vocabulary subtest of the Wechsler-Bellevue Intelligence Scale-II a continuous variable, was entered as a regression in the model. This model also generated three interaction terms, group by sex, group by age, and group by vocabulary score. Each main effect term was tested with the other main effects co-varied out. Hence, in the tests for differences between patients and normals the effects of age, sex, and vocabulary score were partialled out.

Table 2

Test Battery

Order of Testing
1. Tapping under free and speed conditions
2. Dot estimation (Fisher, Williams, & Lubin)
3. Aiming (Moran & Mefferd)
4. Time estimation
5. Unpaced digit symbol substitution (Wechsler)
6. Clock reversal
7. Shift test (Friedman)
8. Stroop Color-Word Interference Test
9. Area Tapping Test (Foulds)
10. Circle Tracing Test (Siegman)
11. Paced Digit Symbol
12. Learning and recall of nonsense syllables
13. Gorham Proverb Test

Results

Patients vs. Normals

There were significant patient-normal differences on 11 of the 13 tests and on 25 of the 33 scores derived from these tests. These results are presented in Table 3. The two tests that failed to show patient-normal differences were Time Estimation and Dot Estimation. Inter-individual variability for both patients and normals was very high on these tests which inflated the error terms and washed out patient-normal differences.

Table 3

Significant Differences Between Depressed Patients and Normal Controls on Cognitive and Psychomotor Tests

	Mean Scores		
Variable	Patients	Normals	F-ratio
A. Tapping			
1. Free condition	69.65	55.93	10.28[b]
2. Additional taps under speed condition	54.17	75.22	25.07[b]
B. Aiming			
1. Total dots in circles	76.34	125.22	116.91[b]
2. Percentage accuracy-4 Trials	69.77	84.05	20.64[b]
3. Estimate by subjects of dots in circles	83.58	102.82	4.34[a]
C. Digit Symbol-Unpaced			
1. Correct symbols-Trial 2	12.07	17.00	76.07[b]
2. Percentage accuracy-Total	95.67	99.55	3.91[a]
3. Guess of time to complete test (seconds)	177.79	137.35	4.67[a]
4. Additional symbols completed Trial 4 vs. Trial 2	.36	1.73	5.26[a]
D. Digit Symbol - Paced			
1. Correct symbols	22.40	34.55	63.20[b]
2. No. errors	1.28	.47	4.20[a]
3. Percentage accuracy	69.56	86.10	20.32[b]
E. Clock reversal			
1. Trial 4 correct	1.77	1.90	4.39[a]
2. Score for speed and accuracy	2.49	3.82	25.45[b]
F. Shift Test			
1. Trial 3 (No. 4's crossed over)	15.88	21.72	62.39[b]
G. Stroop Color-Naming Test			
1. Total errors in reading	3.20	1.82	5.32[a]
2. Ratio of time to complete line 1, Card C and Card C total	16.42	14.28	9.23[b]
3. Critical difference score time to read Card C vs. Card B	42.34	34.07	6.62[a]
H. Area tapping			
1. Estimate of time to complete (seconds)	44.78	22.68	6.37[a]
I. Circle Tracing			
1. Time to trace (seconds) (slow time bast)	43.35	68.55	16.35[b]
J. Learning nonsense syllables			
1. No. attempted	3.38	6.75	102.48[b]
2. No. correct	1.26	2.17	27.60[b]
K. Gorhams Proverbs Test			
1. Abstract sum	5.57	8.12	47.64[b]
2. Concrete sum	1.18	.59	18.06[b]
3. Abstract and concrete sum + 6	9.68	13.53	57.13[b]

[a] Significant at .05 level (2-tailed).
[b] Significant at .01 level (2-tailed).

The number and breadth of the differences between patients and normals was surprising. A prior study by one of the authors (Friedman 1964) had found only modest differences between depressed patients and normals on psychomotor and cognitive tests, and most of these differences were on patient estimates of how well they did on the tests rather than in actual performance. Patients in the earlier study by Friedman (1964) were generally better educated than patients in the present study which may account, in part, for the differences in results between the two studies. The Friedman study also led us to expect patients to deprecate their actual performance on the tests by underestimating how well they did. Some evidence of this was apparent in their tendency to overestimate the time it took them to complete the unpaced digit symbol subtest which has a 120-second time limit, and in their estimate of time spent on the area tapping test. The actual time difference between patients and normals on the area tapping test was not significant under both the non-speed and speed conditions. However, it is also interesting that patients had fewer dots in circles in the Aiming Test than normals, and this difference was also reflected in their estimates of the number of dots they had placed in circles. Hence, in this instance their low estimate is an accurate reflection of their actual performance rather than an example of a low level of aspiration or feelings of inadequacy.

Table 4

Significant Age-Group Differences on Cognitive and Psychomotor Tests

Variable	Under 40		40 Plus		F-ratio	Difference^{c}
	Pt(1)	Norm(2)	Pt(3)	Norm(4)		
Number	139	31	138	81		
A. Aiming						
1. Total dots in circles	90.54	120.33	62.14	130.11	19.65^{b}	3-4
2. Percentage accuracy 4 trials	76.40	81.44	63.15	86.65	9.50^{b}	3-4
B. Time estimation						
1. Time off from 15 seconds	12.28	28.25	34.15	15.58	4.92^{a}	4-1
C. Digit Symbol-Unpaced						
1. Correct symbols Trial 2	14.28	16.85	9.86	17.16	19.21^{b}	4-3
2. Guess of time to complete test	124.83	140.35	230.76	134.35	9.86^{b}	4-1
D. Shift Test						
1. No. 4's crossed over last trial	18.95	21.80	12.81	21.64	18.01^{b}	2,1,4-3
E. Digit Symbol-Paced						
1. Percentage accuracy	79.89	86.90	59.23	85.31	7.44^{b}	2,4,1-3
F. Gorham Proverbs						
1. Abstract sum	6.37	8.23	4.76	8.00	3.85^{a}	2,4,1-3
2. Concrete sum	.79	.57	1.57	.60	7.82^{b}	3-1,4,2
3. Abstract plus concrete plus 6	11.08	13.66	8.28	13.40	6.84^{b}	2,4,1-3

[a] Significant at .05 level (2-tailed).

[b] Significant at .01 level (2-tailed).

[c] Comma indicates no significant difference; dash indicate significant difference.

Differences between the patients and normals emerged on psychomotor and perceptual tasks in which speed, fine eye-hand coordination, or accuracy were important. In this context it is interesting that the patients performed significantly *better* than the normals on finger tapping under the free condition, i.e., under instructions to tap at a rate that was "comfortable" for them. Hence, they were not deficient in psychomotor performance per se, but deficits did appear when they needed to sustain attention and concentration or where other factors such as energy or motivation were important. As expected, the depressed patients did appear to have more difficulty with the paced digit symbol subtest than with the unpaced version of this test. However, their difficulty was primarily in errors generated and in accuracy which dropped from 95 percent under the unpaced condition to 69 percent under the paced condition. The drop in accuracy for the normal subjects was from 99 to 86 percent which was not nearly as dramatic a drop.

Perceptual flexibility as reflected on Clock Reversal of the Stroop Test and the Shift Test was also an area where there were consistent differences favoring the normal subjects over the patients.

Concrete thinking as measured by the Concrete Sum on the Gorham Proverbs Test was also more prevalent in the depressed sample than in the normals. There were also deficits in the ability of depressed patients to learn nonsense syllables. They not only learned fewer correct symbols but were also more cautious than the normals in guessing at possible correct symbols following the presentation period on the memory drum.

Age-Group Differences

There were 10 significant age-group differences (*see* Table 4). As indicated in the "Difference" column in Table 4, the over-40 patients were most dissimilar from the other groups. They performed slower, with less accuracy, and showed more perceptual rigidity and concreteness in thinking than normal subjects in the same age group. It is also noteworthy that on a number of measures, normal subjects over 40 did as well or better than the under-40 normals. Hence, although age per se plays some role in psychomotor and cognitive decline, it is the combination of age and depression that seems to have the greatest negative impact on skills in these areas.

Sex-Group Differences

There were only six significant sex-group differences, and in four of these the significant difference was between male patients and male normals. Although the range tests were not significant, the trend in the two other scores was also in the same direction, i.e., with the normal males performing better than the male patients.

Discussion

These results provide compelling evidence that depression does have a negative effect on psychomotor and cognitive skills. The deficits appear to be very general and include tasks requiring sustained effort and concentration, perceptual flexibility or fluidity, abstract thinking, motivation, and accuracy. Simple motor tasks such as finger tapping were not adversely affected by the depression. The results indicate that there is also a tendency for depressed patients to undervalue or deprecate their performance but, in contrast to Friedman's (1964) earlier results, there was some basis in fact for this view, i.e., depressed patients did perform more poorly than their normal counterparts.

The deficits noted in the depressed patients were more pronounced in older patients and the differences were more striking between male patients and male normals than between female patients and female normals. Uhlenhuth (1981) also found a sex difference in the psychomotor performance of depressed patients. He found male depressed patients less efficient than normal men in performing even simple repetitive tasks under various schedules of positive reinforcement. However, depressed women performed more efficiently than their normal counterparts.

There was a general trend in the study for older subjects (patients and normals) to perform poorly on the psychomotor and cognitive tests and for women to perform more poorly than men. Depression tends to magnify these existing age and sex differences but in a somewhat selective fashion. Older depressed patients did more poorly than older normals and male depressed patients performed more poorly than normal males. Dif-

Table 5

Significant Sex-Group Differences on Cognitive and Psychomotor Tests

Variable		Female		Male			
		Pt(1)	Norm(2)	Pt(3)	Norm(4)	F-ratio	Difference[c]
	Number	189	74	88	38		
A. Aiming							
1. No. dots in circles		80.20	119.42	72.48	131.02	5.26[a]	4-3
2. Percentage accuracy for 4 trials		72.60	80.74	66.95	87.35	4.39[a]	4-3
B. Time Estimation							
1. Time off from 15 seconds		-2.12	-4.84	-2.76	-1.67	5.46[a]	
C. Clock Reversal							
1. Combined speed and accuracy score		2.54	3.33	2.43	4.31	4.90[a]	4-3
D. Area Tapping							
1. Speed condition		34.90	44.98	35.24	27.44	8.47[b]	
E. Nonsense Syllable Learning							
1. Syllables attempted		3.66	5.86	3.10	7.63	14.19[b]	4-3

[a] Significant at .05 level (2-tailed).
[b] Significant at .01 level (2-tailed).
[c] Dash indicates significant difference.

ferences were less pronounced between under-40 depressed patients and normals and between female depressed patients and female normals. Hence, it is the patients who are either beginning to experience declines in performance and cognitive skills (older patients) or who have the greatest premorbid strengths in these areas (males) who show the greatest vulnerability to the negative effects of depressive illness.

Although the present study was designed to test a variety of hypotheses related to the effects of depression on psychomotor performance and cognitive skills, this effort was essentially atheoretical. However, study results, particularly the findings that perceptual rigidity and concrete thinking appear to be very prevalent in moderately to severely depressed patients, suggest a possible organic basis for the depression in many of these patients. This is not a new or original thought, but it would be very interesting to select a sample of depressed patients who do poorly on tests such as the Gorham Proverbs and Stroop Color-Naming Test and conduct positron emmission tomography (PET) scans on these patients as has recently been done with schizophrenics.

References

Ayd, F. *Recognizing the Depressed Patient.* New York:Grune & Stratton, 1961.

Friedhoff, A.J., and Alpert, M. The effect of chlorpromazine on the variability of motor task performance in schizophrenics. *J. Nerv. Ment. Dis.*, 130:110-116, 1960.

Hall, K.R.L., and Stride, E. Some factors affecting reaction times to auditory stimuli in mental patients. *J. Ment. Sci.*, 100:402, 1954.

Henry, G.M., Weingartner, H., and Murphy, D.F. Influence of affective states and psychoactive drugs on verbal learning and memory. *Am. J. Psychiatry*, 130:966-971, 1973.

Huston, P.E., and Senf, R. Psychopathology of schizophrenia and depression. I. Effect of amytal and amphentamine sulfate on level and maintenance of attention. *Am. J. Psychiatry*, 109:131, 1952.

Lehmann, H.E. Depression: Categories, mechanisms, and phenomena. Presented at the annual meeting of the American College of Neuropsychopharmacology, Washington, D.C., January 1965.

Sternberg, D.E., and Jarvik, M.E. Memory functions in depression. *Arch. Gen. Psychiatry*, 33:219-224, 1976.

Uhlenhuth, E.H. Personal communication. 1981.

Desglycinamide-9-Arginine-8-Vasopressin (DGAVP, Organon 5667) in Cognitively Impaired Patients[1]

Jared R. Tinklenberg, M.D.,[2] Robert Pigache, M.D.,[3] Philip A. Berger, M.D.,[2] and Bert S. Kopell, M.D.[2]

Animal studies and some human trials indicate that vasopressin (VP) peptides can enhance learning and memory in certain conditions (Tinklenberg et al., in press). The following describes a small clinical trial of one VP peptide, desglycinamide-9-arginine-8-vasopressin (D AVP, Organon 5667), which is of interest because animal studies indicate it is devoid of cardiovascular and antidiuretic hormone (ADH) activity, while retaining behavioral effects (van Riezen 1978).

Method

Eleven men over the age of 50 who had mild to moderate cognitive impairment were studied. They were unable to function occupationally, but could still live independently, did not become disoriented in familiar settings, and showed no marked personality deterioration. The criteria were designed to exclude anyone with severe cognitive limitations or anyone who had always demonstrated low levels of intellectual functioning.

Seven subjects satisfied the Diagnostic and Statistical Manual (DSM-III) requirements for Primary Degenerative Dementia (PDD) (290.10) and met the following additional criteria: insidious onset before age 65 with memory impairment as the initial feature, progressive dementia without stepwise deterioration for at least 2 years before his study, and a Hachinski score of less than 4. There was no evidence suggesting other causes of dementia, i.e., no cerebral vascular symptoms or signs, hypertension, or other cardiovascular disease, alcoholism, drug abuse, head trauma, epilepsy, or mental retardation. There were no localizing signs on EEG, CT, or neurological exams. X-ray and laboratory exams including B12, T3, T4, and folic acid were normal. There was no indication of significant depression or other psychiatric disturbances on two independent exams.

---

[1] This study was supported by the Medical Research Service of the Veterans Administration and the Stanford Mental Health Clinical Research Center Grant MH-30854.

[2] Psychiatry Service (116A), Veterans Administration Medical Center, Palo Alto, CA 94304 and Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305.

[3] Scientific Development Group, Organon, International, Os The Netherlands.

Four patients satisfied the DSM-III requirements for Dementia Associated with Alcoholism (291.22). As with PDD, other causes of dementia were excluded by history, physical, and laboratory exams. There was at least one hospitalization explicitly for alcoholism.

The learning and memory measures, which were chosen on the basis of demonstrated sensitivity to VP or cholinomimetics, were: A 12-word high and low imagery selective reminding learning task and a 20-word delayed free-recall task. To prevent rehearsal between the presentation of the 20 words and their recall 12 minutes later, the subjects were engaged in a distractor task. Behavior and mood were assessed with the Hamilton Depression Scale (Ham-D), Profile of Mood States (POMS), the Sandoz Clinical Assessment -Geriatric (SCAG), and the Nurses Observation Scale for Inpatient Evaluation (NOSIE). The study was conducted at the Stanford Mental Health Clinical Research Center, an inpatient unit at the Palo Alto Veterans Administration Medical Center.

Daily measures of vital parameters and frequent laboratory assessments were also made. After baseline assessments, patients were stratified according to diagnosis and then randomly assigned to one of two parallel groups. Four PDD patients were assigned to the active group and three to placebo. Two alcohol patients were assigned to each treatment group. Each treatment group received placebo DGAVP spray intranasally (i.n.) three times a day (t.i.d.) for 5 days. Then the placebo group continued to receive placebo treatment for 5 more days, whereas the active group received DGAVP 92 μg i.n., t.i.d. (about 202 μg/-day free peptide) for the same period. The measures of learning, memory, mood, and general behavior were obtained during baseline, three times during the first treatment period (when both groups received placebo) and three times during the second treatment period.

Results

Preliminary analyses indicated there were no significant differences between the PDD and alcoholic groups, so the two were combined according to which treatment they received. As indicated in the Table, DGAVP did not enhance overall group performance on the two verbal learning measures. Subjects receiving active treatment did remember words with low imagery value better than placebo subjects, but this trend did not reach statistical significance.

Subjects receiving active treatment did improve clinically as indicated by somewhat better scores on the SCAG, but the magnitude of this improvement was small. The Ham-D and POMS-vigor subscale changes suggest the possibility of DGAVP inducing central nervous system stimulation but, again, any such effect was not pronounced. There were no indications of any DGAVP-related side effects and no evidence for pressor or antidiuretic activity.

Comment

The results of this study combined with those of the authors' previous DGAVP study (Tinklenberg et al. 1982) indicate that any effects of this dosage schedule may be too small to be of clinical significance. Since the few patients who did improve during the active treatment period generally had higher scores on initial measures of depression, the possibility of this VP peptide inducing mild mood elevation should be considered, especially since other VP peptides may ameliorate certain forms of depression (Gold et al. 1979). The failure of PDD patients to respond significantly to DGAVP in this study is consistent with unimpressive findings in two earlier studies of related VP peptides lysine-vasopressin and desamino-8-D-arginine vasopressin (DDAVP) in PDD patients (Chase et al. 1982; Tamminga et al. 1981; Tinklenberg et al. 1982). However, these unconvincing results are in contrast to the recent positive treatment of very early PDD pa-

Table

		Mean of First Treatment Period (Placebo/Placebo)	Mean of Second Treatment Period (DGAVP/Placebo)	Standard Error of Difference
12-Word Selective Reminding Learning Total Recall	Active Group (*N* = 6)	8.56	8.78	
	Placebo Group (*N* = 5)	7.0	7.4	0.35
20-Word Delayed Free Recall	Active Group	2.22	2.22	
	Placebo Group	2.93	3.73	0.93
Sandoz Clinical Assessment Geriatric (SCAG)[a]	Active Group	40.6	37.6	
	Placebo Group	31.9	31.6	0.99
Hamilton Depression (Ham-D)[a]	Active Group	8.2	7.8	
	Placebo Group	2.1	2.3	1.45
Profile of Mood States (POMS): Vigor	Active Group	55.0	60.6	
	Placebo Group	56.0	55.75	4.03

[a] Lower score indicates improvement

tients with DDAVP (Weingartner 1981). Further studies of these interesting peptides using more extensive dosage schedules and larger numbers of patients are being conducted to resolve these apparent discrepancies.

Acknowledgment: We thank Dr. Henk van Riezen and his colleagues at Organon for their assistance.

References

Chase, T.N., Durso, R., Fedio, P., and Tamminga, C.A. Vasopressin treatment of cognitive deficits in Alzheimer's disease. In: Corkin, S., Davis, K.L., Growdon, J.H., Usdin, E., and Wurtman, R.L. (eds.), *Alzheimer's Disease: A Report of Progress in Research.* New York: Raven Press, 1982.

Gold, P.W., Weingartner, H., Ballenger, J.C., Goodwin, F.K., and Post, R.C. Effects of l-desamino-8-D-arginine vasopressin on behavior and cognition in primary affective disorder. *Lancet,* I:992-994, 1979.

Tamminga, C.A., Durso, R., Fedio, P., and Chase, T.N. Vasopressin studies in Alzheimer's disease. *Psychopharmacol. Bull.,* 18(1):48-49, 1982.

Tinklenberg, J.R., Peabody, C.A., and Berger, P.A. Vasopressin effects on cognition and affect in the elderly. In: Ordy, J.M., Sladek, J.R., and Reisberg, B. (eds.), *Neuropeptide and Hormone Modulation of Brain Function and Homeostasis.* New York: Raven Press. (In press)

Tinklenberg, J.R., Pigache, R., Pfefferbaum, A., and Berger, P.A. Vasopressin peptides and dementia. In: Corkin, S., Davis, K.L., Growdon, J.H., Usdin, E., and Wurtman, R.L. (eds.), *Alzheimer's Disease: A Report of Progress in Research.* New York: Raven Press, 1982, pp. 461-466.

van Riezen, H. Unpublished paper presented at the Scientific Development Group, Organon International, Oss, The Netherlands, 1978.

Weingartner, H., Gold, P., Ballenger, J.C., Smallberg, S.A., Summers, R., Rubinow, D.R., Post, R.M., and Goodwin, F.K. Effects of vasopressin on human memory functions. *Science,* 211:601-603, 1981.

Weingartner, H., Kaye, W., Gold, P., Smallberg, S.A., Peterson, R., Gillin, J.C., and Ebert, M. Vasopressin treatment of cognitive dysfunction in progressive dementia. *Life Sci.,* 29:2721-2726, 1981.

How Does Methylphenidate (MP) Affect Information Processing in Man?

Enoch Callaway, M.D.[1] Roy Halliday, Ph.D.,[1]
Shirley Peeke, Ph.D.,[1] and Victor Reus, M.D.[1]

The purpose of this paper is to argue that methylphenidate (MP) and probably other short-acting stimulants act on response-related processes at the output end of information flow and that they have little effect on input function such as stimulus evaluation.

The latency of the P3 component in the average evoked potential appears to reflect time spent evaluating the stimulus. For example, degrading the quality of a stimulus slows both reaction time and P3. Response factors such as response competition, response readiness, and response complexity influence reaction time as do stimulus related factors. However, in contrast to stimulus related factors, these response related factors do not influence P3 latency (McCarthy & Donchin 1981).

The authors found that MP speeded reaction time in a group of older hyperactive children but had no effect on the latency of the visual evoked potential P3 component. By contrast, when the comparisons were made between children, reaction time and the P3 latency were strongly related. Apparently the changes due to maturation and P3 latency influenced both reaction time and P3 latency, while changes induced by MP only affected reaction time and did not affect P3. This is illustrated in the Figure. Thus, maturation seems to speed stimulus evaluation, since it speeds both P3 latency and reaction time. MP seems to speed reaction time without influencing stimulus evaluation as indicated by P3 latency.

Another study of hyperactive children done in this laboratory also suggested that MP is not effective in altering perceptual processes. In this study moderate doses of MP improved memory performance. By contrast, MP had no effect on a span of apprehension test. This latter task requires searching a tachistoscopically projected array for a hidden item. Presumably, performance on this task is a function of speed in perceptual processing.

The fact that P3 latency reflects stimulus evaluation and methylphenidate does not affect P3 latency is further illustrated in another study from this laboratory. This one involved eight women between the ages of 30 and 40. A test was designed to include two levels of stimulus complexity and two levels of response complexity that could be combined to provide four difference tasks. The easy stimulus was an "X" that appeared in any one of four possible horizontal positions. The hard stimuli consisted of the "X" target with three stars which occupied the other three positions. Easy response consisted of pressing one key every time an X appeared. The hard response consisted of pressing one of four keys depending on the horizontal location of the target.

Reaction times and latencies of P3 were collected for all four tasks both before and 45 minutes after taking a pill. The pill contained either a placebo or MP in doses of 5, 10, or 20 mg.

MP speeded RT for all tasks but did not change P3 latency. Increasing both stimulus complexity and response complexity showed reaction time. The increase of stimulus complexity also increased P3 latency, but response complexity did not. Thus, MP acts after the processes involved in stimulus evaluation have been completed.

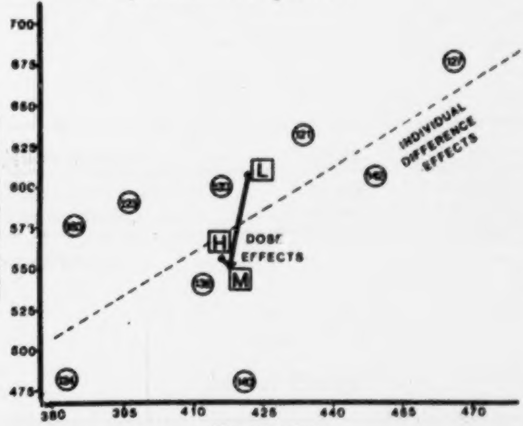


FIGURE: Effects of MP and maturation on reaction time and P3 latency. 0= average across doses of MP for individual subjects. Figure in circle is age in months. / /= average across subjects for each dose. L=Low .16 mg/kg. M=Medium .33 mg/kg. H=High .66 mg/kg.

---

[1] Langley Porter Psychiatric Institute, University of California, San Francisco Medical Center, San Francisco, CA 94143.

The notion that MP speeds response-related operations is consistent with reports in the literature. For example, Mohs et al. (1978) presented rows of print that were to be scanned for a single character and reported that a short-acting stimulant speeded this ordered search. Frowein (1981) has reported that amphetamine did not react with stimulus variables in a series of tasks where varying degrees of stimulus response complexity were combined. However, it did speed the motor response component of this task.

To summarize, then, the available data suggest that MP and perhaps other stimulants do not influence stimulus evaluation processes, but rather act on the performance end of the stimulus/response arc.

References

Frowein, H. Selective effects of barbiturate and amphetamine on information processing and response selection. *Acta. Psychol.*, 47:105-115, 1981.

McCarthy, G., and Donchin, E. A metric for thought: A comparison of P300 latency and reaction time. *Science*, 211:77-80, 1981.

Mohs, R., Tinklenberg, J., Roth, W., and Kopell, B. Methamphetamine and diphenhydramine effects on the rate of cognitive processing. *Psychopharmacology (Berlin)*, 59:13-19, 1978.

Parental Reports of Adverse Responses to Food Substances in Child Psychiatry Patients and Normal Controls

Jovan G. Simeon, M.D.,[1,2] H. Bruce Ferguson, Ph.D.,[1,3] Carole Anne Ralph,[1] and D. Mistry, M.D.[1]

Adverse responses to food substances have long been implicated as etiological factors of hyperactivity, conduct problems, and learning disorders in children. Most of the claims in the older literature associating food substances and behavior disorders are based on poor scientific methodology and anecdotal reports. An important drawback in research regarding allergic reactions has been the lack of reliable and valid diagnostic tests and criteria for allergies. Nevertheless, in the past decade, the popularity of this general approach has grown and publications advocating special diets for children with hyperkinetic and learning disorders have proliferated in North America. Such dietary management has been reported to result in relief of chronic disabling mental and physical symptoms (Crook 1980; Feingold 1975; Rapp 1979).

Controlled research studies examining hypotheses of detrimental effects of general food allergies (Trites et al. 1980) or adverse responses (of an unknown nature) to dyes and additives (Conners 1980; Goyette et al. 1978; Harley et al. 1978) have reported generally negative findings. There seems to be some agreement that a small proportion of children, perhaps the younger ones, are affected adversely by these latter substances. However, this conclusion leaves the clinician in a difficult position until valid and reliable diagnostic tests are evolved. To obtain a different perspective on the seriousness of the problem of adverse responses to food substances for child psychiatry, the authors compared parental reports

---

[1] The Royal Ottawa Hospital, Ottawa, Canada.

[2] Department of Psychiatry, School of Medicine, University of Ottawa, Ottawa, Canada.

[3] Department of Psychology, Carleton University, Ottawa, Canada.

Note: Copies of the questionnaires may be obtained by request from: Jovan G. Simeon, M.D., The Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa, Canada K1Z 7K4.

of such responses in a psychiatric sample with those of a control sample of unscreened school children. Their research hypothesis was that if adverse responses to food substances were an important etiological contributor to psychiatric problems in children, then parental reports of a referral sample ought to reveal a higher frequency of such associations than parental reports from a control sample.

Method

Psychiatric Referral Sample

Two hundred "active" files were selected from the records of the Children's Outpatient Psychiatric Department, Royal Ottawa Hospital. Current addresses were available for 190 of these children and questionnaires regarding any adverse responses to food substances and allergies were mailed out with stamped, return envelopes.

Control Sample

Permission was obtained from the Ottawa Board of Education to distribute questionnaires to elementary school students. Five hundred children, approximately evenly distributed through Grades 1 - 6 (age - 6.5-11.5) were given cover letters and questionnaires with stamped, return envelopes. All these children were in two schools chosen in consultation with Board officials to represent a broad range of socioeconomic status variables.

Questionnaires also obtained information about the child's age and sex, sibling sex and age, medical and academic problems, and allergic responses among family members.

Table 1

Number (and Percent) of Questionnaires Returned by Group

	Sent Out	Returned	Percent Returned
Psychiatric Group	190	57	30.0
Control Group	500	192	38.4

$X^2 = 3.85$ $p < .05$

Results

Response Rate

The response rate of the control sample was significantly higher than that of the psychiatric group (*see* Table 1).

Age Characteristics of Groups

The age range of the psychiatric group was 6-18 years with only 8 of 57 returned forms for children over 13. Those returning questionnaires in the school group had an age range of 5-13 years with relatively few children aged 5, 12, or 13. For the purpose of group comparison, age was divided into "young"(5-8 years inclusive) and "old"(9+ years) categories. The significant chi-square (*see* Table 2) reflects the preponderance of the psychiatric group in the "old" category, while the control sample was evenly split with regard to age.

Sex

There were relatively more males in the psychiatric group. This difference was significant (*see* Table 3) and is consistent with the generally accepted preponderance of boys in child psychiatric populations.

Table 2

Age by Group

Number (percent)	Young	Old
Psychiatric Group	14 (25)	43 (75)
Control Group	93 (48)	96 (52)

$X^2 = 9.28$ $p < .01$

Table 3

Sex of Group

Number (percent)	Male	Female
Psychiatric Group	44 (77)	13 (23)
Control Group	90 (47)	102 (53)

$X^2 = 15.09$ $p < .01$

Reported Adverse Responses or Allergies

Frequency of reported allergies was first examined collapsing across age and sex. The categories examined were: a) reaction only to foods; b) reaction to foods plus has allergies to other substances; and c) reaction to foods or has allergy to other substance. Although the rate of reported reactions was higher for the psychiatric group, there were no significant differences between groups (chi-square). Expressing the frequency of adverse responses to food as a proportion of all reported adverse effects (psychiatric group: 17/28-61 percent; control group: 39/79-49 percent) again revealed no significant difference between the groups.

Adverse Responses or Allergies: Group × Sex: Separate 2 × 2 comparisons of the groups for each sex showed no significant differences, despite the increased difference between groups for males on some variables (*see* Table 4). In addition, there was no difference between groups on adverse responses to foods expressed as a proportion of other allergies.

Table 4

Type of Adverse Response/Allergy as a Function of Group and Sex

Number (percent)	Psychiatric Group		Control Group	
	Male (*N* = 44)	Female (*N* = 13)	Male (*N* = 90)	Female (*N* = 102)
Reacts to food only	5 (11)	0 (0)	8 (9)	15 (15)
Reacts to food *plus* other	14 (32)	3 (23)	17 (18)	22 (22)
Reacts to other only	3 (7)	3 (23)	12 (13)	5 (5)
Reacts to food *or* other	22 (50)	6 (46)	37 (40)	42 (41)

Adverse Responses or Allergies: Group × Age: Although some of the psychiatric group values appeared higher for "young" subjects (*see* Table 5), the small number of psychiatric group children in this category make these figures unreliable. Once again, separate 2 × 2 chi-square comparisons of the groups for each age category showed no difference on any variable. In addition, there was no difference for adverse responses to food expressed as a proportion of other allergies.

Table 5

Type of Adverse Response/Allergy as a Function of Group and Age

Number (percent)	Psychiatric Group		Control Grou	
	Young (*N* = 14)	Old (*N* = 43)	Young (*N* = 93)	Old (*N* =
Reacts to food only	2 (14)	3 (7)	15 (16)	8 (9)
Reacts to food *plus* other	5 (36)	12 (28)	18 (19)	21 (21)
Reacts to other food	1 (7)	4 (9)	2 (2)	15 (15)
Reacts to food *or* other	8 (57)	19 (44)	35 (38)	44 (44)

Type of Symptom Shown to Food Substances

Symptoms were divided into three categories: a) physical symptoms, e.g., nausea; b) behavioral symptoms, e.g., hyperactivity, irritability; c) both physical and behavioral. In addition, the behavioral and "both" categories were combined to give a "total behavioral" symptoms category. The small numbers involved made it necessary to carry out this analysis collapsed across age and sex. Again, though the psychiatric group rates were higher for some variables (both, total behavioral), there were no statistically significant differences.

Substances Causing Symptoms

Both groups were sensitive to the same substances, both food and non-food. An exception was the high incidence of problems of the psychiatric group with pollens (15 vs. 4). Another point of note is that "sweets" (sugar plus chocolate) were reported to cause problems for twice as many children as food dyes or additives (25 vs. 11).

Role of Adverse Responses in Problems

Since the psychiatric group by definition had all been referred for emotional/behavioral/school problems, the role of adverse responses in producing medical, emotional, and school problems was examined in the school group (*see* Table 6).

Chi-square comparisons showed that the "food plus" group had significantly more medical and emotional problems than the "other" or "none" groups and that the "food plus" group had significantly more school problems than the "none" group only ($p < .05$). Thus, it appears that such reports of adverse responses to foods and other substances may indeed be related to incidence of such problems.

Table 6

Type of Adverse Response in the School Group

Number (percent) Adverse Response to:		Problem Area	
	Medical	Emotional	School
Food only ($N = 21$)	6 (29)	1 (5)	5 (24)
Food plus other ($N = 15$)	10 (67)	5 (33)	7 (47)
Other ($N = 41$)	13 (32)	3 (7)	8 (20)
None ($N = 102$)	17 (17)	7 (7)	18 (18)

Relation to Family Problems with Allergies

Only one psychiatric subject had a family member with adverse responses to food, while seven school subjects had family members with such responses. All eight of these children had adverse responses to foods. No family of a child without adverse responses reported a family member with an adverse response to a food substance.

The incidence of reported "allergies" among family members was higher among families of children reported to have adverse responses or allergies (78 vs. 53 percent). Whether or not the child showed adverse responses, the incidence of allergies reported for family members is about 10 percent higher in the school sample. However, chi-square analysis indicated that there were no significant differences between the psychiatric and school groups among subjects either with or without adverse responses.

Conclusion

The most noteworthy finding was the similarity between psychiatric and school groups in frequency and type of adverse responses and the substances to which they were reported to respond. While the problems appeared to be relatively more marked for boys and "young" subjects in the psychiatric sample, these differences did not reach significance. However, some care must be exercised in interpreting these results. Neither sample produced a satisfactory response rate and the school group's response rate was higher than the psychiatric group's. This low response rate leaves open the possibility that real differences in the populations are masked by some unknown sampling bias. Finally, the data showing that children in the school group with adverse responses to food and other substances were reported to have more problems than other children suggests that such adverse responses may indeed play some role in producing physical, behavioral, and school problems.

References

Conners, C.K. *Food Additives and Hyperactive Children.* New York:Plenum Press, 1980.

Crook, W.G. Can what a child eats make him dull, stupid, or hyperactive? *J. Learn. Disabil.*, 13:53-58, 1980.

Feingold, B.F. *Why Your Child is Hyperactive.* New York: Random House, 1975.

Goyette, C.H., Conners, C.K., Petti, T.A., and Curtis, L.E. Effects of artificial colors on hyperkinetic children: A double-blind challenge study. *Psychopharmacol. Bull.*, 13:39-40, 1978.

Harley, J.P., Ray, R.S., Tomasi, L., Eichman, P.L., Matthews, C.G., Chun, R., Cleeland, C.R., and Traisman, E. Hyperkinesis and food additives: Testing the Feingold hypothesis. *Pediatrics*, 61:818-828, 1978.

Rapp, D.J. *Allergies and the Hyperactive Child.* New York: Cornerstone Library, 1979.

Trites, R.L., Tryphonas, H., and Ferguson, H.B. Diet treatment for hyperactive children with food allergies. In:Knights, R.M., and Bakker, D.J. (eds.), *Treatment of Hyperactive and Learning Disordered Children.* Baltimore: University Park Press, 1980.

Classical Conditioning of Cocaine's Stimulatory Effects

Wagner H. Bridger, M.D.,[1] Stanley R. Schiff, M.D.,[1] Stanley S. Cooper, M.D.,[1] William Paredes, M.D.,[2] and Gordon A. Barr, M.D.[1]

The ability of environmental cues that become associated with drug administration to elicit behaviors originally due to the drug alone is well established. Pavlov (in 1927) first suggested that cues paired with drug treatment could be viewed as conditioned stimuli within the framework of classical conditioning.

However, although conditioning of opiates effects is now well accepted, the ability of conditioned stimuli to elicit stimulant-like behavior is not as established. (Irwin & Armstrong 1961; Pickins & Crowder 1967; Pickens & Dougherty 1973; Pilil & Altman 1971; Schiff, in press; Segal 1975; Tilson & Rech 1973). More recently, Post and his colleagues have argued that conditioned stimuli alone are not able to elicit increased activity and stereotypic behaviors typical of cocaine (Post & Rose 1976; Post et al. 1981). On the other hand, stimuli associated with reinforcing intravenous infusions of cocaine act as "priming" doses to facilitate responding for cocaine during extinction (deWit & Stewart 1981).

In the present series of experiments, the following questions were asked: 1) Can stereotyped behavior and hyperactivity elicited by cocaine be classically conditioned? 2) For how long can the conditioned stimuli continue to elicit cocaine-like behaviors with and without extinction?

Experiment I

Male Long-Evans hooded rats from Blue Spruce Farms (Altamont, N.Y.) aged about 90 days, were used. Two groups of rats, conditioned and pseudoconditioned controls, were used for all experiments. Both groups were given training trials in which they were placed into a 10-gallon glass aquarium for 1 minute during which time a tone which served as a conditioned stimulus was presented (2800 Hz Sonalert). Following this, the rats were injected with either 15.0 mg/kg cocaine HCL (Malincrodt) or 0.9 percent saline (1ml/kg) and placed into the second aquarium in a separate room. This procedure was done on 10 consecutive days. On the test day the procedures were identical except that all animals were injected with saline. After each training session, animals were returned to their home cages where they received, approximately 1 hour later, an injection of the opposite drug or vehicle. This served to equate the amount of cocaine received by both groups.

Seven separate behaviors were measured by an experienced rater blind to the experimental conditions through a one-way mirror from a separate room. These behaviors have been defined previously (Schiff, in press). Separate behaviors were measured rather than combining them into a single "stereotypy" score, because most stereotypy scales are defined to be linear and interval scales rather than being empirically derived as such. Thus, they are examples of what Torgerson (1967) calls measurement by fiat. Second, the authors and others (Costall & Naylor 1980; Eichler et al. 1980; Iverson 1977; Schiff 1980) reported that individual stereotyped behaviors may be mediated by different physiological systems.

Because there existed some question about the ability of conditioned stimuli to elicit increased activity and stereotypy, the initial experiment was designed to determine if, using the authors' methods, conditioned cocaine-like effects could be demonstrated.

Results

The conditioned group was compared to the pseudoconditioned group for each behavior by independent *t*-tests. These data are presented in the first table. Seven of the eight behaviors showed significant differences between groups, with licking not being conditioned.

Experiment II

It was established in the first experiment that seven of eight behaviors elicited by cocaine could be conditioned. Yet, for these findings to have practical significance it is necessary, although not sufficient, to demonstrate that the conditioned effect has some permanence. In this second experiment, we delayed testing the animals with saline for 5 days to see if the conditioned effect would last that long. Since it did, we tested twice more at 5-day intervals.

---

[1] Department of Psychiatry, Albert Einstein College of Medicine, Bronx, NY 10461.

[2] Department of Psychology, Hunter College, City University of New York, New York, NY 10021.

The methods were similar to those in the first experiment except that the initial test day was 5 days after the 10th training day rather than 1 day. Subsequent test days (saline injections) were 10 and 15 days posttraining.

Results

The data were analyzed by a two-way analysis of variance (Group × Day of testing) with particular attention paid to the interaction term. First, licking, grooming, and chewing did not show significant differences between groups and also failed to show significant interactions ($p < .05$). This suggests that the conditioned drug effects were dissipated by the first day of testing, Day 5, for these two behaviors; licking failed to show conditioning in Experiment 1. Sniffing and head-bobbing both demonstrated significant

Table 1

Behaviors Elicited by the CS for Conditioned and Pseudoconditioned Groups

	Licking	Head Bobbing	Chewing	Sniffing	Grooming	Rearing Time	Crossing	Rearing Frequency
Condit.	.29	91.37[a]	2.41[b]	99.75[b]	15.65[a]	33.81[b]	10.78[b]	8.27[b]
	.14	5.22	0.88	4.32	3.79	4.60	1.04	1.10
Pseud Condit.	.26	52.04	5.81	62.31	28.51	14.11	5.36	4.03
	.13	5.97	1.39	6.55	4.57	2.86	1.01	.71

[a] $p < .05$

[b] $p < .01$

Note- Entries are Means and Standard Errors of the Mean in seconds/ 120 second period except for crossings and rearing frequencies which are number/ 120 second period. Statistical significance was tested with independent *t*-tests. $N = 16$/ group.

Table 2

Differences Between Conditioned and Unconditioned Groups to the CS 5, 10, and 15 Days Posttraining

	Day	Licking	Head Bobbing	Chewing	Sniffing	Grooming	Rearing Time	Rearing Frequency	Crossing
Condit. Group	5	0.97	65.76	1.91	85.02	21.05	26.87	8.29	10.79
		0.45	4.51	1.20	5.57	7.47	5.02	1.03	1.61
	10	0.52	67.55	0.90	87.08	15.81	20.39	6.38	10.71
	15	1.60	54.61	1.99	80.06	16.04	18.29	6.66	9.33
		0.72	3.47	0.75	4.89	4.07	3.10	0.76	1.16
Pseudo-Condit. Group	5	2.56	33.51	5.27	45.98	27.12	11.98	3.25	4.04
		0.97	4.26	2.20	5.15	6.92	3.88	0.81	0.91
	10	2.40	27.79	2.89	43.15	28.28	9.17	2.46	2.92
		1.13	6.29	1.39	9.06	7.49	3.59	0.84	1.06
	15	3.22	41.64	4.48	63.01	22.39	15.45	4.16	5.91
		0.78	5.29	1.64	5.79	8.11	4.15	0.94	0.82

Note- Entries are Means and Standard Errors of the Mean in seconds/120 second period except for crossings and rearing frequencies which are numbers/120 second period. For statistics see text. $N = 8$/group.

group effects ($p < .001$) and significant interactions ($p < .05$). Subsequent analysis of the interactions by tests of simple main effects (Kirk 1968) showed that there were significant differences between groups on Days 5 and 10 but not on Day 15. Finally, the number of crossings and the frequency of rearing showed significant group differences but failed to show significant interactions (although there was a trend for a significant interaction for crossing, $p < .09$). This suggests that any decay for these two behaviors over the 15 days was minimal. The data are presented in Table 2.

Experiment III

In part because the second experiment which studied decay of the conditioned response contained an extinction component, and in part to determine if the conditioned effect could be decreased by extinction, the conditioned stimuli was presented without the unconditioned stimulus for 4 consecutive days. The ability or inability to extinguish the conditioned response could have implications for the treatment of stimulant abusers. The methods were identical to those of the second experiment, except that there were 4 consecutive test days beginning with Day 11.

Results

Data were analyzed in an identical manner to those in the second experiment. An analysis of variance was done on the data with a significant interaction indicating differential changes in the two groups over the 4 days of testing. This analysis failed to show significant differences between the conditioned and pseudo-conditioned groups for licking, chewing, or grooming. For licking this was a replication of the failure of this behavior to condition, but for the latter two behaviors it indicates caution in concluding that these two behaviors reliably condition. Rearing time only showed a trend towards conditioning ($p < .07$) and the comments above also apply here. Rearing frequency, crossings, sniffing, and head bobbing all showed significant group differences ($p < .05$, $< .01$, $< .001$, $< .05$, respectively) but no behavior showed any significant interactions or trends towards significant interactions ($p < .10$). Again, while nonsignificant differences must be interpreted with caution, this suggests that these behaviors did not show major extinction during the 4 extinction days. Table 3 presents the data.

Table 3

Differences Between Conditioned and Unconditioned Groups to the CS During 4 Days of Extinction

	Day	Licking	Head Bobbing	Chewing	Sniffing	Grooming	Rearing Time	Rearing Frequency	Crossing
Condit. Group	1	0.72	51.80	1.06	72.30	27.04	19.24	5.33	6.92
		0.28	4.07	0.31	2.97	8.81	4.01	0.84	0.85
	2	1.15	47.05	2.31	64.92	27.86	13.67	4.62	6.08
		0.75	6.54	1.09	8.72	6.67	3.46	1.22	1.66
	3	0.84	48.56	1.64	61.62	27.32	17.08	5.88	8.21
		0.32	6.95	0.47	6.55	6.84	2.19	0.80	1.12
	4	1.18	36.13	2.15	52.18	25.30	11.19	.3.79	5.21
		0.56	10.74	1.08	11.14	992	5.20	1.69	1.99
Pseudo-Condit. Group	1	1.40	35.23	4.08	53.60	23.47	9.07	2.29	3.86
		0.62	5.34	1.55	7.26	8.57	2.59	0.79	0.54
	2	0.97	37.73	4.22	49.65	17.17	8.36	2.41	3.71
		0.48	6.94	2.13	8.99	6.58	3.77	0.96	0.88
	3	1.25	24.80	2.05	32.18	36.15	6.58	2.04	2.75
		0.38	4.74	0.55	6.22	4.54	2.66	0.76	0.64
	4	1.18	26.58	8.38	34.09	35.83	7.71	1.92	3.83
		0.52	5.86	0.21	5.55	8.28	3.40	0.68	0.97

Note- Entries are Means and Standard Errors of the Mean (see Table 1). *N* = 8/group.

Discussion

The results of these experiments demonstrate that cocaine-like behaviors can be readily elicited by previously neutral stimuli that had been paired with cocaine and that these effects, for some of the behaviors, are stable over time.

The differences between the results found here and those of Post and his colleagues are likely due to one of two major methodological differences (Post & Rose 1976; Post et al. 1981). Conditioned stimuli were presented for the experimental group only with cocaine. In contrast, the National Institute of Mental Health (NIMH) group allowed 20 minutes of adaptation to the test chamber prior to drug injection. Thus, along with each conditioning trial was an extinction period. Others have reported relatively rapid extinction of the enhancement of cocaine's effects by conditioned stimuli (Hinson & Poulos 1981). Moreover, the authors attempted to increase the likelihood of conditioning by having multiple conditioned stimuli such as tone, injection, novel chamber, and removal to the observation room. It is likely that the conditioned drug effect requires these multiple cues.

A second procedural difference is the dependent measure. We examined individual behaviors and found that not all conditioned with equal ease. Most other investigators have used rating scales that combine behaviors. That some behaviors show more conditioning than others supports the argument that the different behavioral components of stereotyped behaviors may have different anatomical or chemical substrates.

These data have implications for the etiology and treatment of drug-seeking behavior. There are two ways in which environmental stimuli can affect stimulant abuse. The first is the enhancement of stimulant action by association with environmental cues (Hinson & Poulos 1981; Post & Rose 1976; Post et al. 1981; Segal & Mandell 1974). This may contribute substantially to resultant drug actions, including hyperactivity, stereotypy, and convulsions (Post et al. 1981). However, an equally important component is the role of these same environmental cues in the absence of drug. These cues can result in behavioral and presumably physiological effects that mimic the stimulant. In as much as "priming" doses of drug can lead to drug-seeking behavior in animals (Davis & Smith 1976; deWit & Stewart 1981; Gerber & Stretch 1975; Pickens & Harris 1968), stimuli associated with drug intake in a Pavlovian manner can also do the same (deWit & Stewart 1981). For opiates, the role of these stimuli in recidivism has been recognized. The authors suggest that similar processes may be functioning for stimulant abuse.

References

Anden, N.E., Roos, B.E., and Werdinius, B. On the occurrence of homovanillic acid in brain and cerebrospinal fluid and its determination by a fluorometric method. *Life Sci.* 2:448-458, 1963.

Costall, B., and Naylor, R.J. Mesolimbic and extrapyramidal sites for the mediation of stereotyped behaviour patterns and hyperactivity by amphetamine and apomorphine in the rat. *Adv. Biochem. Psychopharmacol.*, 24:47-76, 1981.

Davis, W.M., and Smith, S.G. Role of conditioned reinforcers in the initiation, maintenance, and extinction of drug-seeking behavior. *Pavlovian J. Biol. Sci.*, 11:222-236, 1976.

deWit, H., and Stewart, J. Reinstatement of cocaine-reinforced responding in the rat. *Pscyhopharmacology (Berlin),* 75:134-143, 1981.

Downs, A.W., and Eddy, N.B. The effect of repeated doses of cocaine on the rat. *J. Pharmacol. Exper. Ther.*, 46:199-200, 1932.

Eichler, A.J., Antelman, S.M., and Black, C.A. Amphetamine stereotypy is not a homogeneous phenomenon: Sniffing and licking show distinct profiles of sensitization and tolerance. *Psychopharmacology (Berlin),* 68:287-290, 1974.

Gerber, G.J., and Stretch, R. Drug-induced reinstatement of extinguished self-administration behavior in monkeys. *Pharmacol. Biochem. Behav.*, 3:1055-1061, 1975.

Hinson, R.E. and Poulos, C. Sensitization to the behavioral effects of cocaine: Modification by Pavlovian conditioning. *Pharmacol. Biochem. Behav.*, 15:559-562, 1981.

Irwin, S., and Armstrong, P.M. Conditioned locomotor response with drug as the unconditioned stimulus: Individual differences. In: Rothlin, E. (ed.), *Neuropsychopharmacology.*, Vol 2. Amsterdam: Elsevier, 1961, pp. 151-157.

Iversen, S.D., and Koob, G.F. Behavioral implications of dopaminergic neurons in the mesolimbic system. *Adv. Biochem. Psychopharm.*, 16:209-214, 1977.

Kirk, R.E. *Experimental Design: Procedures for the Behavioral Sciences.* Belmont, Calif:Brooks/Cole, 1968.

Pavlov, I.P. *Conditioned Reflex.* London: Oxford, 1927.

Pickens, R.W., and Crowder, W.F. Effects of CS-US interval on conditioning of drug response with assessment of speed of conditioning. *Psychopharmacology (Berlin),* 11:88-94, 1967.

Pickens, R.W., and Dougherty, J. Conditioning of the activity effects of drugs. In: Thompson, T., and Schuster, C. (eds.), *Stimulus Properties of Drugs.* New York:Appleton-Century Crofts, 1971, pp. 39-50.

Pickens, R., and Harris, W.C. Self-administration of *d*-amphetamine by rats. *Psychopharmacology (Berlin)*, 12:158-163, 1968.

Pihl, R.O., and Altman, J. An experimental analysis of the placebo effect. *J. Clin. Pharmacol.*, 11:91-95, 1971.

Post, R.M., Lockfeld, A., Squillace, K.M., and Contel, N.R. Drug-environment interaction: Context dependency of cocaine-induced behavioral sensitization. *Life Sci.*, 28: 755-760, 1981.

Post, R.M., and Rose, H. Increasing effects of repetitive cocaine administration in the rat. *Nature*, 260:731-732, 1976.

Schiff, S.R. Conditioned dopaminergic activity. *Biol. Psychiatry*. (In press)

Schiff, S.R. Classical conditioning of *d*-amphetamine and apomorphine induced behavior in the rat. Doctoral Dissertation, The Albert Einstein College of Medicine, New York, N.Y. 1980.

Segal, D.S. Behavioral and neurochemical correlates of repeated *d*-amphetamine administration. In: Mandell, A.J. (ed.), *Neurobiological Mechanisms of Adaptation and Behavior*. New York:Raven Press, 1975, pp. 247-262.

Segal, D., and Mandell, A.J. Long-term administration of *d*-amphetamine: Progressive augmentation of motor activity and stereotypy. *Pharmacol. Biochem. Behav.*, 2:249-255, 1974.

Tatum, A.L., and Seevers, M.H. Experimental cocaine addiction. *J. Pharmacol. Exper. Ther.*, 36:401-410, 1929.

Tilson, H.A., and Rech, R.A. Conditioned drug effects and absence of tolerance to *d*-amphetamine-induced motor activity. *Pharmacol. Biochem. Behav.*, 1:149-153, 1973.

Torgerson, W.S. *Theory and Methods of Scaling*. New York: John Wiley & Sons, 1958.

Naloxone Potentiates Cocaine Effect in Man

Robert Byck, M.D.,[1,3] Alan Ruskis, M.D.,[2] James Ungerer,[3] and Peter Jatlow, M.D.[3,4]

The effects of cocaine on mood and physiological parameters in man are well established. Naloxone (an opioid antagonist) has minimal mood and cardiovascular effects. The proposal for a common mechanism of euphoria mediated by endorphins (Byck 1976) would imply a possible block of cocaine euphorigenic effects by naloxone. Similar reasoning by Huey et al.(1980) led to an experiment examining the effects of naloxone on methylphenidate-induced mood enhancement. No block was found, but some effects of methylphenidate appeared to be enhanced, although not at a statistically significant level.

The authors examined the effects of 20 mg IV naloxone on mood and physiological parameters on seven male volunteers who had received 2 mg/kg cocaine intranasally. Cocaine effects in the predictable directions occurred, but naloxone given at 15 minutes after cocaine enhanced rather than blocked cocaine "high;" there was an increase in "euphoria" and a depression of "lethargy," "malaise," and other psychological measures consistent with enhanced cocaine effect. The effect on physiological parameters was variable. When naloxone was given at 5 minutes before cocaine or 25 minutes after cocaine, no significant changes in cocaine effects were seen.

Holaday and others (Faden et al. 1981) have reported naloxone reversal of endotoxin and spinal shock by a postulated central dopaminergic mechanism. The authors suspect that their observed potentiation of cocaine effect occurs by a similar dopaminergic mechanism and that administration of cocaine or methylphenidate "sets up" a dopamine agonist response to naloxone similar to that caused by shock-inducing mechanisms.

The apparent necessity for naloxone dosage to follow cocaine rather than precede it implies a

---

[1] Departments of Pharmacology, [2] Anesthesiology, [3] Psychiatry, and [4] Laboratory Medicine, Yale University School of Medicine, New Haven, CT 06510.

cocaine effect on a naloxone sensitive system which may not be a traditional opiate receptor mechanism. Since naloxone effects are, if anything, the reverse of cocaine effects, the finding of a potentiation is clearly more than an additive interaction.

References

Byck, R. Peptide transmitters: A unifying hypothesis for euphoria, respiration, sleep, and the action of man. *Lancet,* 2:72-73, 1976.

Huey, L.Y., Janowsky, D.S., Judd, L.L., Roitman, N.A., Clopton, P.L., Segal, D., Hall, L., and Parker, D. The effects of naloxone on methylphenidate-induced mood and behavioral changes: A negative study, *Psychopharmacology (Berlin),* 67:125-130, 1980.

Faden, A.I., Jacobs, T.P., Feuerstein, G., and Holaday, J.W. Dopamine partially mediates the cardiovascular effects of naloxone after spinal injury. *Brain Res.,* 213:415-421, 1981.

Rapid Acquisition of Conditioned Responses to Hydromorphone in Detoxified Heroin Addicts

Joseph W. Ternes, Ph.D.,[1] Charles P. O'Brien, M.D., Ph.D.,[1] and Thomas T. Testa, Ph.D.[1]

A Pavlovian conditioning procedure was used to study conditioned drug states in human subjects. Six recently detoxified heroin addicts received six training trials in which two arbitrarily selected stimuli, a strawberry-flavored solution and a 700 Hertz (Hz) tone, were used to signal an infusion of 4 mg of hydromorphone.

Subjects' verbal reports of craving, withdrawal, and high, and two autonomic variables, skin temperature and pupil diameters, were recorded to assess the effects of this training. The unconditioned response to hydromorphone included an increase in skin temperature, pupilary constriction, reports of feeling high, and a reduction in craving and withdrawal symptoms. During *training* with hydromorphone, the conditioned stimulus (CS) elicited a mixed anticipatory response pattern. It partially resembled the unconditioned drug reaction, since the subjects reported feeling high and had fewer withdrawal symptoms. On the other hand, it partially resembled unconditioned withdrawal since they also reported an increase in craving, their pupils became dilated, and their skin temperature decreased. During *test* trials, when physiological saline was substituted for hydromorphone, both the subjective reports and autonomic variables changed in the opposite direction from the drug's unconditioned effects. Additionally, subjects displayed extreme negative affect 15 to 20 minutes after the saline infusion. The authors believe this is the phenomemon which is commonly referred to as "conditioned withdrawal."

Classical conditioning readily occurs when opiate drugs are used as unconditioned stimuli (UCSs). Thompson and Pickens (1971) demonstrated that a drug-produced state can act as an interoceptive stimulus in control of operant behaviors. Wikler (1973) observed that opiate drugs elicit compensatory physiological changes which are conditioned responses CRs. Recently Siegel (1976) demonstrated that tolerance to morphine in rats is a Pavlovian CR. Conditioning can also produce an interoceptive state which resembles abstinence symptoms and which motivates opiate-seeking behavior in detoxified addicts (Goldberg & Schuster 1970). This latter CR is sometimes called "conditioned withdrawal" (Wikler 1965).

---

[1] Department of Psychiatry, University of Pennsylvania and Veterans Administration Medical Center, Philadelphia, PA 19104.

The evidence for the phenomenon known as "conditioned withdrawal" is still somewhat speculative. Teasdale (1973) found that showing slides of drug-related scenes to post-addicts resulted in significant changes in mood. O'Brien et al. (1977) reported that conditioned abstinence symptoms were produced by pairing a tone/odor CS with naloxone injection in methadone addicts. Ternes et al. (1979) and Hugdal and Ternes (1981) have shown that naturalistic stimuli such as syringes, bags of heroin, and video sequences of self-injection were capable of eliciting electrodermal arousal and autonomic changes similar to opiate withdrawal signs in detoxified addicts. Ternes and O'Brien (1982) have also reported that when detoxified addicts were allowed to self-inject saline, autonomic changes occurred which were in opposition to the usual effects of an opiate. They argue that the syringe and self-injection procedure are naturally conditioned CSs which elicit anticipatory CRs which resemble withdrawal signs. These CRs may also be correlates of a conditioned emotional state which motivates behavior as a means of avoiding abstinence syndrome. However, to date no clear demonstration of how conditioned withdrawal responses are acquired in human subjects has been published.

The Laboratory at the Veterans Administration Drug Research center in Philadelphia has been engaged in studying the role of Pavlovian conditioned responses in human opiate addiction for the last 10 years. In earlier works, the authors have attempted to demonstrate experimental extinction of naturalistic stimuli normally associated with heroin self-administration (O'Brien et al. 1979). It could be argued, however, that what appeared to be conditioned reactions to stimuli normally associated with self-injection were in fact unconditioned arousal responses and movement artifacts which were unconditionally elicited by the syringe and the act of self-injection. The present experiment controlled for these possibilities. This was accomplished by pairing entirely arbitrary stimuli, a strawberry flavor and a 700 Hz tone, with a 4 mg dose of hydromorphone delivered within a 30-second interval as a 2 ml bolus of solution superimposed on the slow infusion of 5 percent dextrose and water which was administered throughout the session. The infusions were administered through an intravenous catheter which was inserted in the median cubital vein prior to each session. The authors believe this procedure is free from the contaminating influences of the subject's prior history of associations with self-injection. It should also be relatively free from the unconditioned arousal effects of the injection stimuli, from movements during drug administration and, finally, from the necessity to use a tourniquet.

Method

Subjects

The subjects were six male heroin addicts with a mean history of heroin use of 5.7 years. Each patient was required to detoxify completely and remain drug-free for 2 days following the last methadone dose. All subjects signed a consent form and became an inpatient on the detoxification ward at the Veterans Administration Medical Center in Philadelphia.

Apparatus

An intermittent infusion set delivered either the UCS or a placebo and was placed in the arm of the subject prior to the beginning of each test session. The administration set was connected to polyethylene tubing which was passed through an aperture in the wall to an adjoining room where it was attached to a Harvard infusion pump.

Procedure

There were 10 daily experimental sessions. Prior to each of these, the subject was prepared for physiological recordings by attaching a thermister to the right index finger. Each session was

60 minutes long. Prerecorded instructions asked the subject to rate his level of craving, high, and withdrawal in order to assess his subjective state at various points throughout the session. He was also asked to drink a flavored liquid when he heard a tone onset. The first 10 minutes of the session were silent except for the verbal self-reports which occurred at 5-minute intervals throughout the session. This constituted the session baseline period. Tone onset (65 db, 700 Hz audiogenerator) occurred at the end of this baseline period. At that time, the patient was also instructed to drink 70 ml of strawberry Hawaiian punch. The tone as well as the highly salient strawberry taste constituted a complex CS for the delivery of the drug. At the end of the 4th minute of the tone, the infusion pump was turned on. On the first 2 days (pretraining), as well as on the last 2 days (testing), physiological saline was infused instead of hydromorphone. During Sessions 3 through 8 (training), 4 mg of hydromorphone was infused. Delivery of the solution on both drug and placebo days was accomplished by a 4 cc syringe attached to a Harvard infusion pump. This was followed by a flush of 5 cc of 5 percent dextrose and water from a second 5 cc syringe, also placed in the pump. At this point, the subject was given the same set of questions. The questions were repeated at 10-minute intervals until the end of the session at minute 60.

The autonomic measures taken from all patients during the 60-minute session were: pupil size and skin temperature. Subjective reports of high, craving, and withdrawal were also elicited from the subjects by requesting a response from fixed choice questions such as: "Do you feel any high, craving, withdrawal/none, mild, moderate, extreme?"

Results

Figure 1 shows the mean change in subjective reports by the subjects after the CS was presented during each of the three conditions of the experiment: pretraining baseline, training with hydromorphone, and testing with saline. During pretraining sessions there were only slight changes in the subject's reports of craving, high, and withdrawal. When the CS was presented during *training*, craving and high increased and withdrawal decreased relative to the severity of these reports during the session baseline period. During *testing*, both craving and withdrawal increased but no reports of feeling high occurred. These results suggest that conditioned high responses were acquired during training with hydromorphone and that these CRs were accompanied by increased levels of craving and decreased withdrawal. However, when a placebo was given, subjective reports of craving were followed in time by withdrawal symptoms.

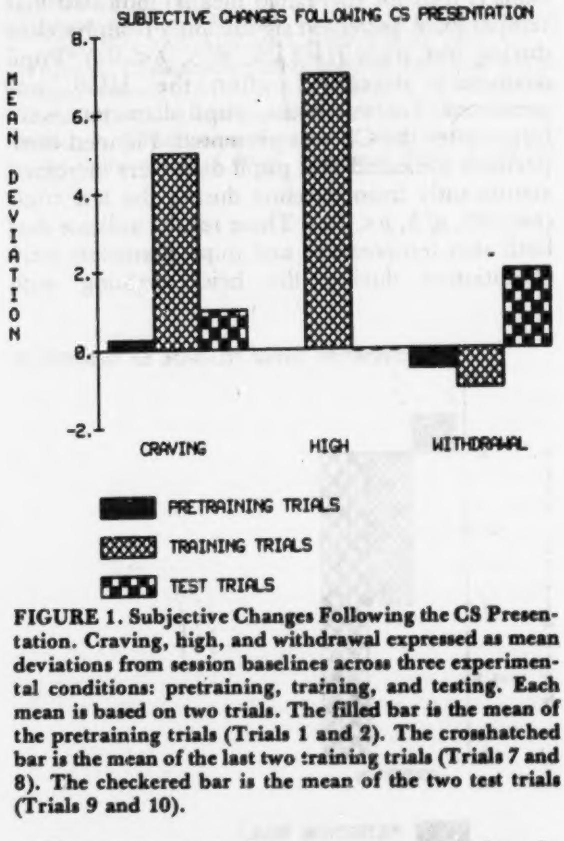


FIGURE 1. Subjective Changes Following the CS Presentation. Craving, high, and withdrawal expressed as mean deviations from session baselines across three experimental conditions: pretraining, training, and testing. Each mean is based on two trials. The filled bar is the mean of the pretraining trials (Trials 1 and 2). The crosshatched bar is the mean of the last two training trials (Trials 7 and 8). The checkered bar is the mean of the two test trials (Trials 9 and 10).

Figures 2 and 3 show the mean deviations in skin temperature and pupil diameters from session baseline which were elicited by the CS presentation during the pretraining, training, and test phases of the experiment. A slight positive change in skin temperature occurred during the pretraining trials. During training and testing, however, all of the changes in skin temperature were in a negative direction relative to the respective session baseline. Pupil diameters decreased slightly during the pretraining trials. During training and testing, all of the changes in pupil diameter were positive relative to the session baselines.

In the presence of CF, both of these autonomic variables changed in the opposite direction from the unconditioned response to hydromorphone. During training, skin temperature increased after the UCS presentation. On test trials when no drug was given, skin temperature decreased following the CS presentation. Planned comparisons (*t*-tests for correlated means) indicated that temperature decreased significantly from baseline during test trials ($t=3.25$, *df* 5, $p<.01$). Pupil diameters decreased after the UCS was presented. On test trials, pupil diameters were larger after the CS was presented. Planned comparisons indicated that pupil diameters increased significantly from baseline during the test trials ($t=2.83$, *df* 5, $p<.01$). These results indicate that both skin temperature and pupil diameters were conditioned during the brief training with hydromorphone. These results also indicate that these autonomic CRs resemble the conditioned compensatory response mechanism which both Wikler and Siegel have proposed.

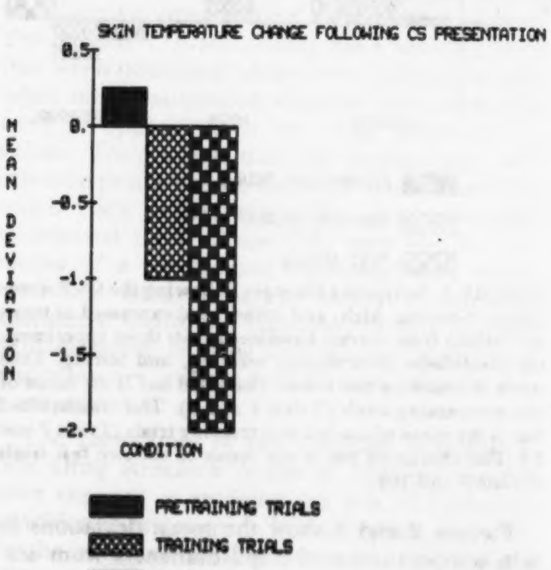


FIGURE 2. Skin Temperature Changes Following the CS Presentation. Mean deviations from session baseline periods during pretraining, training, and test trials. Each mean is based on two trials. The solid bar represents the pretraining trials. The crosshatched bar represents the training trials, and the checkered bar represents the test trials.

Discussion

The authors found that the unconditioned response to hydromorphone in detoxified addicts was skin temperature increase, pupil constriction, and reports of feeling high and attenuation of withdrawal symptoms and craving. The CS presentations during training with hydromorphone elicited anticipatory responses which preceded these drug effects. These included autonomic changes such as skin temperature decrease and pupilary dilation. Subjectively, the subjects reported feeling high, increased craving for opiates, and a reduction in withdrawal symptoms.

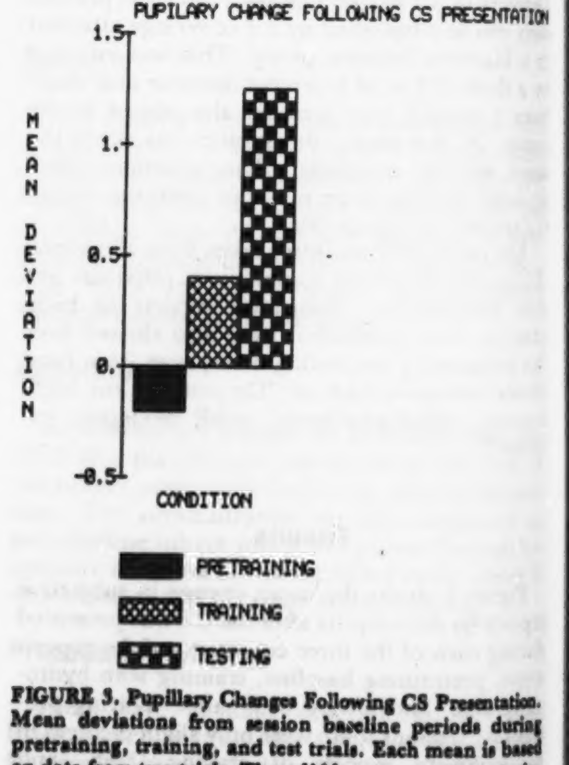


FIGURE 3. Pupillary Changes Following CS Presentation. Mean deviations from session baseline periods during pretraining, training, and test trials. Each mean is based on data from two trials. The solid bar represents pretraining trials, the crosshatched bar represents training trials, and the checkered bar represents test trials.

It was also found that during test trials, when physiological saline was infused instead of hydromorphone, CS presentation elicited skin temperature decrease, pupil dilation, and an increase in craving for opiates relative to baseline. No euphoria or high was reported. However, subjects experienced an increase in withdrawal symptoms. These results may appear contradictory, since subjects frequently reported feeling high prior to the drug infusion during training. Although they did not report feeling high on test trials, reports of withdrawal symptoms usually did not occur until 15 or 20 minutes after CS presentation. This suggests that the CS caused a brief delay in the onset of the withdrawal syndrome.

The authors believe these results indicate the complex nature of the CR to an opiate UCS in human addicts. It is comprised of both drug-negative and drug-positive components. Immediately following CS presentation, the subject may experience either euphoria or relief of withdrawal symptoms or delayed onset of withdrawal. However, in either case, eventually a negative affective reaction follows which is accompanied by an increased craving and withdrawal symptoms. Therefore the CR is essentially biphasic, a positive affective reaction followed in time by a negative reaction. Most addicts are relatively tolerant to opiates and therefore the negative component is in ascendency. This tends to reduce the initial positive drug effects when a good dose is administered. When a placebo or low dose is given, it results in labeling the negative affect as withdrawal symptoms.

References

Goldberg, S., and Schuster, C.R. Conditioned nalorphine-induced abstinence changes: Persistence in post morphine-dependent monkey. *J. Exp. Anal. Behav.*, 14:33-46, 1970.

Hugdal, K., and Ternes, J.W. An electrodermal measure of arousal in opiate addicts to drug-related stimuli. *Biol. Psychol.*, 12:291-298, 1981.

O'Brien, C.P., Testa, T., O'Brien, T.J., Brady, J.P., and Wells, B. Conditioned narcotic withdrawal in humans. *Science*, 175:1000-1002, 1977.

O'Brien, C.P., Greenstein, R., Ternes, J., McLellan, A.T., and Grabowski, J. Unreinforced self-injections: Effects on rituals and outcome in heroin addicts. Proceedings of the 41st annual scientific meeting of the Committee on Problems of Drug Dependence, Philadelphia, Pa., 1979, NIDA Research Monograph #27, 1980.

Siegel, S. Morphine analgesic tolerance: Its situation specificity supports a Pavlovian conditioning model. *Science*, 193:323-325, 1976.

Teasdale, J. Conditioned abstinence in narcotic addicts. *Int. J. Addict.*, 8:273-292, 1973.

Ternes, T.W., and O'Brien, C.P. Associative and nonassociative responses to opiates: An opponent-process view of addiction. Proceedings of the scientific meeting of the Committee of Problems of Drug Dependence, San Francisco, Ca., NIDA Research Monograph, 40, 1982.

Ternes, J.W., O'Brien, C.P., Grabowski, J., Wellerstein, H., and Jordan-Hays, J. Conditioned drug responses to naturalistic stimuli. NIDA Research Monograph #27, 1980.

Thompson, T., and Pickens, R. (eds.) *Stimulus Properties of Drugs*. New York:Appleton-Century-Crofts, 1971.

Wikler, A. Conditioning factors in opiate addiction and relapse. Wilner, D.M., and Kasselbaum, G.G. (eds.), *Narcotics*. New York:McGraw Hill Book Co., 1965.

Wikler, A. Conditioning of successive adaptive responses to the initial effects of drugs. *Conditioned Reflex*, 8:193-210, 1973.

Lofexidine in Abrupt Methadone Withdrawal[1]

Arnold M. Washton, Ph.D.,[2] and
Richard B. Resnick, M.D.[2]

Introduction

Previous studies have shown that the alpha-2 noradrenergic agonist, clonidine hydrochloride, is a safe and effective non-opiate treatment for opiate withdrawal and that clonidine can be extremely useful in facilitating a rapid transition from opiate dependence to aftercare treatment with the opiate antagonist, naltrexone (*see* review by Washton & Resnick 1981). However, clonidine is not without clinical risks and potential drawbacks. Clonidine's potent hypotensive and sedative effects have limited its clinical usefulness with some patients, suggesting that other alpha-2 noradrenergic agonists lacking these side effects might be safer and more efficacious.

Lofexidine hydrochloride (Merrell-Dow Pharmaceuticals) is an investigational analogue of clonidine that has been shown to significantly reduce opiate withdrawal in morphine-dependent rats (Shearman et al. 1980). Clinical testing of lofexidine as an antihypertensive agent has shown it to be less sedating and hypotensive than clonidine (Maner et al. 1980; St. John LaCorte et al. 1981). The present study was a preliminary clinical trial of lofexidine in abrupt methadone withdrawal. As in earlier studies with clonidine in this facility (Washton & Resnick 1981), the test of lofexidine's usefulness was conducted in an outpatient setting with the measure of success defined by induction onto naltrexone.

Method

The subjects were 15 methadone-dependent male outpatient volunteers who showed no evidence of medical or psychiatric illness and gave informed consent to the study which involved an abrupt switch from methadone to lofexidine. On Day 1, subjects received their usual methadone dose (10-25 mg) and began a self-administered lofexidine dose regimen of 0.1 mg two or three times daily. On Day 2, methadone was abruptly discontinued with subjects receiving a matched placebo methadone solution, and the lofexidine dosage was increased to 0.1 mg four times daily. Subsequently, the lofexidine dose was increased as needed to no more than 0.4 mg four times daily according to symptoms and side effects. All subjects were told that the detoxification procedure would take 11 days and that naltrexone could be started on Day 11 (10 days post-methadone), provided that they used no illicit opiates during the study as confirmed by the absence of a precipitated withdrawal reaction to intravenous naloxone challenge (2.0 mg) on Day 11. Subjects who did use illicit opiates during the first 10 days post-methadone were allowed to continue on lofexidine, and the naloxone challenge was postponed to the first opportunity where it posed minimal risk of precipitating a withdrawal reaction (i.e., to at least 5 days after the last opiate use) but no later than Day 21 of the study. The detoxification was considered successful if the subjects passed the naloxone challenge and started naltrexone on Days 11-21. Subjects who returned to using opiates and failed to begin naltrexone by Day 21 were considered unsuccessful.

Results

Successful detoxification and induction onto naltrexone was accomplished with 10 of the 15 subjects. All patients rated lofexidine as moderately to extremely effective in reducing most of the commonly experienced withdrawal symptoms. Insomnia, lethergy, and muscle/bone pain were the most frequent residual complaints. None of the 10 subjects reported unacceptable withdrawal symptoms while taking lofexidine. Those who failed to complete the detoxification procedure cited opiate craving rather than withdrawal discomfort as the major reason for returning to opiate use. No one reported oversedation, dizziness, or lightheadedness from lofexidine, despite rapid increases in the dose to as much as 1.6 mg per day within the first 5 days. The maximum daily lofexidine dose ranged from 0.6 mg to 1.6 mg across the 10 subjects with an average of 1.2 mg. There was no significant lowering of blood pressure (BP) even at the maximum lofexidine dose (mean prelofexidine BP, 115/74 mm Hg; mean BP at maximum dose 115/76 mm Hg). Dry mouth and mild drowsiness were the most commonly reported side effects. Upon study completion, reductions in the daily lofexidine dose by 0.2 to 0.6 mg per day produced no symptomatic complaints or significant changes in blood pressure.

---

[1] The authors' research studies cited in this paper were conducted in a treatment program at New York Medical College sponsored by the New York State Office of Alcoholism and Substance Abuse, Division of Substance Abuse Services. Research funds were provided by the National Institute on Drug Abuse, Boehringer Ingleheim Ltd., and Merrell-Dow Pharmaceuticals, Inc.

[2] Department of Psychiatry, Division of Drug Abuse Research and Treatment, New York Medical College, New York, NY 10029.

Discussion

This open clinical trial provides preliminary evidence of lofexidine's efficacy in reducing symptoms of opiate withdrawal. The present findings are similar to earlier results with clonidine (Washton & Resnick 1981) in terms of detoxification success rates and withdrawal symptom relief, but lofexidine was found to be considerably less sedating and hypotensive. Lofexidine may therefore prove to be safer and more clinically useful than clonidine, especially in outpatient opiate detoxification. These findings suggest that lofexidine might allow opiate-addicted outpatients even greater access to naltrexone or drug-free modalities without hospital admission. A controlled study comparing lofexidine with gradual methadone detoxification is currently being conducted at this facility.

References

Maner, T., Mehta, J., Johnson, C., and Conti, C.R. Comparative efficacy of two centrally acting imidazoline derivatives, clonidine and lofexidine. *Clin. Res.*, 28:33a, 1980.

Shearman, G.T., Lal, H., and Ursillo, R.C. Effectiveness of lofexidine in blocking morphine-withdrawal in the rat. *Pharmacol. Biochem. Behav.*, 12:573-575, 1980.

St. John Lacorte, W., Jain, A.K., Ryan, J.R., and McMahon, F.G. Comparative efficacy and tolerability of lofexidine and clonidine given alone or concomitantly with hydrochlorothiazide in hypertensive outpatients. *Clin. Pharmacol. Ther.*, 29:259, 1981.

Washton, A.M., and Resnick, R.B. Clonidine in opiate withdrawal: Review and appraisal of clinical findings. *Pharmacotherapy*, 1:140-146, 1981.

Effects of Desipramine on Diurnal Rhythms of Plasma 3-Methoxy-4-Hydroxyphenylglycol (MHPG) in Depressed Patients[1]

Edward M. DeMet, Ph.D.,[2] Angelos E. Halaris, M.D., Ph.D.,[2] Harry E. Gwirtsman, M.D.,[2] Rochelle M. Reno, Ph.D.,[2] and Phyllis I. Becker, M.D.[2]

A number of studies have suggested that manic-depressive illness may be associated with a decrease in noradrenergic activity. A noradrenergic role is supported by findings of low levels of the major norepinephrine (NE) metabolite 3-methoxy-4-hydroxyphenylglycol (MHPG) in the urine and plasma of some depressed patients (Halaris & DeMet 1979; Maas et al. 1968). MHPG changes in these fluids are believed to largely reflect changes in central NE turnover (DeMet & Halaris 1979). However, it has been shown that successful treatment of depressed patients with tricyclic antidepressants fails to produce a sustained increase in urinary MHPG levels, as might be expected if NE activity were directly related to the depressed mood state (Beckmann & Goodwin 1975; Halaris & DeMet 1980). One possible explanation for this discrepancy could be related to the fact that MHPG levels follow a circadian rhythm with elevated levels during the daytime and reduced levels during the evening and night hours (Halaris & DeMet 1981; Wehr et al. 1980). Both of the above cited studies showed that the circadian rhythm of MHPG in manic-depressive patients was phase-advanced by 1 to 2 hours as compared to normal subjects. Moreover, another study has shown that the tricyclic antidepressant, imipramine, exerts effects on diurnal rhythms of adrenergic receptor binding in rat brain (Wirz-Justice et al. 1980). In that study, chronic

---

[1] This study was supported by USPHS Grant MH-35824 from the National Institute of Mental Health, and the Veterans Administration.

[2] Department of Psychiatry, UCLA School of Medicine and Veterans Administration Medical Center, Brentwood Division, Los Angeles, CA 90073.

Address reprint requests to: Edward M. DeMet, Ph.D., VA Hospital Brentwood, 11301 Wilshire Blvd., Los Angeles, CA 90073.

imipramine treatment resulted in a phase retardation of the normal diurnal rhythms of alpha- and beta-adrenergic receptor binding. Whether the antidepressant effect of these agents is directly related to their ability to delay the phase of the diurnal rhythm of NE remains to be established.

The present investigation was undertaken to determine whether treatment with a tricyclic antidepressant might cause a phase delay of the circadian pattern of NE turnover in depressed patients. Three hospitalized depressed patients meeting Research Diagnostic Criteria (RDC) for primary major depressive disorder, endogenous type, were compared with three normal volunteers. Patients were free of any psychoactive medication for at least 3 weeks prior to the study. No attempt was made to impose dietary or activity restrictions on either patients or volunteers, since no significant effect on MHPG blood levels had been found in preliminary studies. A history of alcohol use in either patients or volunteers served as exclusion criterion, and all subjects were requested to refrain from the use of any alcoholic beverages for at least three days prior to the experiment. A log of activity and foods ingested was maintained. A written informed consent was obtained from each participant in the study. Blood samples were obtained from an indwelling antecubital catheter which was kept patent by flushing it with sterile citrate-phosphate-dextrose buffer (CPD-A). A baseline diurnal rhythm of plasma MHPG was determined for each subject using the gas chromatographic method of Halaris et al. (1977). Blood samples were collected at 3-hour intervals around the clock, with the exception that the 6 a.m. sample was omitted in the patient collections. Patients were then treated with a daily dose of 150 mg desipramine-HCl (DMI) for a total of 4 weeks. Changes in mental status and clinical improvement were determined weekly by means of the Hamilton Rating Scale for Depression. The diurnal rhythm of MHPG levels in plasma was reexamined following the fourth week of treatment.

Figure 1 shows that both the normal volunteers and the depressed patients had pronounced diurnal rhythms of plasma MHPG levels. However, the rhythms differed in the two groups, with the depressed patients leading normal controls by about 3 hours. The averaged rhythms shown for both depressed patients and normals follow a true circadian rhythm with a 24-hour periodicity. Individual normal subjects also showed sinusoidal patterns with a 24 hour periodicity. When these rhythms for the normals were averaged, the resultant curve was actually slightly distorted as compared to the individual curves due to minor differences in intra-subject amplitude variability. The opposite was true of depressed patients. Individual patients significantly deviated from a 24-hour periodicity, and several exhibited secondary peaks in the late afternoon and evening. Averaging of the individual rhythms tended to mask these differences such that a secondary peak is only barely evident in Figure 1, and the net response approximates a 24-hour period. Both the amplitudes and baselines of the MHPG rhythms were similar in the depressed and normal subjects.

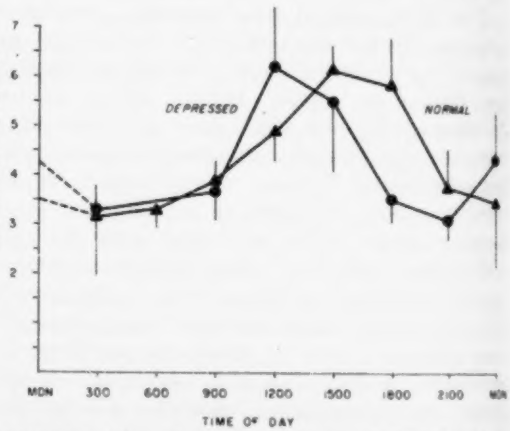


FIGURE 1. Diurnal pattern of plasma MHPG levels in three normal subjects (▲ — ▲) and three endogenously depressed patients (● — ●).

All three patients showed significant improvement with DMI treatment, as evidenced by a decrease in Hamilton rating scores (change score = 23 ± 2.08 S.E.M.). Figure 2 shows that DMI treatment resulted in the normalization of the phase of diurnal plasma MHPG rhythms. This change was accompanied by a slight reduction in both the baseline MHPG level and the amplitude of the MHPG cycle. Normalization was evident in the individual rhythms as well as in the composite sample.

The results of the present study clearly showed that plasma MHPG rhythms were phase-advanced in the three endogenously depressed patients studied. Clinical improvement with DMI treatment was associated with the normalization of the phase of the MHPG rhythm. The fact that phase normalization occurred in all three patients studied suggests that MHPG phase shifts may be specific biochemical indicators of clinical improvement. Since the amplitudes of the diurnal rhythms of normal and depressed subjects were actually more similar before DMI treatment than after, the results further suggest that behavioral normalization after tricyclic treatment may be independent of changes in the amplitude of noradrenergic activity. Finally, the present results suggest that the circadian pattern of MHPG is a state-dependent trait that may be of diagnostic value.

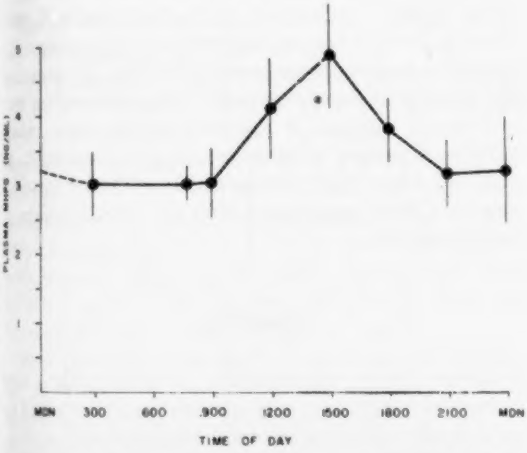


FIGURE 2. Diurnal pattern of plasma MHPG levels in the same three endogenously depressed patients after treatment with DMI.

References

Beckmann, H., and Goodwin, F.K. Antidepressant response to tricyclics and urinary MHPG in unipolar patients. *Arch. Gen. Psychiatry*, 32:17-21, 1975.

DeMet, E.M., and Halaris, A.E. Origin and distribution of 3-methoxy-4-hydroxyphenylglycol in body fluids. *Biochem. Pharmacol.*, 28:3043-3050, 1979.

Halaris, A.E., DeMet, E.M., and Halari, M.E. Determination of plasma 3-methoxy-4-hydroxyphenylglycol by pulsed electron capture gas chromatography. *Clin. Chim. Acta.*, 78:285-294, 1977.

Halaris, A.E., and DeMet, E.M. Studies of norepinephrine metabolism in manic and depressive states. In: Usdin, E. (ed.), *Catecholamines: Basic and Clinical Frontiers.* New York:Pergamon Press, 1979, pp. 1866-1868.

Halaris, A.E., and DeMet, E.M. Open trial evaluation of a pyrrolidine derivative (AHR-1118) on norepinephrine metabolism. *Prog. Neuro-Psychopharmacol.*, 4:43-49, 1980.

Halaris, A.E., and DeMet, E.M. Parameters affecting norepinephrine metabolism in healthy and depressed populations. Paper read at the 20th Annual Meeting, American College of Neuropsychopharmacology, Coronado, California, December 16-18, 1981.

Maas, J.N., Fawcett, J.A., and Dekirmenjian, H. Catecholamine metabolism, depressive illness, and drug response. *Arch. Gen. Psychiatry*, 26:252-262, 1972.

Wehr, T.A., Muscettola, G., and Goodwin, F.K. Urinary 3-methoxy-4-hydroxyphenylglycol circadian rhythm. *Arch. Gen. Psychiatry*, 37:257-263, 1980.

Wirz-Justice, A., Kafka, M.S., Naber, D., and Wehr, T.A. Circadian rhythms in rat brain alpha- and beta-adrenergic receptors are modified by chronic imipramine. *Life Sci.*, 27:341-347, 1980.

β-Endorphin, Cortisol, and Prolactin in Serum of Schizophrenic Patients During Long-Term Neuroleptic Treatment and After Withdrawal: Relationships to Psychopathology[1]

**Dieter Naber, M.D.,[2] Margot Albus, M.D.,[2]
Franz Muller, M.D.,[2] Horst Burke, M.D.,[2]
Doris Welter,[2] Manfred Ackenheil, M.D.,[2]
and Hanns Hippius, Prof., M.D.[2]**

The effectiveness of neuroleptic maintenance therapy to prevent relapse of chronic schizophrenia is well established (Davis et al. 1976; Gardos & Cole 1976; Hogarty et al. 1976; Prien & Klett 1972; Wistedt 1981; Woggon 1979). However, there is evidence that some patients do not profit from neuroleptic treatment or even improve after withdrawal (Andrews et al. 1976; Leff & Wing 1971; Marder et al. 1979; Tobias & MacDonald 1974). With regard to the neuroleptics' serious side-effects such as tardive dyskinesia, there is a strong effort to minimize the neuroleptic dosage and to determine which patients do not require maintenance therapy.

Investigating any potential predictors for the effect of neuroleptic withdrawal in chronic schizophrenia, age of patients, duration of illness, and previous neuroleptic dosage have been found to correlate with psychopathological changes and probability of relapse (Davis et al. 1976; Marder et al. 1979; Prien & Klett 1972; Woggon 1979). In other studies, low serum level of prolactin was associated with early relapse after drug discontinuation (Brown & Laughren 1981; Zander et al. 1981). This study is an attempt to replicate these previous findings and to see whether serum levels of β-endorphin and cortisol are related to psychopathological changes after neuroleptic withdrawal.

Method

Twenty-four chronic schizophrenic patients, diagnosed according to the ICD-system, participated in the study. Leading symptoms were delusions, hallucinations, behavioral disorders, and disturbances of affect and energy level. Their age was 27 - 65 (mean ± SD 46 ± 8) years; they were treated with different neuroleptics for 1 - 24 (8 ± 7) years at a daily dosage of 560 ± 490 mg of chlorpromazine equivalents. After the first serum sampling, neuroleptic treatment was discontinued and placebo was given instead for 12 days. Blood was collected via an indwelling intravenous catheter from fasting, reclining patients in the morning 12 hours after the last neuroleptic dosage and again 12 days after drug withdrawal. The Brief Psychiatric Rating Scale (BPRS) was used to rate psychopathological syndromes on the 2 days of blood collection. Prolactin, cortisol, and β-endorphin were measured by commercially available radioimmunoassays (NEN). To increase the validity of these hormonal measurements, two individual samples 5 minutes apart were taken from each patient during neuroleptic treatment as well as after drug withdrawal. The statistical analyses were performed with the mean value of both samples.

Results

Serum levels of prolactin, β-endorphin, and cortisol during long-term neuroleptic treatment as well as after drug withdrawal are listed in Table 1. Drug withdrawal caused significant changes of all three hormones: Prolactin levels decreased (*t*-test, $df=23$; $t=3.92$, $p<0.001$), while levels of β-endorphin ($t=4.62$, $p<0.0005$), and cortisol ($t=5.19$, $p<0.0001$) both increased. Correlating serum levels during neuroleptic treatment and after withdrawal, significant relationships were found (Pearson correlation, $N=24$): prolactin $r=0.71$, $p<0.001$; β-endorphin $r=0.61$, $p<0.005$; cortisol $r=0.53$, $p<0.01$. The two serum samples, taken 5 minutes apart during neuroleptic treatment as well as after withdrawal, were also significantly correlated: prolactin $r=0.84$, $p<0.0001$ and $r=0.86$, $p<0.0001$; β-endorphin $r=0.67$, $p<0.001$ and $r=0.85$, $p<0.0001$; cortisol $r=0.67$, $p<0.001$ and $r=0.81$, $p<0.0001$. During withdrawal, β-endorphin and cortisol serum levels were significantly correlated ($r=0.63$, $p<0.001$).

---

[1] This work was supported by the Deutsche Forschungsgemeinschaft.

[2] Psychiatrische Klinik der Universität München, München, Federal Republic of Germany.

Table 1

Levels of Prolactin, β-Endorphin, and Cortisol in Serum of 24 Male Chronic Schizophrenic Patients During Long-Term Neuroleptic Therapy (NL) and After Drug Withdrawal for 12 Days (WL)

Hormone	NL Mean ± SD (% of Patient Above Normal Range)	WL Mean ± SD (% of Patient Above Normal Range)
Prolactin (ng/ml)	25.2 ± 22.6 (41%)	10.6 ± 12.2 (13%)
β-Endorphin (pg/0.1 ml)	8.9 ± 1.8 (4%)	11.4 ± 3.1 (46%)
Cortisol (μg/100 ml)	17.9 ± 4.5 (8%)	23.6 ± 5.4 (42%)

Normal range: Prolactin 5-20 ng/ml; β-endorphin 5-12 pg/0.1 ml; cortisol 12-25 μg/100ml.

Drug withdrawal caused distinct changes in the psychopathology of most patients, but within the whole group the total BPRS score did not change (43.6 ± 10.9 pts vs. 42.6 ± 12.2 pts). Of the five different subscales, only "anergia" showed a significant decrease (14.5 ± 5.2 pts vs. 12.5 ± 5.8 pts; $t=3.63$, $p<0.05$). Correlating hormonal measurements with psychopathological scores, only β-endorphin serum level after neuroleptic withdrawal was significantly related to total BPRS score ($r=-0.44$, $p<0.05$) and to "angergia" ($r=-0.46$, $p<0.05$).

Relationships between serum levels of prolactin, β-endorphin, and cortisol to changes of BPRS scores after drug withdrawal are listed in Table 2. Six subjects worsened (6-16 points) and 8 subjects improved (6-12 points) by more than 6 points of the total BPRS score. These two groups did not differ in serum levels of prolactin or cortisol, but improved subjects had significantly higher levels of β-endorphin during neuroleptic treatment (10.0±2,1 pg/0.1 ml vs. 7.5±7.4 pg/0.1 ml; $t=3.15$, $p<0.02$) as well as after withdrawal (13.8±1.7 pg/0.1 ml vs. 9.8±3.5 pg/0.1 ml; $t=2.65$, $p<0.05$).

There were no significant relationships between BPRS scores or their changes after withdrawal and age, duration, or dosage of neuroleptic treatment.

Discussion

The individually very different psychopathological response to withdrawal of neuroleptics is in agreement with numerous previous studies (Andrews et al. 1976; Davis et al. 1976; Leff & Wing 1971; Prien & Klett 1972; Marder et al. 1979; Zander et al. 1981). However, looking for variables which discriminate between patients who improve and those who worsen after drug discontinuation, this study did not replicate findings that age, duration of illness, previous neuroleptic therapy (Davis et al. 1976; Marder et al. 1979; Prien & Klett 1972; Woggon 1979) or prolactin serum levels (Brown & Laughren 1981; Laughren et al. 1979; Zander et al. 1981) are valid predictors.

Only the β-endorphin serum level was found to correlate significantly with the effects on psychotic behavior: While patients with low levels mostly worsened, high levels of β-endorphin were associated with improvement or lack of change. It

Table 2

Relationships Between Hormonal Serum Levels in 24 Male Chronic Schizophrenic Patients During Neuroleptic Treatment (NL) and After 12 Days of Drug Withdrawal (WL) to Changes in BPRS Psychopathology Scores

	Changes of BPRS Psychopathology Scores (WL score-NL score, improvement = negative numbers)					
	Total Score	Anxiety Depress.	Anergia	Thought Disord.	Activat.	Hostility
Prolactin NL	−0.03	0.36	0.28	−0.25	−0.16	−0.16
Prolactin WL	−0.07	0.31	0.08	−0.15	−0.02	−0.12
β-Endorphin NL	−0.48*	−0.15	−0.54**	−0.23	0.17	−0.23
β-Endorphin WL	−0.41*	−0.23	−0.43*	0.17	−0.06	−0.45*
Cortisol NL	0.01	0.00	−0.17	0.03	0.10	0.13
Cortisol WL	−0.32	−0.32	−0.45*	0.08	0.12	0.01

Pearson correlation: * = $p<0.05$; ** $p<0.01$.

has to be considered that neuroleptic withdrawal for 12 days is a rather short period, but psychotic relapses often occur already within 8-14 days after discontinuation of long-term neuroleptic treatment (Davis et al. 1976; Zander et al. 1981). Further studies are obviously needed to investigate the possible relationship between the β-endorphin serum level and psychotic relapse following neuroleptic withdrawal.

The neuroendocrine results are similar to previous studies: Long-term neuroleptic treatment seems to induce tolerance of the tuberoinfundibular system, at least in some patients; therefore the prolactin-stimulating effect does not exist any more in all patients and the mean serum level is close to the normal range (Brown & Laughren 1981; Naber et al. 1979; Zander et al. 1981). The effect of neuroleptics on serum levels of β-endorphin in humans is controversial: Emrich et al. (1980) found a significant increase, but Brambilla et al. (1981) did not observe a significant change. Ongoing studies show that neuroleptic treatment for 2-6 weeks induces a significant increase of β-endorphin serum levels only in about 40 percent of patients (Naber et al. unpublished). The mostly normal levels found in this study could reflect the development of tolerance. The increase after neuroleptic withdrawal is probably a nonspecific stress effect, since coritsol, not affected by chronic neuroleptic therapy (Franzen 1971; Naber 1980), also increased significantly.

References

Andrews, P., Hall, J.N., and Snaith, R.P. A controlled trial of phenothiazine withdrawal in chronic schizophrenic patients. *Br. J. Psychiatry,* 128(4):451-455, 1976.

Brambilla, F., Genazzani, A.R., Facchinetti, F., Parrini, D., Petraglia, F., Sacchetti, E., Scarone, S., Guastalla, A., and D'Antona, N. β-Endorphin and β-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. *Psychoneuroendocrinology,* 6(4):321-330, 1981.

Brown, W.A., and Laughren, T.P. Tolerance to the prolactin elevating effects of neuroleptics. *Psychiatry Res.,* 5(3): 317-322, 1981.

Brown, W.A., and Laughren, T. Low serum prolactin and early relapse following neuroleptic withdrawal. *Am. J. Psychiatry,* 138(2):237-239, 1981.

Davis, J.M., Gosenfeld, L., and Tsai, C.C. Maintenance antipsychotic drugs to prevent relapse: A reply to Tobias and MacDonald. *Psychol. Bull.,* 83(3):431-447, 1976.

Emrich, H.M., Höllt, V., Bergmann, M., Kissling, W., Schmid, W., Zerssen, D.V., and Herz, A. Plasma levels of β-endorphin in schizophrenic patients: Failure of naloxone to counteract curative effects of neuroleptic drugs. In: Costa, E., and Tabucchi, M. (eds.), Neural Peptides and Neuronal Communications. New York:Raven Press, 1980, pp. 489-502.

Franzen, G. Serum cortisol in chronic schizophrenia. *Psychiatr. Clin.,* 4(2):237-246, 1971.

Gardos, G., and Cole, J.O. Maintenance antipsychotic therapy: Is the cure worse than the disease? *Am. J. Psychiatry,* 133(1):32-36, 1976.

Hogarty, G.E., Ulrich, R.F., Mussare, F., and Aristigueta, N. Drug discontinuations among long-term, successfully maintained schizophrenic outpatients. *Dis. Nerv. Syst.,* 37(4):494-500, 1976.

Laughren, T.P., Brown, W.A., and Williams, B.W. Serum prolactin and clinical state during neuroleptic treatment and withdrawal. *Am. J. Psychiatry,* 136(1):108-110, 1979.

Leff, J.P., and Wing, J.K. Trial of maintenance therapy in schizophrenia. *Br. Med. J.,* 3(4):599-604, 1971.

Marder, S.R., van Kammen, D.P., Docherty, J.P., Rayner, J., and Bunney, W.E., Jr. Predicting drug-free improvement in schizophrenic psychosis. *Arch. Gen. Psychiatry,* 36(9):1080-1085, 1979.

Naber, D., Ackenheil, M., Fischer, H., Zander, K., Laakman, G., and von Werder, K. Neuroendocrine effects of long-term treatment with neuroleptic drugs. In: Usdin, E., Eckert, H., and Forrest, I.S. (eds.), *Phenothiazines and Structurally Related Drugs.* New York:Elsevier/North Holland Biomedical Press, 1980, pp. 223-226.

Naber, D., Fischer, B., and Ackenheil, M. Effect of long-term neuroleptic treatment on dopamine tuberoinfundibular system: Development of tolerance? *Commun. Psychopharmacol.,* 3(1):59-65, 1979.

Prien, R.F. and Klett, C.J. An appraisal of the long-term use of tranquilizing medication with hospitalized chronic schizophrenics: A review of the drug discontinuation literature. *Schizophren. Bull.,* 5(1):64-73, 1972.

Tobias, L.L., and MacDonald, M.L. Withdrawal of maintenance drugs with long-term hospitalized mental patients: A critical review. *Psychol. Bull.,* 31(2):107-125, 1974.

Wistedt, B. A depot neuroleptic withdrawal study. *Acta Psychiatr. Scand.,* 64(1):65-84, 1981.

Woggon, B. Neuroleptika-Absetzversuche bei chronisch schizophrenen Patienten. (Study of neuroleptic discontinuation in chronic schizophrenic patients.) *Int. Pharmacopsychiatry,* 14(1):34-56, 1979.

Zander, K.J., Fischer, B., Zimmer, R., and Ackenheil, M. Long-term neuroleptic treatment of chronic schizophrenic patients: Clinical and biochemical effects of withdrawal. *Psychopharmacology (Berlin),* 73(1):43-47, 1981.

Psychopharmacology—A Recurring Bibliography

The bibliography below is offered to our readers to alert them to recent papers on psychopharmacology from the world literature. It was computer-generated by the Medical Literature Analysis and Retrieval System (MEDLARS) of the National Library of Medicine, National Institutes of Health, and represents papers which were entered into the system during the 3 months before the *Bulletin* went to press.

The subject headings from Index Medicus were selected by the WHO International Reference Center at the NIMH to reflect significant current interest of the international scientific community. Some nonrelevant citations may appear, and some relevant ones may be absent, but this is usual for machine-generated searches. Each subsequent issue of the *Bulletin* will provide such a bibliography, which contains two parts—a Subject Section and an Author Section.

Comments and suggestions are invited.

ISSN 0048-5764

SUBJECT SECTION

ACETYLCHOLINE

Properties of an acetylcholine-induced conductance in the rabbit atrial myocardium. Nilius B. **Acta Biol Med Ger** 1981;40(7-8):1031-42

The action of putative neurotransmitter substances in the cat labyrinth. Felix D, et al. **Acta Otolaryngol (Stockh)** 1982 Jan-Feb; 93(1-2):101-5

Brain level and synthesis of acetylcholine during exposure to vibration and organic-phosphorus and phenol-derived pesticides. Górny D, et al. **Acta Physiol Pol** 1981;32(4):469-76

Interactions between GABA, dopamine, acetylcholine, and glutamate-containing neurons in the extrapyramidal and limbic systems. Bartholini G, et al. **Adv Biochem Psychopharmacol** 1981;30:119-28

Hemicholinium-3 and related ether analogues on the synthesis of acetylcholine by mouse brain (in vitro). Bove FC, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):278-93

Uncoupling of acetylcholine uptake from the Torpedo cholinergic synaptic vesicle ATPase. Anderson DC, et al. **Biochem Biophys Res Commun** 1981 Nov 30;103(2):422-8

Decreases in the release of acetylcholine in vitro with low oxygen. Gibson GE, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):111-5

Cholinergic muscarinic stimulation of steroidogenesis in bovine adrenal cortex fasciculata cell suspensions. Hadjian AJ, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):157-63

Increase of acetylcholine-receptor sensitivity by adenosine triphosphate: a novel action of ATP on ACh-sensitivity. Akasu T, et al. **Br J Pharmacol** 1981 Oct;74(2):505-7

Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Glickman RD, et al. **Brain Res** 1982 Feb 18;234(1):81-99

At the frog neuromuscular junction prostaglandin synthase inhibitors depress and PGE partially restores quantal acetylcholine release. Madden KS, et al. **Brain Res** 1982 Feb 25;234(2):464-8

Chemoreceptors for serotonin (5-HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma-aminobutyric acid (GABA) on rabbit visceral afferent neurons. Higashi H, et al. **Brain Res Bull** 1982 Jan; 8(1):23-32

2-chloroadenosine inhibits brain acetylcholine turnover in vivo. Haubrich DR, et al. **Can J Physiol Pharmacol** 1981 Nov;59(11):1196-8

Distribution and activity of adrenergic and cholinergic innervation of the extrahepatic biliary system in the rabbit. Tessitore V, et al. **Cell Mol Biol** 1981;27(5):527-37

Muscarinic acetylcholine receptors of the small intestine and pancreas of the rat: distribution and the effect of vagotomy. Isaacs PE, et al. **Clin Sci** 1982 Feb;62(2):203-7

Development and aging of cholinergic synapses. VI. Mechanisms of acetylcholine biosynthesis in the chick iris. Marchi M, et al. **Dev Neurosci** 1981;4(6):442-50

Preparation and characterisation of homogeneous neurotoxin type A from Clostridium botulinum. Its inhibitory action on neuronal release of acetylcholine in the absence and presence of beta-bungarotoxin. Tse CK, et al. **Eur J Biochem** 1982 Mar 1;122(3):493-500

Simultaneous measurement of acetylcholine and choline in brain by pyrolysis-gas chromatography-mass spectrometry. Khandelwal JK, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):145-56

Autoregulation of acetylcholine release in isolated hippocampal nerve endings. Marchi M, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):75-9

Effects of ketotifen, a benzocycloheptathiophene, on metacholine- and acetylcholine-induced contractions of canine respiratory smooth muscle. Polson JB, et al. **Immunopharmacology** 1982 Feb;4(1):69-72

Effect of immobilization stress & ascorbic acid on acetylcholine & plasma cortisol in albino rats. Gode JD, et al. **Indian J Exp Biol** 1981 Dec; 19(12):1175-6

On the ionic mechanism underlying adrenergic-cholinergic antagonism in ventricular muscle. Josephson I, et al. **J Gen Physiol** 1982 Jan; 79(1):69-86

Increase in exogenous choline fails to elevate the content or turnover rate of cortical, striatal, or hippocampal acetylcholine. Brunello N, et al. **J Neurochem** 1982 Apr;38(4):1160-3

Aging decreases oxidative metabolism and the release and synthesis of acetylcholine. Gibson GE, et al. **J Neurochem** 1981 Oct; 37(4):978-84

Effect of motor and premotor cortex ablation on concentrations of amino acids, monoamines, and acetylcholine and on the ultrastructure in rat striatum. A confirmation of glutamate as the specific cortico-striatal transmitter. Hassler R, et al. **J Neurochem** 1982 Apr;38(4):1087-98

Continuous determination by a chemiluminescent method of acetylcholine release and compartmentation in Torpedo electric organ synaptosomes. Israël M, et al. **J Neurochem** 1981 Dec;37(6):1475-83

The effect of ouabain on the release of [14C]acetylcholine and other substances from synaptosomes. Vyas S, et al. **J Neurochem** 1981 Dec; 37(6):1467-74

The kinetics of acetylcholine turnover in a resting cholinergic nerve terminal and the magnitude of the cytoplasmic compartment. Weiler M, et al. **J Neurochem** 1982 May;38(5):1187-91

Neuronal cell surfaces: distinctive glycoproteins of cultured adrenergic and cholinergic sympathetic neurons. Braun SJ, et al. **J Neurosci** 1981 Dec;1(12):1397-406

Comparison of effects of cyanide and acetylcholine on renal hemodynamics and sodium excretion. Williams RL, et al. **J Pharm Sci** 1982 Jan;71(1):47-50

Studies on isolated smooth muscle cells. VII. Response to agonists and the contraction velocity of taenia coli of guinea pig and the single smooth muscle cells. Momose K, et al. **J Pharmacobiodyn** 1981 Sep; 4(9):670-6

Effects of phosphatidylcholine administration to rats on choline in blood and choline and acetylcholine in brain. Jope RS. **J Pharmacol Exp Ther** 1982 Feb;220(2):322-8

Alteration in sensitivity to isoproterenol and acetylcholine in the rat heart after repeated administration of isoproterenol. Nomura Y, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):411-6

gamma-Aminobutyric acid (GABA) receptor stimulation. IV. Effect of progabide (SL 76002) and other GABAergic agents on acetylcholine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):689-95

Effects of acetylcholine on respiratory neurones in the nucleus ambiguus-retroambigualis complex of the cat. Jordan D, et al. **J Physiol (Lond)** 1981 Nov;320:103-11

Mouse pancreatic acinar cells: voltage-clamp study of acetylcholine-evoked membrane current. McCandless M, et al. **J Physiol (Lond)** 1981 Sep;318:57-71

A study of desensitization of acetylcholine receptors using nerve-released transmitter in the frog. Magleby KL, et al. **J Physiol (Lond)** 1981 Jul; 316:225-50

Interaction of adenosine and acetylcholine on the bullfrog atrium. Goto M, et al. **Jpn J Physiol** 1981;31(4):501-13

Effects of atropine on nicotinic transmission in bullfrog sympathetic ganglia. Yamada M. **Kurume Med J** 1981;28(2):119-23

Acetylcholine metabolism in the rat hippocampus and striatum following one-trial passive training. Barker LA, et al. **Neuropharmacology** 1982 Feb;21(2):183-5

Simultaneous reduction in the turnover rates of septal gamma-aminobutyric acid and hippocampal acetylcholine following administration of nabilone. Revuelta AV, et al. **Neuropharmacology** 1981 Nov;20(11):1111-4

Mechanisms of tolerance to the anticholinesterase, DFP: acetylcholine levels and dynamics in the rat brain. Russell RW, et al. **Neuropharmacology** 1981 Dec;20(12A):1197-201

Analog of a conditioned reflex of sensomotor cortical units following microinjection of acetylcholine. Kopytova FV, et al. **Neurosci Behav Physiol** 1981 May-Jun;11(3):213-20

Cholinergic actions of false neurotransmitters: acetyldiethylcholine. Aronstam RS, et al. **Neurosci Lett** 1982 Jan 22;28(1):51-6

The effect of 2-amino-4-phosphonobutyrate (APB) on acetylcholine release from the rabbit retina: evidence for on-channel input to cholinergic amacrine cells. Neal MJ, et al. **Neurosci Lett** 1981 Nov 4;26(3):301-5

Intracellular observations on the disinhibitory action of acetylcholine in the hippocampus. Ben-Ari Y, et al. **Neuroscience** 1981;6(12):2475-84

Spontaneous and potassium-induced release of acetylcholine from mouse forebrain minces. Carroll PT, et al. **Neuroscience** 1981;6(12):2555-9

Disinhibitory action of acetylcholine in the rat's hippocampus: extracellular observations. Krnjević K, et al. **Neuroscience** 1981; 6(12):2465-74

Primary monolayer cultures of the rat corpus striatum: morphology and properties related to acetylcholine and gamma-aminobutyrate. Messer A. **Neuroscience** 1981;6(12):2677-87

Electrophysiologic evidence for involvement of acetylcholine as a neurotransmitter in the lateral vestibular nucleus. Ito J, et al. **Otolaryngol Head Neck Surg** 1981 Nov-Dec;89(6):1025-9

Cholinesterases and postnatal development of the negative chronotropic effects of acetylcholine in albino rats. Vlk J. **Physiol Bohemoslov** 1981; 30(6):497-503

The effects of intracerebroventricularly applied kainic acid on acetylcholine content and release in rat brain cortex and striatum. Kleinrok A, et al. **Pol J Pharmacol Pharm** 1981;33(4):453-8

Effect of neuroleptics on release on acetylcholine to the lateral cerebral ventricle in the rat. Plech A, et al. **Pol J Pharmacol Pharm** 1981; 33(4):393-400

Changes in neuromuscular junction endplate current time constants produced by sulfhydryl reagents. Steinacker A, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7806-9

Effect of acetylcholine, gastrin, and glucagon alone and in combination with secretin and cholecystokinin on the secretion of the isolated perfused rat pancreas. Sommer H, et al. **Res Exp Med (Berl)** 1981; 179(3):239-47

Syncytiotrophoblast membrane vesicles: a model for examining the human placental cholinergic system. Fant ME, et al. **Teratology** 1981 Oct; 24(2):187-99

Effect of synaptic transmitter drugs on receptive fields of rabbit retinal ganglion cells. Daw NW, et al. **Vision Res** 1981;21(11):1643-7

[Effect of phentolamine on carotid reflexes induced by acetylcholine] Silva Carvalho L, et al. **C R Soc Biol (Paris)** 1981;175(6):913-5 (Eng. Abstr.) (Fre)

[Ontogenesis of the acetylcholine system in the brain of the South African clawed toad (Xenopus laevis Daudin)] Schlesinger C. **J Hirnforsch** 1981; 22(5):543-53 (Eng. Abstr.) (Ger)

[Studies on catecholamine secretion from adrenal medulla—acetylcholine stimulation (author's transl)] Komiya E, et al. **Horumon To Rinsho** 1981 Aug;29(8):915-8 (Jpn)

[Adaptation of the peripheral organs of rats to noradrenaline deficiency following chronic desympathization] Berdysheva LV, et al. **Fiziol Zh SSSR** 1981 Nov;67(11):1636-42 (Eng. Abstr.) (Rus)

[Effect of the level of cholinergic processes in the body on pulmonary surfactant] Kriuchkova VI. **Fiziol Zh SSSR** 1981 Nov;67(11):1643-6 (Rus)

[Effect of central cholinergic structures on the activity of the cardiovascular system] Pastukhov VA. **Fiziol Zh SSSR** 1981 Nov; 67(11):1661-9 (Eng. Abstr.) (Rus)

[Effect of acetylcholine on gastric secretory function and its vascular tonus] Skliarov AIa. **Fiziol Zh SSSR** 1982 Jan;68(1):90-9 (Eng. Abstr.) (Rus)

ACHIEVEMENT

A four-year follow-up study of the effects of methylphenidate on the behavior and academic achievement of hyperactive children. Charles L, et al. **J Abnorm Child Psychol** 1981 Dec;9(4):495-505

AFFECT

Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Phillips RH. **Psychosomatics** 1982 Jan;23(1):81-7

AFFECTIVE DISORDERS

Juggling act on a tightrope: using psychotropics in the elderly [editorial] Schell NB. **NY State J Med** 1981 Nov;81(12):1737

Biological factors in affective disorders and their relevance to lithium prophylaxis. Mendlewicz J. **Pharmacopsychiatria** 1982 Jan;15(1):11-8

Circadian rhythm mechanisms in affective illness and in antidepressant drug action. Wehr TA, et al. **Pharmacopsychiatria** 1982 Jan; 15(1):31-9 (59 ref.)

beta-Endorphin and beta-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. Brambilla F, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):321-30

[Biological perturbations in affective disorders in man] Rafaelsen OJ. **Encephale** 1981;7(4 Suppl):413-9 (Eng. Abstr.) (Fre)

AFFECTIVE DISORDERS, PSYCHOTIC

Effectiveness of verapamil in the treatment of a manic patient. Dubovsky SL, et al. **Am J Psychiatry** 1982 Apr;139(4):502-4

Carbamazepine treatment of selected affectively disordered inpatients. Folks DG, et al. **Am J Psychiatry** 1982 Jan;139(1):115-7

Lithium and glycine levels [letter] Prakash R. **Am J Psychiatry** 1982 Jan; 139(1):132

Cerebral fluoride in mania and the effect of lithium: a hypothesis. Gal EM. **Commun Psychopharmacol** 1980;4(5):405-9

[Recurrence prophylaxis of affective diseases with lithium and their results] Felber W. **Psychiatr Clin (Basel)** 1981;14(3):161-6 (Eng. Abstr.) (Ger)

[Lithium in the prophylaxis of recurrent affective disorders. Effectiveness of low plasma levels and predictors to clinical response (author's transl)] Faravelli C, et al. **Riv Patol Nerv Ment** 1980 Nov-Dec; 101(6):261-71 (Eng. Abstr.) (Ita)

AFFECTIVE SYMPTOMS

Anxiety and other neurotic symptoms in patients suffering from dans la conception des états limitrophes et des mécanismes d'action clinique des tranquillisants. Skovronsky O, et al. **Agressologie** 1981 Oct; 22(C):25-6

Prescribing of minor tranquillizers for emotional problems in a family practice. Bass MJ, et al. **Can Med Assoc J** 1981 Dec 1; 125(11):1225-6

[New trends in the concept of border states and mechanisms of clinical action of tranquilizers] Alexandrovsky YA. **Agressologie** 1981 Oct; 22(C):19-24 (Fre)

AGGRESSION

Localization of the site of the anticonflict action of benzodiazepines in the amygdaloid nucleus of rats. Shibata K, et al. **Brain Res** 1982 Feb 25;234(2):442-6

Variations in plasma and adrenal catecholamines and related enzymes in isolated-aggressive mice. Tizabi Y, et al. **Commun Psychopharmacol** 1980;4(5):433-9

Apomorphine-induced aggression in rats chronically treated with oral clonidine: modulation by central serotonergic mechanisms. Hahn RA, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):389-93 gamma-Aminobutyric acid in brain areas of isolated aggressive or non-aggressive inbred strains of mice. Simler S, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):57-61

Effect of tryptophan administration on spontaneous and P-CPA-induced muricidal aggression in laboratory rats. Valzelli L, et al. **Pharmacol Res Commun** 1981 Oct;13(9):891-7

[Biological basis of aggression] Chida AM, et al. **Rev Paul Enferm** 1981 Jul-Aug;(1):13-5 (Eng. Abstr.) **(Por)**

[Sensitization of male rats to aggressive behavior by apomorphine] Alikmets LKh, et al. **Zh Vyssh Nerv Deiat** 1982 Jan-Feb; 32(1):130-5 (Eng. Abstr.) **(Rus)**

[Role of corticosteroids in the development of fear and aggression reactions] Malyshenko NM. **Zh Vyssh Nerv Deiat** 1982 Jan-Feb; 32(1):144-51 (Eng. Abstr.) **(Rus)**

AMINO ACIDS

Lithium and amino acids [letter] Goodnick PJ, et al. **Am J Psychiatry** 1982 Apr;139(4):538-9

Protein turnover in pulmonary macrophages. Utilization of amino acids derived from protein degradation. Hammer JA 3d, et al. **Biochem J** 1981 Jul 15;198(1):53-65

On the formation of amino acids deriving from spermidine and spermine. Seiler N, et al. **Biochem J** 1981 Oct 15;200(1):123-32

Disposition of the acid-extractable amino acid pool in mammalian cells. Wheatley DN. **Cytobios** 1981;31(122):117-34

Effects of phencyclidine on excitatory amino acid activation of spinal interneurones in the cat. Lodge D, et al. **Eur J Pharmacol** 1982 Jan; 77(2-3):203-4

K+-stimulated release of endogenous glutamate, GABA and other amino acids from neuron- and glia-enriched cultures of the rat cerebellum. Pearce BR, et al. **FEBS Lett** 1981 Nov 30;135(1):215-8

Effect of antiepileptic drugs on the cerebral amino acid uptake in vitro. Saladini M, et al. **Ital J Neurol Sci** 1981 Dec;2(4):351-60

Tryptophan overload in the pregnant rat: effect on brain amino acid levels and in vitro protein synthesis. Fando JL, et al. **J Neurochem** 1981 Oct; 37(4):824-9

A regional study of 4-aminobutyrate metabolism and amino acid levels in rat brain following chronic oral administration of ethanolamine O-sulphate. Fletcher A, et al. **J Neurochem** 1982 Apr;38(4):1022-8

In vitro release of endogenous amino acids from granule cell-, stellate cell-, and climbing fiber-deficient cerebella. Flint RS, et al. **J Neurochem** 1981 Dec;37(6):1425-30

Effect of motor and premotor cortex ablation on concentrations of amino acids, monoamines, and acetylcholine and on the ultrastructure in rat striatum. A confirmation of glutamate as the specific cortico-striatal transmitter. Hassler R, et al. **J Neurochem** 1982 Apr;38(4):1087-98

Motor effects following application of putative excitatory amino acid antagonists to the region of the mesencephalic dopamine cell bodies in the rat. Dawbarn D, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(2):100-4

The effect of 6-aminonicotinamide on the levels of brain amino acids and glucose, and their labeling with 14C after injection of [U-14C] glucose. Gaitonde MK, et al. **Neurochem Res** 1981 Oct; 6(10):1159-67

AMITRIPTYLINE

Amitriptyline levels and clinical effects. Quednow B, et al. **Agressologie** 1981 Nov;22(E):15-8

Recurrence of depression after discontinuation of long-term amitriptyline treatment. Bialos D, et al. **Am J Psychiatry** 1982 Mar;139(3):325-9

Demethylation and hydroxylation of amitriptyline, nortriptyline, and 10-hydroxyamitriptyline in human liver microsomes. Mellström B, et al. **Drug Metab Dispos** 1981 Nov-Dec;9(6):565-8

Two-phase derivatization of amitriptyline and structurally related tertiary amines for gas chromatography with electron-capture detection. Karlsson KE. **J Chromatogr** 1981 Dec 18;219(3):373-8

A controlled comparison of trimipramine and amitriptyline. Kline NS. **J Clin Psychiatry** 1981 Mar;43(3):100-4

Adverse reactions to benzodiazepine-tricyclic antidepressant compound. Beresford TP, et al. **J Clin Psychopharmacol** 1981 Nov;1(6):392-4

Quantitative assessment of the pre- and postsynaptic alpha adrenoceptor antagonist potency of amitriptyline. Leighton HJ. **J Pharmacol Exp Ther** 1982 Feb;220(2):299-304

The influence of amitriptyline, imipramine and chlorpromazine on activity of arginase in rat's brain and liver. Grabowska-Hibner J, et al. **Mater Med Pol** 1981 Jan-Mar;13(1):54-7

Depression, antidepressants, and plasma DBH. Mathew RJ, et al. **Psychiatry Res** 1981 Dec;5(3):331-4

Binding of amitriptyline and nortriptyline in plasma determined from their equilibrium distributions between red cells and plasma, and between red cells and buffer solution. Burch JE, et al. **Psychopharmacology (Berlin)** 1981;75(3):262-72

[Comparison of the effectiveness of tranylcypromine, nortriptyline, thioridazine and amitriptyline in two syndromological types of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981;77(4):245-52 (Eng. Abstr.) **(Cze)**

AMOBARBITAL

[Industrial and pharmaceutical novelties. Prontalgin] **Chir Dent Fr** 1981 Nov 19;51(134):55 **(Fre)**

AMPHETAMINE

Evaluation of amphetamine-induced in vivo electrochemical response. Dayton MA, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):141-4

Stereospecific long-term effects of amphetamine on striatal dopamine neurons in rats. Steranka LR. **Eur J Pharmacol** 1981 Dec 17; 76(4):443-6

Age-related decline in brain stimulation reward: rejuvenation by amphetamine. Lewis MJ. **Exp Aging Res** 1981 Fall;7(3):225-34

Drug-induced circling after unilateral 6-hydroxydopamine lesions of the nigro-striatal pathway is mediated via the midbrain periaqueductal grey and adjacent reticular formation (angular complex). Reavill C, et al. **Life Sci** 1981 Dec 7;29(23):2357-65

Amphetamine psychosis and schizophrenia: a dual model. Kokkinidis L, et al. **Neurosci Biobehav Rev** 1981 Winter;5(4):449-61 (173 ref.)

Ontogeny of fenfluramine and amphetamine anorexia compared in rat pups. Leshem M. **Pharmacol Biochem Behav** 1981 Dec;15(6):859-63

Differential effects of l-amphetamine on ontogeny of active avoidance, intertrial responses, and locomotor activity. Bauer R, et al. **Psychopharmacology (Berlin)** 1981;75(3):299-304

A comparison of some behavioural effects of amphetamine and electrical brain stimulation of the mesolimbic dopamine system in rats. D'Mello GD. **Psychopharmacology (Berlin)** 1981;75(2):184-92

Amphetamine-associated myoglobinuric renal failure. Scandling J, et al. **South Med J** 1982 Feb;75(2):237-40

[Effect of phenamine and haloperidol on stereotyped behavior in response to electric stimulation of the substantia nigra in cats] Arushanian EB, et al. **Biull Eksp Biol Med** 1981 Oct;91(10):444-7 (Eng. Abstr.) **(Rus)**

[Effect of high doses of phenamine on instrumental defensive reflexes in intact and striatectomized rats] Baturin VA. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec;31(6):1305-7 **(Rus)**

[Effect of N-(4-picolyl)-3,5 dimethylbenzamide (M-14012-4) on stereotyped behavior induced by apomorphine and amphetamine in the rat and mouse] Casais PL, et al. **Arch Farmacol Toxicol** 1981 Apr; 7(1):65-72 **(Spa)**

[Peripheral mechanisms implicated in the interaction of atropine, amphetamine and reserpine on body temperature in the conscious rat] Milanés MV, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):77-8 **(Spa)**

AMPHETAMINES

Stereochemical aspects of para-chloroamphetamine metabolism. Rabbit liver microsomal metabolism of RS-, R(-)-, and S(para-chloroamphetamine. Ames MM, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):5-9

Conversion of N-hydroxyamphetamine to phenylacetone oxime by rat liver microsomes. Matsumoto RM, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):105-8

The effects of 2,5-dimethoxy-4-methylamphetamine (DOM) on operant behavior: interactions with other neuroactive agents. Commissaris RL, et al. **Commun Psychopharmacol** 1980;4(5):393-404

Neurochemical and behavioural correlates of the interaction between amphetamine and delta 9-tetrahydrocannabinol in the rat. Lew EO, et al. **Drug Alcohol Depend** 1981 Sep;8(2):93-101

p-Chloroamphetamine: effects on tonic immobility, activity, and temperature in chickens. Boren JL, et al. **J Comp Physiol Psychol** 1981 Dec;95(6):991-1002

ANOREXIA NERVOSA

A double-blind controlled trial of lithium carbonate primary anorexia nervosa. Gross HA, et al. **J Clin Psychopharmacol** 1981 Nov; 1(6):376-81

[Therapy of anorexia nervosa aimed at depressive manifestations] Kadlecová B. **Cesk Pediatr** 1981 Nov;36(11):666-7 **(Cze)**

ANTIDEPRESSIVE AGENTS

Comparison of the dosage schedules during the administration of retarded lithium carbonate. Balon R, et al. **Act Nerv Super (Praha)** 1981; 23(4):278-80

Treatment of enuresis with sydnocarb. Polák L, et al. **Act Nerv Super (Praha)** 1981;23(4):263-4

Duration of REM sleep latency as predictor of effect of antidepressant therapy. A preliminary report. Svendsen K, et al. **Acta Psychiatr Scand** 1981 Sep;64(3):238-43

Relationship between plasma antidepressant levels and clinical outcome for inpatients receiving imipramine. Simpson GM, et al. **Am J Psychiatry** 1982 Mar;139(3):358-60

The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy, each alone and in combination.

Blackburn IM, et al. **Br J Psychiatry** 1981 Sep;139:181-9

Zimelidine and norzimelidine protein binding measured by equilibrium dialysis and cerebrospinal fluid. Calil HM, et al. **Clin Pharmacol Ther** 1982 Apr;31(4):522-7

The new generation of antidepressants. Davis JM, et al. **Curr Psychiatr Ther** 1981;20:293-7

Brain histamine H1- and H2-receptors and histamine-sensitive adenylate cyclase: effects of antipsychotics and antidepressants. Coupet J, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):149-55

alpha 1-Adrenoceptor-mediated responses in the lateral geniculate nucleus are enhanced by chronic antidepressant treatment. Menkes DB, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):27-35

Effect of norepinephrine uptake blocker on beta-adrenergic receptors of the rat cerebral cortex. Sethy VH, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):53-6

Poor prophylactic lithium response due to antidepressants. Reginaldi D, et al. **Int Pharmacopsychiatry** 1981;16(2):124-8

Rapid cyclers and antidepressants. Tondo L, et al. **Int Pharmacopsychiatry** 1981;16(2):119-23

Changes in saliva secretion and accommodation width during short-term administration of imipramine and zimelidine in healthy volunteers. von Knorring L. **Int Pharmacopsychiatry** 1981;16(2):69-78

Determination of the antidepressant agent citalopram and metabolites in plasma by liquid chromatography with fluorescence detection. Oyehaug E, et al. **J Chromatogr** 1982 Jan 8;227(1):129-35

Gas chromatographic determination of noxyptyline in substance, tablets and in biological material. Szyszko E, et al. **J Chromatogr** 1981 Dec 4;219(2):291-6

Methodological problems in studies of depressive disorder: utility of the discontinuation design. Quitkin FM, et al. **J Clin Psychopharmacol** 1981 Sep;1(5):283-8

How capable of driving are hospitalized psychiatric patients under psycho-active drug therapy? Hobi V, et al. **J Int Med Res** 1981; 9(6):434-47

Pyrazolodiazepines. 3. 4-Aryl-1,6,7,8-tetrahydro-1,3-dialkylpyrazolo[3,4-e][1,4]diazepines as antidepressant agents. DeWald HA, et al. **J Med Chem** 1981 Aug; 24(8):982-7

A new nontricyclic antidepressant agent. Synthesis and activity of N-[trans-2-(dimethylamino)cyclopentyl]-N-(3,4-dichlorophenyl)propa and related compounds. Szmuszkovicz J, et al. **J Med Chem** 1981 Oct; 24(10):1230-6

Active conformation of polycyclic antidepressants. Asscher Y, et al. **J Pharm Sci** 1982 Jan;71(1):122-4

Comments on multicenter trials of antidepressant drugs. Hippius H, et al. **Mod Probl Pharmacopsychiatry** 1981;16:95-9

The effects of antidepressant drugs on conditioned taste aversion learning of the olfactory bulbectomized rat. Jancsár SM, et al. **Neuropharmacology** 1981 Dec;20(12B):1341-5

Neuroleptics as antidepressants. Robertson MM, et al. **Neuropharmacology** 1981 Dec;20(12B):1335-6

Effect of antidepressant drugs on carbachol chloride-induced wet dog shake behaviour in rats. Turski L, et al. **Neuropharmacology** 1981 Dec; 20(12A):1193-6

Atypical antidepressant drugs - psychopharmacological profile and mechanism of action. Maj J. **Pharmacopsychiatria** 1982 Jan; 15(1):26-30

Circadian rhythm mechanisms in affective illness and in antidepressant drug action. Wehr TA, et al. **Pharmacopsychiatria** 1982 Jan; 15(1):31-9 (59 ref.)

Effects of cholinomimetics, cholinolytics and atypical antidepressants in the behavioral despair test in the rat. Herman ZS, et al. **Pol J Pharmacol Pharm** 1981;33(5):485-9

The effect of pyrazidol on the central serotonergic system. Sypniewska M, et al. **Pol J Pharmacol Pharm** 1981;33(3):313-9

Advances in antidepressant treatment? Jenner FA. **Practitioner** 1981 Oct; 225(1360):1378-85

Non-tricyclic antidepressants. van Dijk J, et al. **Prog Med Chem** 1978; 15:261-320 (351 ref.)

The biotransformation of [14C]minaprine in man and five animals species. Davi H, et al. **Xenobiotica** 1981 Nov;11(11):735-47

[Therapy of anorexia nervosa aimed at depressive manifestations] Kadlecová B. **Cesk Pediatr** 1981 Nov;36(11):666-7 (Cze)

[On the position of pyrazidol in the group of antidepressants in treatment of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981 Oct;77(5):315-21 (Eng. Abstr.) (Cze)

[Influence of the seasons on the course and therapeutic results of depressive phases of maniomelancholy (author's transl)] Sedivec V. **Cesk Psychiatr** 1981 Oct;77(5):326-30 (Eng. Abstr.) (Cze)

[Treatment of endogenous depressions with maprotiline, clomipramine, dibenzepine and pyrlindole (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Jun;77(3):198-203 (Eng. Abstr.) (Cze)

[Therapists and therapeutic choice (author's transl)] Ayme J. **Encephale** 1981;7(4 Suppl):507-11 (Eng. Abstr.) (Fre)

[Depressed patients and their treatment. Therapeutic mistakes and toxicity (author's transl)] Crome P. **Encephale** 1981;7(4 Suppl):499-506 (Eng. Abstr.) (Fre)

[Role of postsynaptic noradrenergic receptors in the mechanism of action of antidepressants] Cuenca E. **Encephale** 1981;7(4 Suppl):397 (Fre)

[Therapeutic implications of the biochemical features about depressive illness (author's transl)] Lôo H. **Encephale** 1981;7(4 Suppl):429-40 (62 ref.) (Eng. Abstr.) (Fre)

[Predicted pharmacology of an antidepressant] Pinder RM. **Encephale** 1981;7(4 Suppl):371-80 (Eng. Abstr.) (Fre)

[Are antidepressants different? (author's transl)] Puech AJ. **Encephale** 1981;7(4 Suppl):401-3 (Eng. Abstr.) (Fre)

[Prescription of antidepressants (author's transl)] Rainaut J. **Encephale** 1981;7(4 Suppl):513-22 (Eng. Abstr.) (Fre)

[Value of the binding site for tritiated imipramine in the pharmacology of antidepressants] Zarifian E. **Encephale** 1981;7(4 Suppl):405-7 (Fre)

[Open study of minaprine in a child psychiatry population (author's transl)] de Villard R, et al. **Neuropsychiatr Enfance Adolesc** 1981 Apr-May; 29(4-5):255-8 (Eng. Abstr.) (Fre)

[Depression. Treatment] Hougardy G. **Rev Med Liege** 1982 Jan 1; 37(1):14-6 (Fre)

[Drug therapy of anxiety states] Laux G. **Krankenpfl J** 1982 Feb 15; 20(2):22-4 (Ger)

[Determination of tofizopame by photoluminescence] Székelyhidi L, et al. **Acta Pharm Hung** 1981 Nov;51(6):270-4 (Eng. Abstr.) (Hun)

[Lithium in the prophylaxis of recurrent affective disorders. Effectiveness of low plasma levels and predictors to clinical response (author's transl)] Faravelli C, et al. **Riv Patol Nerv Ment** 1980 Nov-Dec; 101(6):261-71 (Eng. Abstr.) (Ita)

[Atypical antidepressants: effect on synaptosomal uptake of serotonin and GABA] Avdulov NA, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):564-6 (Eng. Abstr.) (Rus)

[Effect of the new antidepressant cephedrine on compensatory hypertrophy of the ovaries and the inhibiting effect of estrogen] Mekhova GM, et al. **Farmakol Toksikol** 1982 Jan-Feb;45(1):52-4 (Eng. Abstr.) (Rus)

[Effect of the tetracyclic antidepressants pyrazidol and inkazan on the adrenergic nerve transmission in the rat vas deferens] Panasiuk LV, et al. **Farmakol Toksikol** 1982 Jan-Feb;45(1):13-7 (Eng. Abstr.) (Rus)

[New information concerning the neurochemical mechanisms of action of antidepressants] Val'dman AV. **Vestn Akad Med Nauk SSSR** 1982; (1):3-8 (Eng. Abstr.) (Rus)

[Antidepressive agents can cause dental damages in children and adults] van Dijken J, et al. **Lakartidningen** 1981 Nov 25;78(48):4366-8 (Swe)

ANXIETY

Do have antidepressants of the second generation anxiolytic properties? Kabes J, et al. **Agressologie** 1981 Nov;22(E):11-3

Some dissociations in the anxiety and mental tension. Molcan J, et al. **Agressologie** 1981 Oct;22(C):17-8

Anxiolytics and beta blockers: evaluation of pharmacodynamics by quantitative EEG, psychometric and physiological variables. Saletu B, et al. **Agressologie** 1981 Oct;22(C):5-16

Effect of beta blockade and beta stimulation on stage fright. Brantigan CO, et al. **Am J Med** 1982 Jan;72(1):88-94

Anxiety as a paradigm case of emotion. Gray JA. **Br Med Bull** 1981 May;37(2):193-7 (46 ref.)

Practical therapeutics management of anxiety. Arap-Mengech HN. **East Afr Med J** 1981 Sep;58(9):631-5

beta-Adrenoceptor antagonists [letter] **N Engl J Med** 1982 Jan 21; 306(3):176-7

The drug treatment of anxiety. Rosenbaum JF. **N Engl J Med** 1982 Feb 18;306(7):401-4 (24 ref.)

[Psychopharmacology of anxiety. 1] **Agressologie** 1981 Oct;22(C):1-53 (Fre)

[Drug therapy of anxiety states] Laux G. **Krankenpfl J** 1982 Feb 15; 20(2):22-4 (Ger)

ANXIETY DISORDERS

Pimozide versus chlordiazepoxide in anxiety neurosis. Doongaji DR, et al. **Acta Psychiatr Belg** 1981 Jul-Aug;81(4):416-23

Anxiolytic properties of neuroleptic drugs. Balon R, et al. **Agressologie** 1981 Nov;22(D):9-10

Neuroleptics in neurotic anxiety. Boleloucky Z. **Agressologie** 1981 Nov; 22(D):15-7

Dothiepin, antianxiety effect in neurotic women. Boriová M, et al. **Agressologie** 1981 Nov;22(E):9-10

A double-blind, placebo-controlled study with tofizopam in anxiety neurosis. Filip V, et al. **Agressologie** 1981 Oct;22(C):27-30

Clinical trial with clobazam. Kabes J, et al. **Agressologie** 1981 Oct; 22(C):41-2

Treatment of anxious depression with intravenous infusions of a combination of drugs. Krebs-Roubicek L, et al. **Agressologie** 1981 Nov; 22(D):25-6

Tofizopam in the therapy of anxious-depressive syndromes. Molcan J, et al. **Agressologie** 1981 Nov;22(D):23-4

Influence of different psychotropic drugs on psychotic anxiety. Nahunek

K. et al. **Agressologie** 1981 Nov;22(D):11-3

Neuroleptics in the treatment of anxiety. Schmidt P. **Agressologie** 1981 Nov;22(D):19-20

Differentiated psychopharmacotherapy in anxiety states of slowly progressive schizophrenia. Smulevitch A. **Agressologie** 1981 Nov;22(D):31-2

Anxiety in climax and its pharmacological treatment. Tendlova H, et al. **Agressologie** 1981 Nov;22(E):7-8

Drug treatment of anxiety. Vinar O. **Agressologie** 1981 Oct;22(C):35-8

Case report of painful ejaculation as a side effect of amoxapine. Kulik FA, et al. **Am J Psychiatry** 1982 Feb;139(2):234-5

Major common symptoms in psychiatry. Anxiety. Tyrer P. **Br J Hosp Med** 1982 Feb;27(2):109-13

Diazepam, propranolol and their combination in the management of chronic anxiety. Hallstrom C, et al. **Br J Psychiatry** 1981 Nov;139:417-21

Recent advances in anxiolytic therapy. Rickels K. **J Clin Psychiatry** 1981 Nov;42(11 Pt 2):40-4

Current therapeutic options in the management of typical anxiety. Schuckit MA. **J Clin Psychiatry** 1981 Nov;42(11 Pt 2):15-26

Specific anxiety syndromes: current therapeutic options. Uhlenhuth EH. **J Clin Psychiatry** 1981 Nov;42(11 Pt 2):27-34

Catecholamine and dopamine-beta-hydroxylase in anxiety. Mathew RJ, et al. **J Psychosom Res** 1981;25(6):499-504

[Personality, antidepressant and neuroses] Bolelouckỳ Z, et al. **Agressologie** 1981 Nov;22(E):3-5 **(Fre)**

[Psychopathology of anxiety] Guensberger E, et al. **Agressologie** 1981 Oct;22(C):31-3 (Eng. Abstr.) **(Fre)**

[Comparative results of the treatment of anxiety in the depressive syndrome with Tolvon, Vivalan and Alival] Ivanov V, et al. **Agressologie** 1981 Nov;22(D):29-30 **(Fre)**

[Interactions between depression and anxiety (author's transl)] Ballus C. **Encephale** 1981;7(4 Suppl):335-7 (Eng. Abstr.) **(Fre)**

[Comparative studies on the tranquilizer effect of fluspirilene and bromazepam] Thilmann J. **Med Welt** 1981 Dec 25;32(51-52):1959-61 **(Ger)**

APOMORPHINE

Androgenic influences on apomorphine-induced yawning in rats. Berendsen HH, et al. **Behav Neural Biol** 1981 Sep;33(1):123-8

Inhibition by apomorphine of the potassium-evoked release of [3H]-gamma-aminobutyric acid from the rat substantia nigra in vitro. Arbilla S, et al. **Br J Pharmacol** 1981 Oct;74(2):389-97

N-n-propyl-norapomorphine: an extremely potent stimulant of dopamine autoreceptors. Argiolas A, et al. **Brain Res** 1982 Jan 7;231(1):109-16

An orally effective, long-acting dopaminergic prodrug: (-)-10,11-methylenedioxy-N-propylnoraporphine. Baldessarini RJ, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):87-8

Pharmacological profiles of the putative dopamine autoreceptor agonists 3-PPP and TL-99. Martin GE, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):15-23

Alterations in local cerebral glucose utilisation in specific thalamic nuclei following apomorphine. McCulloch J, et al. **J Cereb Blood Flow Metab** 1981;1(1):133-6

Apomorphine-induced aggression in rats chronically treated with oral clonidine: modulation by central serotonergic mechanisms. Hahn RA, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):389-93

Interaction of apomorphine and stressors in the production of hyperthermia in the rabbit. Snow AE, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):335-9

Drug-induced circling after unilateral 6-hydroxydopamine lesions of the nigro-striatal pathway is mediated via the midbrain periaqueductal grey and adjacent reticular formation (angular complex). Reavill C, et al. **Life Sci** 1981 Dec 7;29(23):2357-65

The use of dopamine agonists in the treatment of schizophrenia. Corsini GU, et al. **Neuropharmacology** 1981 Dec;20(12B):1309-13

Behavioural and neurochemical studies on apomorphine-induced hypomotility in mice. Sumners C, et al. **Neuropharmacology** 1981 Dec;20(12A):1203-8

Dopaminergic agonistic and antagonistic drugs in the ventral tegmentum of rats inhibit and facilitate changes of food-search behaviour. Oades RD. **Neurosci Lett** 1981 Nov 18;27(1):75-80

The effects of quipazine, fenfluramine and apomorphine on the morphine potentiation of tonic immobility. Wallnau LB. **Pharmacol Biochem Behav** 1981 Dec;15(6):895-901

Substance P levels in the rat forebrain after apomorphine and haloperidol treatment. Janicki P, et al. **Pol J Pharmacol Pharm** 1981;33(5):499-502

Haloperidol and clonidine increase, and apomorphine decreases ultrasonic vocalizations by gerbils. Thiessen DD, et al. **Psychopharmacology (Berlin)** 1981;75(3):287-90

[Effects of different doses of apomorphine on the glutamate decarboxylase activity of the substantia nigra and the medial basal hypothalamus] Giammona G, et al. **Boll Soc Ital Biol Sper** 1981 Oct 30;57(20):2074-9 (Eng. Abstr.) **(Ita)**

[Effect of amizil and galantamin on the behavioral effects of apomorphine in rats] Bandman AL, et al. **Biull Eksp Biol Med** 1981 Nov;92(11):566-9 (Eng. Abstr.) **(Rus)**

[Sensitization of male rats to aggressive behavior by apomorphine] Allikmets LKh, et al. **Zh Vyssh Nerv Deiat** 1982 Jan-Feb;32(1):130-5 (Eng. Abstr.) **(Rus)**

[Effect of N-(4-picolyl)-3,5 dimethylbenzamide (M-14012-4) on stereotyped behavior induced by apomorphine and amphetamine in the rat and mouse] Casais PL, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):65-72 **(Spa)**

APPETITE

A neurochemical theory of appetite and weight changes in depressive states. Hopkinson G. **Acta Psychiatr Scand** 1981 Sep;64(3):217-25

ATTENTION

Methylphenidate compared with behavioral self-control in attention deficit disorder: preliminary report. Anderson EE, et al. **JDBP** 1981 Dec;2(4):137-41

Effects of levodopa on attention deficit disorder, residual type. Wood D, et al. **Psychiatry Res** 1982 Feb;6(1):13-20

AVOIDANCE LEARNING

Piribedil-induced anti-hypoxic protection in rats. Saligaut C, et al. **Aviat Space Environ Med** 1982 Jan;53(1):35-9

Lesions of the olfactory pathways affecting neophobia and learned aversion differentially. Royet JP, et al. **Behav Brain Res** 1982 Mar;4(3):251-62

Effects of metenkephalin on the formation and fixation of defensive temporal associations and on the incorporation of C14-leucine in brain proteins of the rat. Kruglikov RI, et al. **Biol Bull Acad Sci USSR** 1980 Sep-Oct;7(5):432-4

Behavioral effects and physiological disposition of some beta-hydroxylated indoleamines in the rat. Gentile NT, et al. **Biol Psychiatry** 1982 Jan;17(1):109-13

Selective associations in one-day-old rats: taste-toxicosis and texture-shock aversion learning. Gemberling GA, et al. **J Comp Physiol Psychol** 1982 Feb;96(1):105-13

Acetylcholine metabolism in the rat hippocampus and striatum following one-trial passive training. Barker LA, et al. **Neuropharmacology** 1982 Feb;21(2):183-5

A circadian rhythm in passive avoidance behavior: the effect of phase shift and the benzodiazepines. Childs G, et al. **Neuropharmacology** 1981 Dec;20(12B):1365-6

The effects of antidepressant drugs on conditioned taste aversion learning of the olfactory bulbectomized rat. Jancsár SM, et al. **Neuropharmacology** 1981 Dec;20(12B):1341-5

Correlation between retention of defensive conditioned reflexes and brain acetylcholinesterase activity in rats. Dish TN. **Neurosci Behav Physiol** 1981 May-Jun;11(3):230-3

Correlation between the rate of avoidance conditioning and the brain catecholamine level in rats. Saul'skaya NB. **Neurosci Behav Physiol** 1981 May-Jun;11(3):221-6

On the interactive role of central noradrenaline neurons and corticosterone in two-way active avoidance acquisition in the rat. Archer T, et al. **Neurosci Lett** 1981 Dec 23;27(3):341-6

Effects of bilateral amygdala lesions on neophobia and conditioned taste aversion in mice. Shimai S, et al. **Percept Mot Skills** 1982 Feb;54(1):127-30

Kyotorphins affect aversive pecking in chicks. Kastin AJ, et al. **Physiol Behav** 1981 Dec;27(6):1073-6

Behavioral and corticosterone effects in conditioned taste aversion following hippocampal lesions. Smotherman WP, et al. **Physiol Behav** 1981 Oct;27(4):569-74

Learned aversions in rats fed a tryptophan-free diet. Treneer CM, et al. **Physiol Behav** 1981 Nov;27(5):757-60

Differential effects of l-amphetamine on ontogeny of active avoidance, intertrial responses, and locomotor activity. Bauer R, et al. **Psychopharmacology (Berlin)** 1981;75(3):299-304

Enhancement of the avoidance-suppressing effects of neuroleptic agents after repeated administration: changes in the discriminated avoidance response in rats. Kuribara H, et al. **Psychopharmacology (Berlin)** 1981;75(2):148-51

Differential reversal of various dopamine antagonists by anticholinergics in Sidman avoidance: possible relationship to adrenergic blockade. Liebman JM, et al. **Psychopharmacology (Berlin)** 1981;75(3):248-53

[Dualistic action of scopolamine on avoidance conditioned response in dogs (author's transl)] Niu XY, et al. **Chung Kuo Yao Li Hsueh Pao** 1981 Mar;2(1):4-8 (Eng. Abstr.) **(Chi)**

[Learning in rats with differing emotional responsiveness and its relation to brain monoamines] Gromova EA, et al. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec;31(6):1238-46 (Eng. Abstr.) **(Rus)**

AZEPINES

Comparison of the in vitro metabolism of N-nitrosohexamethyleneimine by rat liver and lung microsomal fractions. Hecker LI, et al. **Cancer Res** 1982 Jan;42(1):59-64

alpha 2-Adrenoceptor agonistic effect of B-HT 920 in isolated perfused hindquarters of rats. Kobinger W, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):101-5

Effect of cetiedil on cation and water movements in erythrocytes. Schmidt WF 3d, et al. **J Clin Invest** 1982 Mar;69(3):589-94

Pyrazolodiazepines. 3. 4-Aryl-1,6,7,8-tetrahydro-1,3-dialkylpyrazolo[3,4-e][1,4]diazepines as antidepressant agents. DeWald HA, et al. **J Med Chem** 1981 Aug; 24(8):982-7

[Effectiveness of the repellent action and the prospects for using clothing chemically bonded with carboxide] Dremova VP, et al. **Med Parazitol (Mosk)** 1982 Jan-Feb;51(1):39-44 (Eng. Abstr.) **(Rus)**

BEHAVIOR

Neurochemistry of behaviour. Warburton DM. **Br Med Bull** 1981 May; 37(2):121-5 (45 ref.)

A four-year follow-up study of the effects of methylphenidate on the behavior and academic achievement of hyperactive children. Charles L, et al. **J Abnorm Child Psychol** 1981 Dec;9(4):495-505

An analysis of commonalities in substance abuse and habitual behavior. Levison PK. **Natl Inst Drug Abuse Res Monogr Ser** 1981 Jul; (37):27-41

Quantitative EEG and behavioral effects in volunteers of a new benzodiazepine (SAS 643) in relation to drug plasma concentration. Sannita WG, et al. **Ther Drug Monit** 1981;3(4):341-9

BEHAVIOR, ANIMAL

Some behavioral effects of antiepileptic drugs during acute and prolonged treatment in the rat. Kulig BM. **Acta Neurol Scand [Suppl]** 1981; 89:59-67

Central neurotropic activity of homovanillic acid. Kleinrok Z, et al. **Acta Physiol Pol** 1981 Sep-Oct;32(5):477-85

Taurine and thermoregulation: behavioral and cellular studies. Carlà V, et al. **Adv Exp Med Biol** 1981;139:361-72

Endorphins and behavior. Bolles RC, et al. **Annu Rev Psychol** 1982; 33:87-101

Circling behavior produced by unilateral lesions of the central vestibular system. Shima F, et al. **Appl Neurophysiol** 1982 May-Jun; 45(3):255-60

Androgenic influences on apomorphine-induced yawning in rats. Berendsen HH, et al. **Behav Neural Biol** 1981 Sep;33(1):123-8

The effect of PEA on serotonin and catecholamines. Widelitz MM, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):1107-11

Amygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst-motivated behavior. Lénárd L, et al. **Brain Res** 1982 Feb 4;233(1):115-32

Neurochemical and behavioural correlates of the interaction between amphetamine and delta 9-tetrahydrocannabinol in the rat. Lew EO, et al. **Drug Alcohol Depend** 1981 Sep;8(2):93-101

The effect of some anti-epilepsy drugs on enhancement of the monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. Bhavsar VH, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):243-7

Suppressive action of cholecystokinin octapeptide on the behavioral effects of L-DOPA in the rat. Itoh S, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):313-6

Lithium dissociates haloperidol-induced behavioral supersensitivity from reduced dopac increase in rat striatum. Meller E, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):25-9

An improved pharmacological procedure for depletion of noradrenaline: pharmacology and assessment of noradrenaline-associated behaviors. Zolovick AJ, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):265-71

3H-Diazepam binding sites in Roman high- and low-avoidance rats. Gentsch C, et al. **Experientia** 1981 Dec 15;37(12):1315-6

Unlimited access intravenous drug self-administration in rhesus monkeys. Balster RL, et al. **Fed Proc** 1982 Feb;41(2):211-5

Time-dependent environmentally-induced changes in cerebral and extra-cerebral morphology and chemistry--the basis of learning, memory and behavior. DeFeudis FV. **Gen Pharmacol** 1982;13(1):1-9 (97 ref.)

Comparative effects of short- and long-term treatment with neuroleptics on behavioural activity as well as dopamine turnover in striatum. Rastogi RB, et al. **Gen Pharmacol** 1982;13(1):35-40

A reliable multichannel commutator for making electrical contact with conscious, freely moving rats. Andrews CD, et al. **J Neurosci Methods** 1982 Jan;5(1-2):73-6

Stereospecificity of behavioural effects of viloxazine in bulbectomized rats does not correlate with its 5-HT-releasing action in vitro. Greenwood DT, et al. **J Pharm Pharmacol** 1982 Jan;34(1):38-41

Sodium valproate exerts anti-conflict activity in rats without any concomitant rise in forebrain GABA level. Rasmussen KJ, et al. **Life Sci** 1981 Nov 23;29(21):2163-70

Drug-induced circling after unilateral 6-hydroxydopamine lesions of the nigro-striatal pathway is mediated via the midbrain periaqueductal grey and adjacent reticular formation (angular complex). Reavill C, et al. **Life Sci** 1981 Dec 7;29(23):2357-65

The behavioural effects of systemically administered kainic acid: a pharmacological analysis. Worms P, et al. **Life Sci** 1981 Nov 23; 29(21):2215-25

Differential drug effects as a function of the controlling consequences. Barrett JE. **Natl Inst Drug Abuse Res Monogr Ser** 1981 Jul; (37):159-81 (40 ref.)

Differential involvement of dopamine-containing tracts in 5-hydroxytryptamine-dependent behaviours caused by amphetamine in large doses. Andrews CD, et al. **Neuropharmacology** 1982 Jan; 21(1):63-8

Repeated administration of triiodothyronine (T3) to rats enhances nigrostriatal and mesolimbic dopaminergic behavioural responses. Heal DJ, et al. **Neuropharmacology** 1982 Feb;21(2):159-62

Pharmacological properties of new antipsychotic agents: use of animal models. Puech AJ, et al. **Neuropharmacology** 1981 Dec; 20(12B):1279-84

Effect of antidepressant drugs on carbachol chloride-induced wet dog shake behaviour in rats. Turski L, et al. **Neuropharmacology** 1981 Dec; 20(12A):1193-6

Behavioral and temperature changes induced by clonidine in the developing rat. Reinstein DK, et al. **Neurosci Lett** 1981 Nov 4; 26(3):251-7

Computer-aided calculation of dose response curves in behavioral pharmacology by using a nonlinear regression procedure. Morgenstern R, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):987-91

Rats' responses to blood and body odors of stressed and non-stressed conspecifics. Mackay-Sim A, et al. **Physiol Behav** 1981 Sep; 27(3):503-10

Behavioral and corticosterone effects in conditioned taste aversion following hippocampal lesions. Smotherman WP, et al. **Physiol Behav** 1981 Oct;27(4):569-74

Studies on the behavioral and hypotensive effects of intraventricular prostacyclin (PGI2) in rats. Brus K, et al. **Pol J Pharmacol Pharm** 1981; 33(4):467-74

Effects of cholinomimetics, cholinolytics and atypical antidepressants in the behavioral despair test in the rat. Herman ZS, et al. **Pol J Pharmacol Pharm** 1981;33(5):485-9

Psychopharmacological effects of cholinomimetic agents administered into hippocampus and various hypothalamic areas in the rat. Thesis. Plech A. **Pol J Pharmacol Pharm** 1981;33(4):415-20

Effect of parachlorophenylalanine on the incidence of abnormal behavior observed following diazepam withdrawal. Suzuki T, et al. **Prog Neuropsychopharmacol** 1981;5(4):415-7

Differential inhibitory effects of ascorbic acid on the binding of dopamine agonists and antagonists to neostriatal membrane preparations: correlations with behavioral effects. Heikkila RE, et al. **Res Commun Chem Pathol Pharmacol** 1981 Dec;34(3):409-21

Effect of prenatal phenytoin administration on postnatal development of the rat: a behavioral teratology study. Elmazar MM, et al. **Teratology** 1981 Oct;24(2):115-24

BENACTYZINE

[Effect of amizil and galantamin on the behavioral effects of apomorphine in rats] Bandman AL, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):566-9 (Eng. Abstr.) **(Rus)**

BENZAZEPINES

Selective action of diltiazem on cerebral vascular smooth muscle in the rabbit: antagonism of extrinsic but not intrinsic maintained tone. Bevan JA. **Am J Cardiol** 1982 Feb 18;49(3):519-24

Comparative electrophysiologic and coronary hemodynamic effects of diltiazem, nisoldipine and verapamil on myocardial tissue. Lathrop DA, et al. **Am J Cardiol** 1982 Feb 18;49(3):613-20

Effect of diltiazem on calcium transport and development of tension in heart muscle. Morad M, et al. **Am J Cardiol** 1982 Feb 18; 49(3):595-601

Electrophysiologic effects of diltiazem in canine myocardium, with special reference to conduction delay during ischemia. Peter T, et al. **Am J Cardiol** 1982 Feb 18;49(3):602-5

Pharmacokinetics of diltiazem in selected animal species and human beings. Piepho RW, et al. **Am J Cardiol** 1982 Feb 18;49(3):525-8

The pharmacokinetics of diltiazem in healthy American men. Zelis RF, et al. **Am J Cardiol** 1982 Feb 18;49(3):529-32

Effects of diltiazem on smooth muscles and neuromuscular junction in the mesenteric artery. Suzuki H, et al. **Am J Physiol** 1982 Mar; 242(3):H325-36

Cold blood-diltiazem cardioplegia. Barner HB, et al. **Ann Thorac Surg** 1982 Jan;33(1):55-63

[Effects of diltiazem on catecholamine release from cat adrenal glands (author's transl)] Yamaguchi I, et al. **Nippon Yakurigaku Zasshi** 1981 Nov;78(5):501-9 (Eng. Abstr.) (Jpn)

BENZODIAZEPINE TRANQUILIZERS

The passage of flunitrazepam into cerebrospinal fluid in man. Aaltonen L, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Apr;48(4):364-8

Neuroleptics in neurotic anxiety. Boleloucky Z. **Agressologie** 1981 Nov;22(D):15-7

A double-blind, placebo-controlled study with tofizopam in anxiety neurosis. Filip V, et al. **Agressologie** 1981 Oct;22(C):27-30

Clinical trial with clobazam. Kabes J, et al. **Agressologie** 1981 Oct;22(C):41-2

Subjective and psychometric assessment of effect in single application of clobazam. Molcan J, et al. **Agressologie** 1981 Oct;22(C):43-5

Tofizopam in the therapy of anxious-depressive syndromes. Molcan J, et al. **Agressologie** 1981 Nov;22(D):23-4

Differentiated psychopharmacotherapy in anxiety states of slowly progressive schizophrenia. Smulevitch A. **Agressologie** 1981 Nov;22(D):31-2

Clinical investigations of some anxiolytics drugs. Welbel SL. **Agressologie** 1981 Oct;22(C):39-40

Cimetidine--benzodiazepine interactions [letter] Mangini RJ. **Am J Hosp Pharm** 1982 Feb;39(2):236, 242

Lorazepam and desipramine serum concentration [letter] Rosenblatt JE. **Am J Psychiatry** 1982 Apr;139(4):536-7

Lorazepam and oxazepam esters. Hydrophobicity, hydrolysis rates and brain appearance. Simon-Trompler E, et al. **Arzneimittelforsch** 1982;32(2):102-5

Sedation for upper gastrointestinal endoscopy [letter] Bardhan KD. **Br J Anaesth** 1981 Dec;53(12):1368

Clobazam kinetics in the elderly. Greenblatt DJ, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):631-6

Hypnotic activity and effects on performance of lormetazepam and camazepam--analogues of temazepam. Nicholson AN, et al. **Br J Clin Pharmacol** 1982 Mar;13(3):433-9

Impaired elimination of lorazepam following subchronic administration in two patients with renal failure [letter] Verbeeck RK, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):749-51

Urinary monoamine oxidase inhibitor and benzodiazepine withdrawal. Petursson H, et al. **Br J Psychiatry** 1982 Jan;140:7-10

Localization of the site of the anticonflict action of benzodiazepines in the amygdaloid nucleus of rats. Shibata K, et al. **Brain Res** 1982 Feb 25;234(2):442-6

Steady-state plasma desmethyldiazepam during long-term clorazepate use: effects of antacids. Shader RI, et al. **Clin Pharmacol Ther** 1982 Feb;31(2):180-3

Lormetazepam - yet another benzodiazepine. **Drug Ther Bull** 1982 Jan 8;20(1):3-4

Pharmacokinetics of N-desmethyldiazepam after a single oral dose of clorazepate: the effect of smoking. Norman TR, et al. **Br J Clin Pharmacol** 1981;21(3):229-33

The kinetics and displacement of [11C]flunitrazepam in the brain of the living baboon. Comar D, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):21-6

Benzodiazepines suppress the light response of retinal dopaminergic neurons in vivo. Kamp CW, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):343-6

Absorption, distribution, elimination and metabolism of tofizopam, a new 2,3-benzodiazepine derivative, in animal experiments. Elekes I, et al. **Farmaco [Prat]** 1981 Dec;36(12):542-52

Quantitative determination of camazepam and its metabolite temazepam in man by gas-liquid chromatography with electron-capture detection. Riva R, et al. **Farmaco [Prat]** 1982 Jan;37(1):15-9

Analysis of the metabolites of ethyl loflazepate by gas chromatography with electron-capture detection. Cano JP, et al. **J Chromatogr** 1981 Dec 11;226(2):413-22

Assay of flunitrazepam, temazepam and desalkylflurazepam in plasma by capillary gas chromatography with electron-capture detection. Jochemsen R, et al. **J Chromatogr** 1982 Jan 8;227(1):199-206

High-performance liquid chromatographic determination of lorazepam in monkey plasma. Walmsley LM, et al. **J Chromatogr** 1981 Nov 13;226(1):155-63

Recent advances in anxiolytic therapy. Rickels K. **J Clin Psychiatry** 1981 Nov;42(11 Pt 2):40-4

Pharmacokinetic comparison of sublingual lorazepam with intravenous, intramuscular, and oral lorazepam. Greenblatt DJ, et al. **J Pharm Sci** 1982 Feb;71(2):248-52

Benzodiazepine inhibition of site-specific binding of nitrobenzylthioinosine, an inhibitor of adenosine transport. Hammond JR, et al. **Life Sci** 1981 Nov 23;29(21):2207-14

Anxiolytic properties of opiates and endogenous opioid peptides and their relationship to the actions of benzodiazepines. Millan MJ, et al. **Mod Probl Pharmacopsychiatry** 1981;17:123-41

The drug treatment of anxiety. Rosenbaum JF. **N Engl J Med** 1982 Feb 18;306(7):401-4 (24 ref.)

Benzodiazepines: clinical use patterns. Rickels K. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(33):43-60

A circadian rhythm in passive avoidance behavior: the effect of phase shift and the benzodiazepines. Childs G, et al. **Neuropharmacology** 1981 Dec;20(12B):1365-6

Effect of benzodiazepines on cyclic GMP formation in rat cerebellar slices. Smith CC, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):29-33

Self-injection of barbiturates and benzodiazepines in baboons. Griffiths RR, et al. **Psychopharmacology (Berlin)** 1981;75(2):101-9

Effect of age and sex on disposition of desmethyldiazepam formed from its precursor clorazepate. Shader RI, et al. **Psychopharmacology (Berlin)** 1981;75(2):193-7

GLC-ECD determination of 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1,3-dihydro-5-(O-fluorophe (SAS 643) in plasma and urine and identification of its main biotransformation products. Mardente S, et al. **Ther Drug Monit** 1981;3(4):351-6

Quantitative EEG and behavioral effects in volunteers of a new benzodiazepine (SAS 643) in relation to drug plasma concentration. Sannita WG, et al. **Ther Drug Monit** 1981;3(4):341-9

[Lorazepam. Evaluation after extensive use] Fouks L. **Agressologie** 1981 Oct;22(C):51-3 (Fre)

[Comparative study of the hypnogenic effect of bromazepam and flunitrazepam] Porot M, et al. **Ann Med Psychol (Paris)** 1981;139(8):919-23 (Fre)

[Relation between the clinical effect and the pharmacokinetics of midazolam following i.m. and i.v. administration/2nd comm.: Pharmacokinetical aspects (author's transl)] Crevoisier C, et al. **Arzneimittelforsch** 1981;31(12a):2211-5 (Eng. Abstr.) (Fre)

[Relationship between clinical effects and pharmacokinetics of midazolam on i.m. and i.v. application to volunteers/1st comm.: Clinical aspects (author's transl)] Ziegler WH, et al. **Arzneimittelforsch** 1981;31(12a):2206-10 (Eng. Abstr.) (Fre)

[Benzodiazepines as psycholeptica (author's transl)] Bouffioux R, et al. **Rev Med Brux** 1982 Jan;3(1):55-61 (Eng. Abstr.) (Fre)

[The antagonistic effect of physostigmine on sedation by lormetazepam (author's transl) Grote B, et al. **Anaesthesist** 1981 Dec;30(12):627-32 (Eng. Abstr.) (Ger)

[Intramuscular application of midazolam. Its effect upon CNS and respiration (author's transl)] Grote B, et al. **Arzneimittelforsch** 1981;31(12a):2224-5 (Eng. Abstr.) (Ger)

[Drug therapy of anxiety states] Laux G. **Krankenpfl J** 1982 Feb 15;20(2):22-4 (Ger)

[Comparative studies on the tranquilizer effect of fluspirilene and bromazepam] Thilmann J. **Med Welt** 1981 Dec 25;32(51-52):1959-61 (Ger)

[Clinical pharmacology of benzodiazepine tranquilizers] Janicki P, et al. **Pol Tyg Lek** 1981 Aug 24;36(34):1313-6 (Pol)

[Molecular mechanisms of the pharmacologic action of benzodiazepines] Korneev AIa, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):20-8 (Eng. Abstr.) (Rus)

[Physicochemical heterogeneity of the GABA receptors and the detection of the differences in their structural relation with benzodiazepine receptors] Korneev AIa, et al. **Zh Nevropatol Psikhiatr** 1981;81(11):1661-2 (Eng. Abstr.) (Rus)

BENZODIAZEPINONES

Clinical trial with clobazam. Kabes J, et al. **Agressologie** 1981 Oct;22(C):41-2

Subjective and psychometric assessment of effect in single application of clobazam. Molcan J, et al. **Agressologie** 1981 Oct;22(C):43-5

Antileptazol activity and kinetics of clobazam and N-desmethyl-clobazam in the guinea-pig. Ballabio M, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):192-9

Anthramycin binding to deoxyribonucleic acid-mitomycin C complexes. Evidence for drug-induced deoxyribonucleic acid conformational change and cooperativity in mitomycin C binding. Kaplan DJ, et al. **Biochemistry** 1981 Dec 22;20(26):7572-80

Clobazam kinetics in the elderly. Greenblatt DJ, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):631-6

Liquid chromatography of demoxepam and phenothiazines using a post-column photochemical reactor and fluorescence detection. Brinkman UA, et al. **J Chromatogr** 1981 Nov 6;217:463-71

Analysis of the metabolites of ethyl loflazepate by gas chromatography with electron-capture detection. Cano JP, et al. **J Chromatogr** 1981 Dec 11;226(2):413-22

Clobazam kinetics: intrasubject variability and effect of food on absorption. Divoll M, et al. **J Clin Pharmacol** 1982 Jan;22(1):69-73

Agonist and antagonist benzodiazepine receptor interaction in vitro. Möhler H, et al. **Nature** 1981 Dec 24;294(5843):763-5

Sympathetic Nerve Stimulation on the perfused rat heart. Affinities of N-methylatropine and pirenzepine at pre- and postsynaptic muscarine receptors. Fuder H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):210-9

Chronic clonazepam administration induces benzodiazepine receptor subsensitivity. Crawley JN, et al. **Neuropharmacology** 1982 Jan;21(1):85-9

Chronic benzodiazepine treatment increases [3H]muscimol binding in mouse brain. Marangos PJ, et al. **Neuropharmacology** 1982 Jan; 21(1):81-4

The effect of pirenzepine and L-hyoscyamine on gastric emptying and salivary secretion in healthy volunteers. Jaup BH, et al. **Scand J Gastroenterol** 1981;16(6):769-73

[Genetic differences in the anticonvulsant effect and rate of metabolism of phenazepam] Seredenin SB, et al. **Biull Eksp Biol Med** 1981 Oct; 91(10):450-3 (Eng. Abstr.) **(Rus)**

BIOGENIC AMINES

Cerebral monoamines and lidocaine toxicity in rats. Niederlehner JR, et al. **Anesthesiology** 1982 Mar;56(3):184-7

The effect of amine structure on complexation with lasalocid in model membrane systems. I. Identification of charged complexes in lipid bilayer membranes. Kinsel JF, et al. **Biochim Biophys Acta** 1982 Jan 22; 684(2):233-40

Distribution and activity of adrenergic and cholinergic innervation of the extrahepatic biliary system in the rabbit. Tessitore V, et al. **Cell Mol Biol** 1981;27(5):527-37

Stress-modulated alteration of brain biogenic amines in the rat: effects of L-tryptophan. Quirce CM, et al. **Commun Psychopharmacol** 1980; 4(5):371-7

Biogenic amines and beta-endorphin responses in the rat vas deferens. Miranda H, et al. **Gen Pharmacol** 1982;13(1):45-8

Selective effect of microembolization on pulmonary removal of biogenic amines. Flink JR, et al. **J Appl Physiol** 1982 Feb;52(2):421-7

Rapid and simple method for measuring biogenic amines and metabolites in brain homogenates by HPLC-electrochemical detection. Zaczek R, et al. **J Neural Transm** 1982;53(1):1-5

Amine modulation of the neurogenic Limulus heart. Augustine GJ, et al. **J Neurobiol** 1982 Jan;13(1):61-74

Effect of motor and premotor cortex ablation on concentrations of amino acids, monoamines, and acetylcholine and on the ultrastructure in rat striatum. A confirmation of glutamate as the specific cortico-striatal transmitter. Hassler R, et al. **J Neurochem** 1982 Apr;38(4):1087-98

In vitro studies of 5, 10-methylenetetrahydrofolate reductase: inhibition by folate derivatives, folate antagonists, and monoamine derivatives. Hollinger JL, et al. **J Neurochem** 1982 Mar;38(3):638-42

Central mechanisms of fenfluramine and related anorectic drugs. Garattini S. **Jpn J Pharmacol** 1981;31 Suppl:29P-35P (26 ref.)

Persistent alteration of rat brain monoamine levels by carbon monoxide exposure: sex differences and behavioral correlation. Shellenberger MK. **Neurotoxicology (Park Forest II)** 1981 Nov;2(3):431-41

[Monoamines and endogenous depression. Biochemical and pharmacological aspects] Scuvée-Moreau J, et al. **Rev Med Liege** 1982 Jan 1;37(1):1-7 **(Fre)**

[Learning in rats with differing emotional responsiveness and its relation to brain monoamines] Gromova EA, et al. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec;31(6):1238-46 (Eng. Abstr.) **(Rus)**

BIPOLAR DISORDER

Lithium levels in the ejaculate, spermiogram and adjuvant psychopharmacological therapy. Kolomaznik M, et al. **Act Nerv Super (Praha)** 1981;23(4):275-6

Flupenthixol decanoate in recurrent manic-depressive illness. A comparison with lithium. Ahlfors UG, et al. **Acta Psychiatr Scand** 1981 Sep;64(3):226-37

Serum lithium concentrations around the clock with different treatment regimens and the diurnal variation of the renal lithium clearance. Lauritsen BJ, et al. **Acta Psychiatr Scand** 1981 Oct;64(4):314-9

Lithium kinetics in single daily dosing. Perry PJ, et al. **Acta Psychiatr Scand** 1981 Oct;64(4):281-94

The use of the antidepressant tradozone in outpatient psychiatric practice. Soucek K, et al. **Agressologie** 1981 Nov;22(D):27

Noradrenergic drugs and affective disorders [letter] Abensour P, et al. **Am J Psychiatry** 1982 Jan;139(1):142-3

Lithium and amino acids [letter] Goodnick PJ, et al. **Am J Psychiatry** 1982 Apr;139(4):538-9

Potentiation of antidepressant effects by L-triiodothyronine in tricyclic nonresponders. Goodwin FK, et al. **Am J Psychiatry** 1982 Jan; 139(1):34-8

Phenelzine treatment without switch to mania [letter] Keitner GI. **Am J Psychiatry** 1982 Mar;139(3):386

Persistent elevation of thyroid-stimulating hormone in women with bipolar affective disorder. O'Shanick GJ, et al. **Am J Psychiatry** 1982 Apr;139(4):513-4

Questions about combined lithium and haloperidol treatment [letter] Rudorfer MV, et al. **Am J Psychiatry** 1982 Apr;139(4):537-8

Mania responsive to lecithin in a 13-year-old girl. Schreier HA. **Am J Psychiatry** 1982 Jan;139(1):108-10

Therapeutic use of the tricyclic-induced switch in bipolar manic-depression. Waters BG, et al. **Am J Psychiatry** 1982 Feb; 139(2):245-6

Treatment of intractable rapid-cycling manic-depressive disorder with levothyroxine. Clinical observations. Stancer HC, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):311-2

A new method for the use of salivary lithium concentrations as an indicator of plasma lithium levels. Selinger D, et al. **Biol Psychiatry** 1982 Jan;17(1):99-102

Poor prophylactic lithium response due to antidepressants. Reginald D, et al. **Int Pharmacopsychiatry** 1981;16(2):124-8

Rapid cyclers and antidepressants. Tondo L, et al. **Int Pharmacopsychiatry** 1981;16(2):119-23

Eye tracking in patients with unipolar and bipolar affective disorders in remission. Iacono WG, et al. **J Abnorm Psychol** 1982 Feb; 91(1):35-44

Plasma GABA in affective illness. A preliminary investigation. Petty F, et al. **J Affective Disord** 1981 Dec;3(4):339-43

Unusual presentation of manic depressive disorder in adolescence. Rogeness GA, et al. **J Clin Psychiatry** 1982 Jan;43(1):37-9

Adverse effects of lithium therapy in the acutely ill elderly patient. Smith RE, et al. **J Clin Psychiatry** 1981 Mar;43(3):94-9

Reduction of vanadate, a possible explanation of the effect of phenothiazines in manic-depressive psychosis [letter] Naylor GG, et al. **Lancet** 1982 Feb 13;1(8268):395-6

beta-Endorphin studies in psychiatric patients. Gorelick DA, et al. **Mod Probl Pharmacopsychiatry** 1981;17:236-45

Establishing lithium clinics in office practice. Hasan MK, et al. **Postgrad Med** 1982 Feb;71(2):182, 186, 190

The psychobiology of depressive disorders: from pathophysiology to predisposition. Depue RA, et al. **Prog Exp Pers Res** 1981;10:1-114 (436 ref.)

Course and relationship of lithium side effects to plasma lithium levels. Peselow ED, et al. **Psychiatr Clin (Basel)** 1981;14(3):178-83

Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Phillips RH. **Psychosomatics** 1982 Jan;23(1):81-7

BRADYKININ

Chemoreceptors for serotonin (5-HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma-aminobutyric acid (GABA) on rabbit visceral afferent neurons. Higashi H, et al. **Brain Res Bull** 1982 Jan; 8(1):23-32

Use of 125I-labeled human serum albumin for quantitation of microvascular permeability in rat skin: reevaluation of an old method for studies on substances with an enhancing effect on microvascular permeability. Gerdin B. **J Pharmacol Methods** 1981 Nov;6(3):167-75

BUTYLAMINES

Histamine release from human basophils and isolated rat mast cells induced by ketobemidone, pethidine and the spasmolytic A29. Grosman N. **Acta Pharmacol Toxicol (Copenh)** 1982 Jan;50(1):78-80

BUTYROPHENONE TRANQUILIZERS

Development of tolerance to the stimulatory effect of neuroleptic butyrophenones on pituitary-adrenal activity in rats. Aimoto T, et al. **J Pharmacobiodyn** 1981 Nov;4(11):827-32

Disposition of timiperone, 4'-fluoro-4-[4-(2-thioxo-1-benzimidazolinyl)piperidino]butyrophenone, a neuroleptic, in the rat on repeated oral dosage. Sudo K, et al. **Xenobiotica** 1981 Oct;11(10):685-91

BUTYROPHENONES

Systemic absorption of ketocaine following epicutaneous administration. Berlin-Wahlén A, et al. **Acta Pharm Suec** 1981;18(3):113-8

Irreversible blockade of [3H]spiperone- but not [3H]dopamine-labeled dopamine receptors with phenoxybenzamine. Titeler M. **Biochem Pharmacol** 1981 Nov 15;30(22):3031-7

Opposed stages of continuous amphetamine administration: parallel alterations in motor stereotypies and in vivo spiroperidol accumulation. Ellison G, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):207-14

Inhibitory effects of ascorbic acid on the binding of [3H]dopamine antagonists to neostriatal membrane preparations: relationship to lipid peroxidation. Heikkila RE, et al. **J Neurochem** 1982 Apr; 38(4):1000-6

Ontogenetic development of the striatal [3H]spiperone binding: regulation by sodium and guanine nucleotide in rats. Nomura Y, et al. **J Neurochem** 1982 Apr;38(4):902-8

Solubilization and characterization of 3H-spiroperidol binding sites of calf caudate. Lerner MH, et al. **Life Sci** 1981 Dec 7;29(23):2367-74

Are striatal [3H]spiperone radioreceptor assays indicative of multiple dopamine receptor interactions? Clements-Jewery S, et al. **Neuropharmacology** 1981 Dec;20(12B):1295-8

Suppression of drinking and induction of sedation by a dopamine agonist is blocked by small doses of spiperone. Dourish CT, et al. **Neuropharmacology** 1982 Jan;21(1):69-72

Dopaminergic agonistic and antagonistic drugs in the ventral tegmentum of rats inhibit and facilitate changes of food-search behaviour. Oude

RD. **Neurosci Lett** 1981 Nov 18;27(1):75-80

Disposition of timiperone, 4'-fluoro-4-[4-(2-thioxo-1-benzimidazolinyl)piperidino]butyrophenon a neuroleptic, in the rat on repeated oral dosage. Sudo K, et al. **Xenobiotica** 1981 Oct;11(10):685-91

CARBAMAZEPINE

Stability of extemporaneous suspensions of carbamazepine. Burckart GJ, et al. **Am J Hosp Pharm** 1981 Dec;38(12):1929-31

Carbamazepine treatment of selected affectively disordered inpatients. Folks DG, et al. **Am J Psychiatry** 1982 Jan;139(1):115-7

Improved isocratic liquid-chromatographic simultaneous measurement of phenytoin, phenobarbital, primidone, carbamazepine, ethosuximide, and N-desmethylmethsuximide in serum. Szabo GK, et al. **Clin Chem** 1982 Jan;28(1):100-4

Severe carbamazepine poisoning. Rockoff S, et al. **Clin Toxicol** 1981 Aug;18(8):935-9

Metabolism of carbamazepine and its epoxide metabolite in human and rat liver in vitro. Tybring G, et al. **Drug Metab Dispos** 1981 Nov-Dec;9(6):561-4

Brain uptake of carbamazepine in the cat. Monaco F, et al. **Epilepsia** 1982 Feb;23(1):19-22

Preliminary study of the effects of carbamazepine on congenital orofacial defects in offspring of A/J mice. Wray SD, et al. **Epilepsia** 1982 Feb;23(1):101-10

The formation of carbamazepine epoxide by rat liver microsomes: an investigation of the biphasic kinetic profile. van Boxtel CJ, et al. **Life Sci** 1981 Dec 21;29(25):2575-84

Acute carbamazepine toxicity resulting from overdose [letter] Lawless L, et al. **Neurology (NY)** 1982 Mar;32(3):328-9

Erythromycin-carbamazepine interaction? [letter] Straughan J. **S Afr Med J** 1982 Mar 20;61(12):420-1

CARBIMAZOLE

Thyroid proliferation, body weight, thyrotropin and thyroid hormones in chronic antithyroid (carbimazole) treatment in rats. Redmond O, et al. **J Anat** 1981 Aug;133(Pt 1):37-47

CATECHOL ESTROGENS

Catecholestrogens and release of anterior pituitary glend hormones. II. Prolactin. Rodriguez-Sierra JF, et al. **Endocrinology** 1982 Feb;110(2):325-9

Catecholestrogens and release of anterior pituitary gland hormones. I. Luteinizing hormone. Rodriguez-Sierra JF, et al. **Endocrinology** 1982 Feb;110(2):318-24

Interactions of catecholestrogens with cytoplasmic and nuclear estrogen receptors in rat pituitary gland and hypothalamus. Kirchhoff J, et al. **J Neurochem** 1981 Dec;37(6):1540-7

Temporal and other effects of catechol estrogens on prolactin secretion in the rat. Shin SH, et al. **Neuroendocrinology** 1981 Dec;33(6):352-7

CATECHOLAMINES

Operant behaviour of rats after aminophylline and DH-ergotoxin in interaction with catecholamines. Tikal K. **Act Nerv Super (Praha)** 1981;23(4):319-20

Effect of manganese on synthesis of brain catecholamines in growing rats. Chandra SV, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Apr;48(4):349-54

Role of some biogenic amines in the pathomechanism of glomerulonephritis. I. Histological examinations of kidneys in acute and chronic serum sickness in rabbits. Szajner-Milart I, et al. **Acta Physiol Pol** 1981;32(4):349-62

Fetal lung maturation: amniotic fluid catecholamines, phospholipids, and cortisol. Divers WA, et al. **Am J Obstet Gynecol** 1982 Feb 15;142(4):440-4

Comparison of dopamine and dobutamine following coronary artery bypass grafting. Salomon NW, et al. **Ann Thorac Surg** 1982 Jan;33(1):48-54

Urinary excretion of catecholamines in the night monkey (Aotus trivirgatus) (Primates, Cebidae). Peyrin L, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):345-56

The involvement of the catecholaminergic system in physostigmine-induced hyperactivity in rats. Egbe PC. **Arzneimittelforsch** 1982;32(1):27-9

The effect of PEA on serotonin and catecholamines. Widelitz MM, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):1107-11

Potent inhibition of diamine oxidase with the hydroxybenzyloxamines NSD-1039, NSD-1531 and NSD-1024. Gaugas JM. **Biochem Pharmacol** 1981 Nov 15;30(22):3121-2

Ionophore mediated catecholamine release from chromaffin granules. Comparison of X-537 A and X-14547 A effects. Scherman D, et al. **Biochem Pharmacol** 1981 Dec 15;30(24):3277-83

Further studies on the effects of intravenously administered 6-hydroxydopamine on the median eminence of the rat. Smith GC, et al. **Brain Res** 1982 Feb 18;234(1):101-10

The effects of catecholamines on hemorrhagic shock in dogs. Sakahira K, et al. **Bull Tokyo Med Dent Univ** 1981 Dec;28(4):125-34

Work as a correlate of canine left ventricular oxygen consumption, and the problem of catecholamine oxygen wasting. Rooke GA, et al. **Circ Res** 1982 Feb;50(2):273-86

Variations in plasma and adrenal catecholamines and related enzymes in isolated-aggressive mice. Tizabi Y, et al. **Commun Psychopharmacol** 1980;4(5):433-9

Neurochemical and behavioural correlates of the interaction between amphetamine and delta 9-tetrahydrocannabinol in the rat. Lew EO, et al. **Drug Alcohol Depend** 1981 Sep;8(2):93-101

The role of catecholamines in the regulation of pituitary luteinizing hormone and follicle-stimulating hormone secretion. Barraclough CA, et al. **Endocr Rev** 1982 Winter;3(1):91-119 (268 ref.)

Distribution of catecholamines and serotonin in 17 portions of rat ventromedial nucleus and effect of acute immobilization stress. Kiss A, et al. **Endocrinol Exp (Bratisl)** 1981 Dec;15(4):219-28

Guanine nucleotide and magnesium ion regulation of the interaction of gonadotropic and beta-adrenergic receptors with their hormones: a comparative study using a single membrane system. Abramowitz J, et al. **Endocrinology** 1982 Feb;110(2):336-46

Effects of catecholamines on plasma free fatty acids in fed and fasted cattle. Blum JW, et al. **Endocrinology** 1982 Feb;110(2):452-6

Inhibition of the enzymatic degradation of Met-enkephalin by catecholamines. Caffrey JL, et al. **Endocrinology** 1982 Jan;110(1):291-3

A sex difference in the activation of hypothalamic catecholaminergic and luteinizing hormone-releasing hormone peptidergic neurons after acute castration. DePaolo LV, et al. **Endocrinology** 1982 Feb;110(2):531-9

Alterations of brown adipose tissue in genetically obese (ob/ob) mice. I. Demonstration of loss of metabolic response to nerve stimulation and catecholamines and its partial recovery after fasting or cold adaptation. Seydoux J, et al. **Endocrinology** 1982 Feb;110(2):432-8

Effects of catecholamines on circular and longitudinal uterine muscle of the rat. Chow EH, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):157-65

Excitability ot beta-endorphin, morphine and catecholamines of the vas deferens of the rat at different stages of development. Huidobro-Toro JP, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):115-8

Haemophilus influenzae induced loss of lung beta-adrenoceptor binding sites and modulation by changes in peripheral catecholaminergic input. Schreurs AJ, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):95-102

Agonistic actions of DPI (2-(3,4-dihydroxyphenylimino)-imidazolidine) on alpha-adrenoceptors and dopamine receptors. Woodman OL, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):11-9

Altered circadian rhythm of catecholamines in patients with apallic syndrome. Ratge D, et al. **Experientia** 1981 Nov 15;37(11):1207-9

The haloperidol effect on the histofluorescence in the caudate nucleus of the rat brain treated with agonistic and antagonistic acetylcholine compounds. Wawrzyniak M, et al. **Folia Histochem Cytochem (Krakow)** 1981;19(3):143-8

Fluorescence-displacement from the median eminence towards the arcuate nucleus at puberty. Marani E, et al. **Histochemistry** 1981;73(2):165-9

Free and conjugated catecholamines and metabolites in cat urine after hypoxia. Claustre J, et al. **J Appl Physiol** 1982 Feb;52(2):304-8

Micro high-performance liquid chromatographic system with micro precolumn and dual electrochemical detector for direct injection analysis of catecholamines in body fluids. Goto M, et al. **J Chromatogr** 1981 Nov 13;226(1):33-42

Automated measurement of catecholamines in urine, plasma and tissue homogenates by high-performance liquid chromatography with fluorometric detection. Mori K. **J Chromatogr** 1981 Nov 20;218:631-7

Cholinergic and catecholaminergic afferents to the olfactory bulb in the hamster: a neuroanatomical, biochemical, and histochemical investigation. Macrides F, et al. **J Comp Neurol** 1981 Dec 10;203(3):495-514

A modified glyoxylic acid-formaldehyde technique for histofluorescence of catecholamine-containing neurons in cryostat sections of the insect brain. Klemm N. **J Histochem Cytochem** 1982 Apr;30(4):398-400

Synthesis and adrenoceptor affinity of some highly polar beta-substituted catecholamines. Henkel JG, et al. **J Med Chem** 1981 Oct;24(10):1258-60

(alpha S)-erythro-alpha-methylepinephrine: preparation and stereoselective binding to adrenergic receptors in rat forebrain. Taylor CA Jr, et al. **J Med Chem** 1981 Oct;24(10):1261-3

Identification and localization of catecholamines in the nervous system of Limulus polyphemus. O'Connor EF, et al. **J Neurobiol** 1982 Jan;13(1):49-60

Quantitative ionophoresis of catecholamines using multibarrel carbon fibre microelectrodes. Armstrong-James M, et al. **J Neurosci Methods** 1981 Dec;4(4):385-406

The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. 2. Model experiments. Björklund A, et al. **J Neurosci Methods** 1980 Jun; 2(3):301-18

The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. I. A detailed account of the methodology for central nervous tissue using paraffin, cryostat or Vibratome sections. Lorén I, et al. **J Neurosci Methods** 1980 Jun;2(3):277-300

Mild zinc deficiency and undernutrition during the prenatal and postnatal periods in rats: effects on weight, food consumption, and brain catecholamine concentrations. Halas ES, et al. **J Nutr** 1982 Mar; 112(3):542-51

On the ability of domperidone to selectively inhibit catecholamine-induced relaxation of circular smooth muscle of guinea-pig stomach. Sahyoun HA, et al. **J Pharm Pharmacol** 1982 Jan; 34(1):27-33

Developmental changes in the accumulation of norepinephrine and the chronotropic effects of catecholamines in isolated rat atria as influenced by dietary lipid. Wince LC, et al. **J Pharmacol Exp Ther** 1982 Feb; 220(2):340-6

Compared efficacy of dobutamine and dopamine in association with calcium chloride on termination of cardiopulmonary bypass. d'Hollander A, et al. **J Thorac Cardiovasc Surg** 1982 Feb; 83(2):264-71

Dobutamine-induced facilitation of norepinephrine efflux from spiral strips of guinea pig pulmonary arteries. Goshima Y, et al. **Jpn J Pharmacol** 1981 Dec;31(6):1091-4

Electropharmacological actions of catecholamine in sympathetic ganglia. Multiple modes of actions to modulate the nicotinic transmission. Koketsu K. **Jpn J Pharmacol** 1981;31 Suppl:27P-28P

Calcium-dependent secretion of catecholamines from the perfused bovine adrenal medulla by sodium deprivation. Sorimachi M, et al. **Jpn J Physiol** 1981;31(5):753-56

Plasma free and sulfate conjugated catecholamine levels during acute physiological stimulation in man. Joyce DA, et al. **Life Sci** 1982 Feb 1;30(5):447-54

The effect of intracerebroventricular administration of catecholamines and their antagonists on rectal temperature of Mastomys natalensis. Shukla R, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec; 318(1):38-42

Catecholamine metabolism in rat brain. The role of neutral and acidic catechol metabolites. Thiede HM, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(1):29-35

Characterization of catecholamine binding sites in the rat brain. Agrawal AK, et al. **Neurotoxicology (Park Forest II)** 1981 Oct;2(2):365-71

The effect of angiotensin II infusion on plasma catecholamines in the conscious rabbit. Rowe BP, et al. **Proc Soc Exp Biol Med** 1981 Oct; 168(1):110-3

Catecholamines and the sodium pump in excitable cells. Phillis JW, et al. **Prog Neurobiol** 1981;17(3):141-84 (320 ref.)

CNS mediated inhibition of gastric secretion by bombesin: independence from interaction with brain catecholaminergic, and serotoninergic pathways and pituitary hormones. Taché Y, et al. **Regul Pept** 1982 Jan; 3(1):51-9

Valid evaluation of plasma catecholamines [letter] Triebig G. **Thorax** 1981 Nov;36(11):880

Identification of subcellular organelles involved in Ba2+- and Cd2+-induced adrenomedullary secretion. Shanbaky NM, et al. **Toxicol Appl Pharmacol** 1982 Jan;62(1):167-71

Cardiac output, vascular resistance and catecholamine release in hemorrhaged anephric dogs. Badder EM, et al. **Trans Am Soc Artif Intern Organs** 1981;27:330-5

[Elimination of urinary catecholamines and their metabolites after administration of atropine and of alpha and beta sympatholytics in healthy volunteers (author's transl)] Veselková A, et al. **Cas Lek Cesk** 1981;120(50):1533-6 (Eng. Abstr.) (Cze)

[Intensive physical training and its effect on the urine excretion of catecholamines and 17-OH corticoids during aerobic exercise on an ergometer (author's transl)] Veselková A, et al. **Cas Lek Cesk** 1982 Jan 22;121(3):71-3 (Eng. Abstr.) (Cze)

[Study of the catecholamines in the notochord of Anura Amphibia embryos. Its possible relationships with the adenyl-cyclase activity and the primordial germ cells migration (author's transl)] Raïs R, et al. **Arch Anat Microsc Morphol Exp** 1981;70(3):149-60 (Eng. Abstr.) (Fre)

[Cardiovascular and adrenal medullo-sympathetic reactions to acute tobacco poisoning] Dumas JP, et al. **C R Soc Biol (Paris)** 1981; 175(6):866-9 (Eng. Abstr.) (Fre)

[Neural origin and modulation by hypothalamic catecholamines of pulsatile secretion of luteinizing hormone in ovariectomized rats (author's transl)] Endo M. **Hokkaido Igaku Zasshi** 1981 Mar; 56(2):185-98 (Eng. Abstr.) (Jpn)

[Studies on catecholamine secretion from adrenal medulla—acetylcholine stimulation (author's transl)] Komiya E, et al. **Horumon To Rinsho** 1981 Aug;29(8):915-8 (Jpn)

[Urinary excretion of catecholamines by various age groups and plasma catecholamine concentrations measured by new radioenzymatic assay (author's transl)] Nakai T, et al. **Horumon To Rinsho** 1981 Aug; 29(8):909-14 (Jpn)

[Effects of diltiazem on catecholamine release from cat adrenal glands (author's transl)] Yamaguchi I, et al. **Nippon Yakurigaku Zasshi** 1981 Nov;78(5):501-9 (Eng. Abstr.) (Jpn)

[Determination of urinary catecholamine by high performance liquid chromatography (author's transl)] Tanabe T, et al. **Rinsho Byori** 1981 Sep;29(9):874-8 (Jpn)

[Changes in catecholamine concentration and myocardial contractility in focal cytotoxic lesions of the heart] Buriakov IE. **Fiziol Zh** 1981 Nov-Dec;27(6):780-5 (Eng. Abstr.) (Rus)

[Effect of damage to the superior cervical sympathetic ganglion in rabbits on microcirculation and catecholamine concentration in tissues of mucous membranes innervated by it] Dychko EN, et al. **Fiziol Zh** 1982 Jan-Feb;28(1):15-9 (Eng. Abstr.) (Rus)

[Changes in catecholamine excretion in adolescents at high altitudes] Nagnibeda NN, et al. **Fiziol Zh** 1982 Jan-Feb;28(1):91-2 (Rus)

[Effect of cold on catecholamine fluorescence in various rat brain structures] Vorodaevskaia GI. **Fiziol Zh** 1982 Jan-Feb;28(1):86-8 (Rus)

[Effect of electric stimulation of the stellate ganglion and inclusion of the adrenals on catecholamine concentration in the isolated heart] Barinov EF. **Fiziol Zh SSSR** 1981 Oct;67(10):1501-5 (Eng. Abstr.) (Rus)

[Comparative characteristics of the reactions of small intestine vessels to neurogenic influences and catecholamine application] Polenov SA, et al. **Fiziol Zh SSSR** 1981 Dec;67(12):1845-52 (Eng. Abstr.) (Rus)

[Catecholamine concentration of the blood of rats after a flight on the Cosmos-936 biosatellite] Kvetnianski R, et al. **Kosm Biol Aviakosm Med** 1982 Jan-Feb;16(1):80-3 (Eng. Abstr.) (Rus)

[Spectrofluorometric determination of catecholamines and dihydroxyphenylalanine in 1 sample] Sominskii VN, et al. **Lab Delo** 1982;(1):11-5 (Eng. Abstr.) (Rus)

[Catecholamine regulation of the liver and kidney ATPase activity in mice] Krut'ko BT. **Probl Endokrinol (Mosk)** 1982 Jan-Feb; 28(1):73-8 (Eng. Abstr.) (Rus)

[Nature of the catecholamine deficiency in the rat hypothalamus at lengthy periods after irradiation] Bazanova NV, et al. **Radiobiologiia** 1982 Jan-Feb;22(1):19-24 (Rus)

[Catecholamine excretion in chronic pyelonephritis] Tkachuk VN, et al. **Sov Med** 1982;(2):22-5 (Eng. Abstr.) (Rus)

[Catecholaminergic and serotoninergic systems in depression] Puzhin'skii S, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):66-8 (Eng. Abstr.) (Rus)

[Nature of urinary catecholamine excretion in the glossalgia syndrome] Dychko EN. **Vrach Delo** 1981 Dec;(12):93-5 (Rus)

[Psychological component of human stress (author's transl)] Vargas Fernández L. **Rev Med Chil** 1981 May;109(5):441-51 (Eng. Abstr.) (Spa)

CHILD BEHAVIOR DISORDERS

Treatment of childhood aggressivity with lithium. Vetro A, et al. **Agressologie** 1981 Nov;22(E):27-30

Biochemical differences in children with conduct disorder socialized and undersocialized. Rogeness GA, et al. **Am J Psychiatry** 1982 Mar; 139(3):307-11

CHLORDIAZEPOXIDE

Pimozide versus chlordiazepoxide in anxiety neurosis. Doongaji DR, et al. **Acta Psychiatr Belg** 1981 Jul-Aug;81(4):416-23

Adverse reactions to benzodiazepine-tricyclic antidepressant compound. Beresford TP, et al. **J Clin Psychopharmacol** 1981 Nov;1(6):392-4

Chronic benzodiazepine treatment increases [3H]muscimol binding in mouse brain. Marangos PJ, et al. **Neuropharmacology** 1982 Jan; 21(1):81-4

Evidence of a role for GABA in benzodiazepine effects on food preference in rats. Hodges HM, et al. **Psychopharmacology (Berlin)** 1981; 75(3):305-10

Effects of chronic chlordiazepoxide treatment on novel and familiar food preference in rats. Hodges HM, et al. **Psychopharmacology (Berlin)** 1981; 75(3):311-4

Chlordiazepoxide and resistance to punishment. Davis NM, et al. **Q J Exp Psychol [B]** 1981 Nov;33(Pt 4):227-39

P-CHLOROPHENYLALANINE

Effect of tryptophan administration on spontaneous and P-CPA-induced muricidal aggression in laboratory rats. Valzelli L, et al. **Pharmacol Res Commun** 1981 Oct;13(9):891-7

Effect of parachlorophenylalanine on the incidence of abnormal behaviors observed following diazepam withdrawal. Suzuki T, et al. **Prog Neuropsychopharmacol** 1981;5(4):415-7

CHLORPROMAZINE

Effect of chlorpromazine on the ultrastructure of Staphylococcus aureus. Kristiansen JE, et al. **Acta Pathol Microbiol Scand [B]** 1981 Dec; 89(6):399-405

Hydrolysis of sarcolemma by lysosomal lipases and inhibition by chlorpromazine. Beckman JK, et al. **Am J Physiol** 1982 Apr; 242(4):H652-6

A study on the effect of chlorpromazine and desipramine on the activity of some adrenal enzymes. Chan MY, et al. **Biochem Pharmacol** 1981 Dec 15;30(24):3365-7

Metabolism of chlorpromazine by pulmonary microsomal enzymes in the rat and rabbit. Ohmiya Y, et al. **Biochem Pharmacol** 1982 Jan 15; 31(2):157-62

Effect of chlorpromazine on isolated rat hepatocytes. Tsao SC, et al. **Biochem Pharmacol** 1982 Feb 15;31(4):491-7

Fluidity of human erythrocyte membrane and effect of chlorpromazine on fluidity and phase separation of membrane. Ogiso T, et al. **Biochim Biophys Acta** 1981 Dec 7;649(2):325-35

Divalent cations and chlorpromazine can induce non-bilayer structures in phosphatidic acid-containing model membranes. Verkleij AJ, et al. **Biochim Biophys Acta** 1982 Jan 22;684(2):255-62

Retinal amacrine cell system tyrosine hydroxylase: the development of responsiveness to light and neuroleptic drugs. Cohen J, et al. **Brain Res** 1982 Jan;255(1):160-3

The effect of long-term chlorpromazine and desipramine treatment on adrenal corticosterone, cyclic AMP, and cholesterol distribution in rats. Hung F, et al. **Clin Exp Pharmacol Physiol** 1981 Dec;8(6):567-74

Interaction of chlorpromazine and nortriptyline in patients with schizophrenia. Loga S, et al. **Clin Pharmacokinet** 1981 Nov-Dec; 6(6):454-62

Cigarette smoking and chlorpromazine disposition and actions. Pantuck EJ, et al. **Clin Pharmacol Ther** 1982 Apr;31(4):533-8

Actions of chlorpromazine metabolites on brain guanylate cyclase. Pajer KA, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):137-9

Simultaneous determination of chlorpromazine and levomepromazine in human plasma and urine by high-performance liquid chromatography using electrochemical detection. Murakami K, et al. **J Chromatogr** 1982 Jan 8;227(1):103-12

Pimozide versus chlorpromazine in chronic schizophrenia: a 52 week double-blind study of maintenance therapy. Wilson LG, et al. **J Clin Psychiatry** 1982 Feb;43(2):62-5

Effect of carboxylic acids on permeation of chlorpromazine through dimethyl polysiloxane membrane. Gasco MR, et al. **J Pharm Sci** 1982 Feb;71(2):239-41

Drug management in chronic schizophrenia. Tune LE, et al. **Johns Hopkins Med J** 1982 Jan;150(1):45-8

The influence of amitriptyline, imipramine and chlorpromazine on activity of arginase in rat's brain and liver. Grabowska-Hibner J, et al. **Mater Med Pol** 1981 Jan-Mar;13(1):54-7

Chlorpromazine reduces the perceptual ambiguity of a reversible visual figure. Harris JP, et al. **Neuropharmacology** 1981 Dec;20(12B):1337-8

Relationship between plasma-levels of chlorpromazine and effects on EEG and evoked potentials in healthy volunteers. Laurian S, et al. **Pharmacopsychiatria** 1981 Nov;14(6):199-204

Does a plasma level of chlorpromazine help? Van Putten T, et al. **Psychol Med** 1981 Nov;11(4):729-34

[Sensitivity of albino and black mice to various drugs chemically related to melanins] Zarach-Krutysza M. **Acta Pol Pharm** 1981;38(4):513-8 **(Pol)** (Eng. Abstr.)

CHOICE BEHAVIOR

The effect of intrahypothalamic serotonin reinforcement on directional preference in rats. Lesiecka M, et al. **Acta Neurobiol Exp (Warsz)** 1981; 41(5):439-46

CLOMIPRAMINE

On the clinical response/plasma level relationship for clomipramine [letter] Dutt JE. **Br J Psychiatry** 1982 Jan;140:105

Clomipramine and exposure for chronic obsessive-compulsive rituals: III. Two year follow-up and further findings. Mawson D, et al. **Br J Psychiatry** 1982 Jan;140:11-8

3-Chlorodibenzazepine binding to cholinergic receptors and ion channels. Aronstam RS, et al. **Res Commun Chem Pathol Pharmacol** 1981 Dec; 34(3):551-4

[Analysis of controlled studies comparing mianserin and clomipramine (author's transl)] de Buck RP. **Encephale** 1981;7(4 Suppl):455-72 (Eng. Abstr.) **(Fre)**

[Clomipramine and desmethylclomipramine: relationship between plasma levels and clinical effect (author's transl)] Vandel B, et al. **Encephale** 1981;7(5):601-8 (Eng. Abstr.) **(Fre)**

COCAINE

The use of diazepam and of cocaine in combination with other drugs by Los Angeles County probationers. Budd RD. **Am J Drug Alcohol Abuse** 1981;8(2):249-55

Fatalities from cocaine overdoses in Los Angeles County. Nakamura GR, et al. **Clin Toxicol** 1981 Aug;18(8):895-905

Origin of cocaine- and lidocaine-induced spindle activity within the olfactory forebrain of the rat. Stripling JS. **Electroencephalogr Clin Neurophysiol** 1982 Feb;53(2):208-19

Cocaine self-administration in humans. Fischman MW, et al. **Fed Proc** 1982 Feb;41(2):241-6

Cocaine effects on gingiva [letter] Dello Russo NM, et al. **J Am Dent Assoc** 1982 Jan;104(1):13

Binding of [3H]cocaine in mouse brain: kinetics and saturability. Reith ME, et al. **J Recept Res** 1981;2(3):233-43

Cocaine-induced supersensitivity of striatal dopamine receptors: role of endogenous calmodulin. Memo M, et al. **Neuropharmacology** 1981 Dec; 20(12A):1145-50

Comparative stimulus properties of two fractions of the coca leaf (E. coca). Bedford JA, et al. **Pharmacol Biochem Behav** 1981 Dec; 15(6):907-9

Reinstatement of cocaine-reinforced responding in the rat. de Wit H, et al. **Psychopharmacology (Berlin)** 1981;75(2):134-43

COGNITION

The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy, each alone and in combination. Blackburn IM, et al. **Br J Psychiatry** 1981 Sep;139:181-9

Cognitive therapy for depression [editorial] Goldberg D. **Br Med J [Clin Res]** 1982 Jan 16;284(6310):143-4

COGNITION DISORDERS

Pharmacological treatment of chronic cognitive deficit: a review. Dowson JH. **Compr Psychiatry** 1982 Jan-Feb;23(1):85-98

Altered circadian rhythm of catecholamines in patients with apallic syndrome. Ratge D, et al. **Experientia** 1981 Nov 15;37(11):1207-9

Vasopressin treatment of cognitive dysfunction in progressive dementia. Weingartner H, et al. **Life Sci** 1981 Dec 28;29(26):2721-6

COLOR PERCEPTION

Subjective colours and brain function. Shute CC. **Endeavour** 1981; 5(4):141-6

Digitalis toxicity mistaken for jaundice. Dickstein ES. **Geriatrics** 1982 Apr;37(4):133, 137-8

Phencyclidine discrimination in the pigeon using color tracking under second-order schedule. McMillan DE, et al. **J Exp Anal Behav** 1982 Jan;37(1):143-7

CONCEPT FORMATION

Effects of chemicals on delayed matching behavior in pigeons I: acute effects of drugs. McMillan DE. **Neurotoxicology (Park Forest II)** 1981 Nov;2(3):485-98

CONDITIONING (PSYCHOLOGY)

Pimozide attenuates conditioned taste preferences induced by self-stimulation in rats. Ettenberg A, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):915-9

Endogenous corticosterone alterations and appetitive learning in the rat. O'Reilly HM, et al. **Physiol Behav** 1981 Sep;27(3):515-22

CONDITIONING, CLASSICAL

Piribedil-induced anti-hypoxic protection in rats. Saligaut C, et al. **Aviat Space Environ Med** 1982 Jan;53(1):35-9

Role of cholinergic and monoaminergic brain systems in dissociated learning. Arkhipov VI, et al. **Neurosci Behav Physiol** 1981 May-Jun; 11(3):226-9

Correlation between retention of defensive conditioned reflexes and brain acetylcholinesterase activity in rats. Dish TN. **Neurosci Behav Physiol** 1981 May-Jun;11(3):230-3

Effect of serotonin injected into the amygdala on conditioned and unconditioned food reflexes and the EEG in cats. Gasanov GG, et al. **Neurosci Behav Physiol** 1981 May-Jun;11(3):207-12

Effect of serotonin on formation and fixation of various conditioned reflexes. Getsova VM. **Neurosci Behav Physiol** 1981 May-Jun; 11(3):280-5

Analog of a conditioned reflex of sensomotor cortical units following microinjection of acetylcholine. Kopytova FV, et al. **Neurosci Behav Physiol** 1981 May-Jun;11(3):213-20

Effects of bilateral amygdala lesions on neophobia and conditioned taste aversion in mice. Shimai S, et al. **Percept Mot Skills** 1982 Feb; 54(1):127-30

[Binding of 3H-diazepam by cerebral cortex synaptic membranes in the rat during conditioned reflex elaboration] Korotkov KO, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):695-6 (Eng. Abstr.) **(Rus)**

[Effect of high doses of phenamine on instrumental defensive reflexes in intact and striatectomized rats] Baturin VA. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec;31(6):1305-7 (Rus)

CONDITIONING, OPERANT

Operant behaviour of rats after aminophylline and DH-ergotoxin in interaction with catecholamines. Tikal K. **Act Nerv Super (Praha)** 1981; 23(4):319-20

The effects of 2,5-dimethoxy-4-methylamphetamine (DOM) on operant behavior: interactions with other neuroactive agents. Commissaris RL, et al. **Commun Psychopharmacol** 1980;4(5):393-404

Unlimited access intravenous drug self-administration in rhesus monkeys. Balster RL, et al. **Fed Proc** 1982 Feb;41(2):211-5

Drugs as reinforcers in animals and humans: introduction. Balster RL, et al. **Fed Proc** 1982 Feb;41(2):209-10

Operant thermoregulation of rats with anterior hypothalamic lesions. Schulze G, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec; 318(1):43-8

Antagonism by methysergide of the effects of L-5-hydroxytryptophan and quipazine on schedule-controlled responding. Leander JD. **Neuropharmacology** 1981 Dec;20(12A):1141-3

Comparative stimulus properties of two fractions of the coca leaf (E. coca). Bedford JA, et al. **Pharmacol Biochem Behav** 1981 Dec; 15(6):907-9

Phencyclidine in combination with pentobarbital: supra-additive effects on complex operant behavior in patas monkeys. Thompson DM, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):159-65

A comparison of some behavioural effects of amphetamine and electrical brain stimulation of the mesolimbic dopamine system in rats. D'Mello GD. **Psychopharmacology (Berlin)** 1981;75(2):184-92

Two opposite effects of diazepam on fear by differential training in the CER-paradigm. Haug T, et al. **Psychopharmacology (Berlin)** 1981; 75(2):110-3

Chlordiazepoxide and resistance to punishment. Davis NM, et al. **Q J Exp Psychol [B]** 1981 Nov;33(Pt 4):227-39

[Effects of afloqualone, a new centrally acting muscle relaxant, on DRL response and CER in rats (author's transl)] Yamamura M, et al. **Nippon Yakurigaku Zasshi** 1981 Oct;78(4):381-92 (Eng. Abstr.) (Jpn)

[Effects of piracetam in healthy dogs and dogs with experimental neuroses] Airapetiants MG, et al. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec; 31(6):1164-70 (Eng. Abstr.) (Rus)

CONFLICT (PSYCHOLOGY)

Sodium valproate exerts anti-conflict activity in rats without any concomitant rise in forebrain GABA level. Rasmussen KJ, et al. **Life Sci** 1981 Nov 23;29(21):2163-70

A water lick conflict paradigm using drug experienced rats. Petersen EN, et al. **Psychopharmacology (Berlin)** 1981;75(3):236-9

CORTICOSTERONE

Conformation-activity relationships of corticotropin segments. Löw M, et al. **Acta Biochim Biophys Acad Sci Hung** 1981;16(1-2):105-8

Glucose and endocrine responses to hypothalamic electrical stimulation in rats. Dubuc PU, et al. **Am J Physiol** 1982 Mar;242(3):R220-6

Effects of petroleum on adrenocortical activity and on hepatic naphthalene-metabolizing activity in mallard ducks. Gorsline J, et al. **Arch Environ Contam Toxicol** 1981 Nov;10(6):765-77

Effect of corticosterone on the urinary output of Nt-methylhistidine in mature male rats. Santidrián S. **Arch Farmacol Toxicol** 1981 Aug; 7(2):283-8

Inhibition of collagen and sulfated glycosaminoglycan synthesis in neonatal mouse dermal fibroblasts by corticosterone. Verbruggen LA, et al. **Biochem Pharmacol** 1981 Dec 15;30(24):3285-9

The effect of the administration of the adrenocorticotrophic hormone to rats on in vivo steroidogenesis and on the reduction cytochrome P-450 in adrenal mitochondria. Koritz SB. **Biochim Biophys Acta** 1982 Feb 2;714(2):382-5

The effect of long-term chlorpromazine and desipramine treatment on adrenal corticosterone, cyclic AMP, and cholesterol distribution in rats. Hung F, et al. **Clin Exp Pharmacol Physiol** 1981 Dec;8(6):567-74

Glucocorticoid regulation of alpha-lactalbumin production in long-term cultures of normal rat mammary cells. Ray DB, et al. **Endocr Res Commun** 1981;8(3):165-78

Stress-induced inhibition of the plasma corticosterone response to a subsequent stress in rats: a nonadrenocorticotropin-mediated mechanism. De Souza EB, et al. **Endocrinology** 1982 Jan; 110(1):23-33

In vivo corticotropin-releasing factor-induced secretion of adrenocorticotropin, beta-endorphin, and corticosterone. Rivier C, et al. **Endocrinology** 1982 Jan;110(1):272-8

Dopaminergic modulation of aldosterone secretion in the rhesus monkey: evidence that dopamine affects the late pathway of aldosterone biosynthesis by inhibiting the conversion of corticosterone to 18-hydroxycorticosterone. Sowers JR, et al. **Endocrinology** 1982 Apr; 110(4):1173-7

Adrenal steroid-induced changes in beta-adrenergic receptor binding in rat hippocampus. Roberts DC, et al. **Eur J Pharmacol** 1981 Aug 27; 74(1):37-41

Sexual differentiation of hepatic metabolism of corticosterone and testosterone in the rat. Rahman R, et al. **J Biochem (Tokyo)** 1981 Dec; 90(6):1567-75

Effect of corticosterone on serum concentrations of alpha 2 micro-globulin and on spermatogenesis in oestrogen-treated rats. [illegible] NM, et al. **J Endocrinol** 1982 Feb;92(2):309-14

Effects of an intermittent lighting schedule on the time of egg-laying and the levels of luteinizing hormone, progesterone and corticosterone in the plasma of the domestic hen. Duplaix M, et al. **J Endocrinol** 1981 Dec;91(3):375-83

Subcellular compartmentation of steroidogenesis in the zona fasciculata/reticularis of the rat adrenal cortex. McCredie E, et al. **J Steroid Biochem** 1981 Dec;14(12):1269-77

Beta-adrenergic stimulation induces an increase of the plasma levels of immunoreactive alpha-MSH, beta-endorphin, ACTH and of corticosterone. Berkenbosch F, et al. **Life Sci** 1981 Nov 30; 29(22):2249-56

On the interactive role of central noradrenaline neurons and corticosterone in two-way active avoidance acquisition in the rat. Archer T, et al. **Neurosci Lett** 1981 Dec 23;27(3):341-6

Arginine vasotocin: effects on open field behavior, whole brain monoamines and plasma corticosterone. Golus P, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):437-40

Repeated administration of pergolide to rats attenuates the acute elevation of serum corticosterone by pergolide. Fuller RW, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):933-6

Endogenous corticosterone alterations and appetitive learning in the rat. O'Reilly HM, et al. **Physiol Behav** 1981 Sep;27(3):513-22

Behavioral and corticosterone effects in conditioned taste aversion following hippocampal lesions. Smotherman WP, et al. **Physiol Behav** 1981 Oct;27(4):569-74

Diurnal patterns of food intake and plasma corticosterone levels in lactating rats. Tachi N, et al. **Physiol Behav** 1981 Sep;27(3):481-6

Changes in corticosterone levels in iron deficient rats. Williamson AM, et al. **Physiol Behav** 1981 Dec;27(6):1085-8

Hyperprolactinemia and hyperadrenocorticism accompanied by normal blood pressure in Sprague-Dawley rats. McMurtry JP, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):114-8

Effect of corticosterone, hydrocortisone and prostaglandin fatty acid precursors on the spontaneous motility of the uterus isolated from ovariectomized rats. Bonacossa A, et al. **Prostaglandins** 1982 Jan; 23(1):113-28

[Effects of the destruction of the suprachiasmatic nuclei on the circadian rhythms of ACTH corticosterone and the general activity of female rats exposed to a aperiodic environment] Szafarczyk A, et al. **C R Soc Biol (Paris)** 1981;175(6):801-10 (Eng. Abstr.) (Fre)

[Effect of arginine vasotocin, oxytocin and their fragments on the corticosterone content in the blood plasma of chickens of different ages] Sirotkin AV, et al. **Fiziol Zh SSSR** 1982 Jan;68(1):112-5 (Eng. Abstr.) (Rus)

CORTICOTROPIN

Conformation-activity relationships of corticotropin segments. Löw M, et al. **Acta Biochim Biophys Acad Sci Hung** 1981;16(1-2):105-8

The effect of ACTH stimulation on plasma steroids in two patients with congenital hypoaldosteronism and in their relatives. Drop SL, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):245-50

Effects of ACTH on the zona glomerulosa of sodium-loaded timolol maleate-treated rats: stereology and plasma hormone concentrations. Nussdorfer GG, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):256-62

The effect of the administration of the adrenocorticotrophic hormone to rats on in vivo steroidogenesis and on the reduction cytochrome P-450 in adrenal mitochondria. Koritz SB. **Biochim Biophys Acta** 1982 Feb 2;714(2):382-5

ACTH 1-24 and lysine vasopressin selectively activate dopamine synthesis in frontal cortex. Delanoy RL, et al. **Brain Res** 1982 Jan 7; 231(1):117-29

Changes in corticotropic responsiveness and mitochondrial ultrastructure of adrenocortical cells from the inner zone of the duck (Anas platyrhynchos) adrenal gland: the effects of cycloheximide, puromycin, and chloramphenicol. Pearce RB, et al. **Cell Tissue Res** 1981; 221(1):45-57

Stress-induced inhibition of the plasma corticosterone response to a subsequent stress in rats: a nonadrenocorticotropin-mediated mechanism. De Souza EB, et al. **Endocrinology** 1982 Jan; 110(1):23-33

Specific inhibition by glucocorticoids of the alpha 2-adrenergic stimulation of adrenocorticotropin release in rat anterior pituitary cells. Giguère V, et al. **Endocrinology** 1982 Apr;110(4):1225-30

Characterization of an early inhibitory effect of glucocorticoids on stimulated adrenocorticotropin and endorphin release from a clonal ain of mouse pituitary cells. Phillips M, et al. **Endocrinology** 1982 Mar;110(3):892-900

In vivo corticotropin-releasing factor-induced secretion of adrenocorticotropin, beta-endorphin, and corticosterone. Rivier C, et al. **Endocrinology** 1982 Jan;110(1):272-8

Adrenergic mechanisms involved in the control of pituitary-adrenal activity in the rat: a beta-adrenergic stimulatory mechanism. Tilders FJ, et al. **Endocrinology** 1982 Jan;110(1):114-20

Biosynthesis of pairs of peptides related to melanotropin, corticotropin and endorphin in the pars intermedia of the amphibian pituitary gland. Martens GJ, et al. **Eur J Biochem** 1982 Feb;122(1):1-10

ACTH1-24 counteracts the prolactin-releasing effect of an opioid. Ferri S, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):143-5

ACTH1-24 increases stimulation-evoked noradrenaline release from sympathetic nerves by acting on presynaptic ACTH receptors. Göthert M. **Eur J Pharmacol** 1981 Dec 3;76(2-3):295-6

A quantitative approach to trace the corticotrophs in culture after adrenalectomy. Kappay G, et al. **Histochemistry** 1981;73(1):131-6

Lipolytic and enkephalinase inhibitory activities of polypeptides from placental autolysate prepared for therapeutic purposes. Nencini P, et al. **Int J Tissue React** 1981 Dec;3(3-4):167-72

Presence of immunoreactive gamma-melanocyte-stimulating hormone, adrenocorticotropin, and beta-endorphin in human gastric antral mucosa. Tanaka I, et al. **J Clin Endocrinol Metab** 1982 Feb;54(2):392-6

Effect of cortisol or adrenocorticotrophin on release of luteinizing hormone induced by luteinizing hormone releasing hormone in the dairy heifer. Matteri RL, et al. **J Endocrinol** 1982 Jan;92(1):141-6

Beta-adrenergic stimulation induces an increase of the plasma levels of immunoreactive alpha-MSH, beta-endorphin, ACTH and of corticosterone. Berkenbosch F, et al. **Life Sci** 1981 Nov 30;29(22):2249-56

Influence of adrenocorticotropin and adrenalectomy on gonadotropin secretion in immature rats. Mann DR, et al. **Neuroendocrinology** 1982 Jan;34(1):20-6

Evidence that the effects of 5-hydroxytryptophan on the secretion of ACTH and growth hormone in dogs are not mediated by central release of serotonin. Zimmermann H, et al. **Neuroendocrinology** 1982 Jan;34(1):27-31

In vivo and in vitro release of ACTH by synthetic CRF. Turkelson CM, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):425-9

Digoxin-like immunoreactivity of certain steroid and other hormones. Schreiber V, et al. **Physiol Bohemoslov** 1981;30(6):569-71

Human lymphocyte production of corticotropin and endorphin-like substances: association with leukocyte interferon. Smith EM, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7530-4

Running elevates plasma beta-endorphin immunoreactivity and ACTH in untrained human subjects. Gambert SR, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):1-4

[Effects of the destruction of the suprachiasmatic nuclei on the circadian rhythms of ACTH corticosterone and the general activity of female rats exposed to a aperiodic environment] Szafarczyk A, et al. **C R Soc Biol (Paris)** 1981;175(6):801-10 (Eng. Abstr.) **(Fre)**

[Effect of allopurinol on the liberation of free fatty acids from isolated rat and rabbit adipose tissue, stimulated by noradrenaline or adrenocortico-tropic hormone] Sziegoleit W, et al. **Acta Biol Med Ger** 1981;40(6):881-3 **(Ger)**

CORTICOTROPIN RELEASING HORMONE

In vivo corticotropin-releasing factor-induced secretion of adrenocorticotropin, beta-endorphin, and corticosterone. Rivier C, et al. **Endocrinology** 1982 Jan;110(1):272-8

Corticotropin-releasing factor: effects on the sympathetic nervous system and oxygen consumption. Brown MR, et al. **Life Sci** 1982 Jan 11;30(2):207-10

Distribution and characterization of corticotropin-releasing factor and arginine vasopressin in rat hypothalamic nuclei. Hashimoto K, et al. **Neuroendocrinology** 1982 Jan;34(1):32-7

In vivo and in vitro release of ACTH by synthetic CRF. Turkelson CM, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):425-9

CREATIVENESS

Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Phillips RH. **Psychosomatics** 1982 Jan;23(1):81-7

CROSS-CULTURAL COMPARISON

A cross-national comparison of patterns of utilization and psychiatric care. Erinosho OA, et al. **Int J Soc Psychiatry** 1981 Winter;27(4):289-96

Cross-cultural study of a biochemical abnormality in paranoid schizophrenia. Jeste DV, et al. **Psychiatry Res** 1981 Dec;5(3):341-52

DANSYL COMPOUNDS

The effect of occlusive treatment on human skin: an electron microscopic study on epidermal morphology as affected by occlusion and dansyl chloride. Lindberg M, et al. **Acta Derm Venereol (Stockh)** 1982;62(1):1-5

5-(dimethylamino)naphthalene-1-sulfonic acid, a fluorescent probe of the medium chain fatty acid binding site of serum albumin. Doody MC, et al. **Biochemistry** 1982 Jan 5;21(1):28-33

Interaction of alpha-dansylated peptide inhibitors with porcine pepsin: detection of complex formation by fluorescence energy transfer and chromatography and evidence for a two-step binding scheme. Dunn BM, et al. **Biochemistry** 1981 Dec 8;20(25):7206-11

Cycloheptaamylose-dansyl chloride complex as a fluorescent label of surface membranes in living ciliates. Wyroba E, et al. **Histochemistry** 1981 Dec;73(3):459-67

Dansyl chloride labeling of Pseudomonas aeruginosa treated with pyocin R1: change in permeability of the cell envelope. Uratani Y. **J Bacteriol** 1982 Feb;149(2):523-8

DEMENTIA

Vasopressin treatment of cognitive dysfunction in progressive dementia. Weingartner H, et al. **Life Sci** 1981 Dec 28;29(26):2721-6

DEPRESSION

Amoxapine, an observation, and a perspective on MAOIs and their safety [editorial] Shader RI, et al. **J Clin Psychopharmacol** 1981 Sep;1(5):263

Alpha 2 adrenergic receptors in depression [editorial] **Lancet** 1982 Apr 3;1(8275):781

beta-Endorphin studies in psychiatric patients. Gorelick DA, et al. **Mod Probl Pharmacopsychiatry** 1981;17:236-45

[Therapy of anorexia nervosa aimed at depressive manifestations] Kadlecová B. **Cesk Pediatr** 1981 Nov;36(11):666-7 **(Cze)**

[Depressions of the third age] Le Goues G. **Soins Psychiatr** 1982 Jan;(15):19-23 **(Fre)**

[Biochemistry of depression. Comments and correction (letter)] Bánki C. **Orv Hetil** 1982 Jan 17;123(3):127 **(Hun)**

[Depression, a public health problem] Calderón Narváez G. **Salud Publica Mex** 1981 Sep-Oct;23(5):503-8 (Eng. Abstr.) **(Spa)**

DEPRESSION, INVOLUTIONAL

A trial of dextroamphetamine in patients with involutional agitated depression. Ward NG, et al. **J Clin Psychiatry** 1982 Jan;43(1):35-6

[Influence of the seasons on the course and therapeutic results of depressive phases of maniomelancholy (author's transl)] Sedivec V. **Cesk Psychiatr** 1981 Oct;77(5):326-30 (Eng. Abstr.) **(Cze)**

[Introduction to the clinical problems of psychological disorders in involution (author's transl)] Vencovský E. **Cesk Psychiatr** 1981;77(4):232-6 (Eng. Abstr.) **(Cze)**

[Depressions in old age] Fedortsov VI. **Med Sestra** 1982 Jan;41(1):14-7 **(Rus)**

DEPRESSIVE DISORDER

A neurochemical theory of appetite and weight changes in depressive states. Hopkinson G. **Acta Psychiatr Scand** 1981 Sep;64(3):217-25

Duration of REM sleep latency as predictor of effect of antidepressant therapy. A preliminary report. Svendsen K, et al. **Acta Psychiatr Scand** 1981 Sep;64(3):238-43

Do have antidepressants of the second generation anxiolytic properties? Kabes J, et al. **Agressologie** 1981 Nov;22(E):11-3

Treatment of anxious depression with intravenous infusions of a combination of drugs. Krebs-Roubicek E, et al **Agressologie** 1981 Nov;22(D):25-6

Tofizopam in the therapy of anxious-depressive syndromes. Molcan J, et al. **Agressologie** 1981 Nov;22(D):23-4

The therapeutic effect of Trazodon with endogenous depressions. Peterova E, et al. **Agressologie** 1981 Nov;22(E):25

Amitriptyline levels and clinical effects. Quednow B, et al. **Agressologie** 1981 Nov;22(E):15-8

Anxiety in climax and its pharmacological treatment. Tondlova H, et al. **Agressologie** 1981 Nov;22(E):7-8

Recurrence of depression after discontinuation of long-term amitriptyline treatment. Bialos D, et al. **Am J Psychiatry** 1982 Mar;139(3):325-9

Potentiation of antidepressant effects by L-triiodothyronine in tricyclic nonresponders. Goodwin FK, et al. **Am J Psychiatry** 1982 Jan;139(1):34-8

Case report of painful ejaculation as a side effect of amoxapine. Kulik FA, et al. **Am J Psychiatry** 1982 Feb;139(2):234-5

True and pseudo cholinesterases in depression. Mathew RJ, et al. **Am J Psychiatry** 1982 Jan;139(1):125-7

Lorazepam and desipramine serum concentration [letter] Rosenblatt JE. **Am J Psychiatry** 1982 Apr;139(4):536-7

Toward a biochemical classification of depressive disorders, V: Heterogeneity of unipolar depressions. Schatzberg AF, et al. **Am J Psychiatry** 1982 Apr;139(4):471-5

Case report of inhibition of ejaculation and retrograde ejaculation as side effects of amoxapine. Schwarcz G. **Am J Psychiatry** 1982 Feb; 139(2):233–4

Relationship between plasma antidepressant levels and clinical outcome for inpatients receiving imipramine. Simpson GM, et al. **Am J Psychiatry** 1982 Mar;139(3):358–60

Steady-state plasma imipramine levels in prepubertal depressed children. Weller EB, et al. **Am J Psychiatry** 1982 Apr;139(4):506–8

Variability of hormonal responses to a series of neuroendocrine challenges in depressed patients. Winokur A, et al. **Am J Psychiatry** 1982 Jan; 139(1):39–44

Adrenergic receptor sensitivity in depression. Effects of clonidine in depressed patients and healthy subjects. Charney DS, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):290–4

The peripheral kinetics of norepinephrine in depressive illness. Esler M, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):295–300

EEG spectral analysis in vital depression: ultradian cycles. Lange H. **Biol Psychiatry** 1982 Jan;17(1):3–21

Platelet serotonin uptake in depressed patients: circadian effect. Rausch JL, et al. **Biol Psychiatry** 1982 Jan;17(1):121–3

The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy, each alone and in combination. Blackburn IM, et al. **Br J Psychiatry** 1981 Sep;139:181–9

Lithium continuation therapy following electroconvulsive therapy. Coppen A, et al. **Br J Psychiatry** 1981 Oct;139:284–7

Nortriptyline therapy in elderly patients: dosage prediction from plasma concentration at 24 hours after a single 50 mg dose. Dawling S, et al. **Br J Psychiatry** 1981 Nov;139:413–6

On the clinical response/plasma level relationship for clomipramine [letter] Dutt JE. **Br J Psychiatry** 1982 Jan;140:105

Cognitive therapy for depression [editorial] Goldberg D. **Br Med J [Clin Res]** 1982 Jan 16;284(6310):143–4

Decreased 3H-imipramine binding in depressed males and females. Asarch KB, et al. **Commun Psychopharmacol** 1980;4(5):425–32

Alterations in noradrenergic function during clorgyline treatment. Pickar D, et al. **Commun Psychopharmacol** 1980;4(5):379–86

Toward a biochemical classification of depressive disorders IV: Pretreatment urinary MHPG levels as predictors of antidepressant response to imipramine. Schatzberg AF, et al. **Commun Psychopharmacol** 1980;4(5):441–5

Therapies of depression. Rosen H. **Curr Psychiatr Ther** 1981; 20:301–11

Poor prophylactic lithium response due to antidepressants. Reginaldi D, et al. **Int Pharmacopsychiatry** 1981;16(2):124–3

Eye tracking in patients with unipolar and bipolar affective disorders in remission. Iacono WG, et al. **J Abnorm Psychol** 1982 Feb; 91(1):35–44

Plasma GABA in affective illness. A preliminary investigation. Petty F, et al. **J Affective Disord** 1981 Dec;3(4):339–43

Clinical conferences: Management of depression in older people. **J Am Geriatr Soc** 1982 Mar;30(3):219–23

Plasma concentrations of tricyclic antidepressants in clinical practice. Hollister LE. **J Clin Psychiatry** 1982 Feb;43(2):66–9

A controlled comparison of trimipramine and amitriptyline. Kline NS. **J Clin Psychiatry** 1981 Mar;43(3):100–4

Viloxazine HCl in the treatment of endogenous depression: a standard (imipramine) controlled clinical study. McEvoy JP, et al. **J Clin Psychiatry** 1981 Mar;43(3):111–2

Maprotiline versus imipramine [letter] Rifkin A. **J Clin Psychiatry** 1981 Mar;43(3):122

Methodological problems in studies of depressive disorder: utility of the discontinuation design. Quitkin FM, et al. **J Clin Psychopharmacol** 1981 Sep;1(5):283–8

Combined use of trimipramine and phenelzine in depression. Zetin M. **J Nerv Ment Dis** 1982 Apr;170(4):246–7

Defective serotonin transport mechanism in platelets from endogenously depressed patients. Malmgren R, et al. **Life Sci** 1981 Dec 21; 29(25):2649–58

Recognition and management of depression in the elderly. Finlayson RE, et al. **Mayo Clin Proc** 1982 Feb;57(2):115–20

Comments on multicenter trials of antidepressant drugs. Hippius H, et al. **Mod Probl Pharmacopsychiatry** 1981;16:95–9

High-affinity 3H-imipramine binding: a new biological marker in depression. Langer SZ, et al. **Pharmacopsychiatria** 1982 Jan; 15(1):4–10 (57 ref.)

The psychobiology of depressive disorders: from pathophysiology to predisposition. Depue RA, et al. **Prog Exp Pers Res** 1981;10:1–114 (436 ref.)

The diagnosis and treatment of hidden depression. Abrams GM. **Psychiatr Q** 1981 Winter;53(4):235–41

Gradients of monoamine metabolites and cortisol in cerebrospinal fluid of psychiatric patients and healthy controls. Bertilsson L, et al. **Psychiatry Res** 1982 Feb;6(1):77–83

Monoamine oxidase inhibitor-responsive depression. Giller E, et al. **Psychiatry Res** 1982 Feb;6(1):41–8

Depression, antidepressants, and plasma DBH. Mathew RJ, et al. **Psychiatry Res** 1981 Dec;5(3):331–4

Subsensitivity of human beta-adrenergic adenylate cyclase aft salbutamol treatment of depression. Lerer B, et al. **Psychopharmacology (Berlin)** 1981;75(2):169–72

Tricyclic continuation and maintenance therapy in unipolar depression. Kleinman I, et al. **Psychosomatics** 1981 Dec;22(12):1031–6

[Comparison of the effectiveness of tranylcypromine, nortriptyline, thioridazine and amitriptyline in two syndromological types of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981;77(4):245–52 (Eng. Abstr.) (Cz

[On the position of pyrazidol in the group of antidepressants in treatmen of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981 Oct;77(5):315–21 (Eng. Abstr.) (Cz

[Influence of the seasons on the course and therapeutic results of depressive phases of maniomelancholy (author's transl)] Sedivec V. **Cesk Psychiatr** 1981 Oct;77(5):326–30 (Eng. Abstr.) (Cz

[Treatment of endogenous depressions with maprotiline, clomipramine, dibenzepine and pyrlindole (author's transl)] Zapletálek M, et al. **Cesk Psychiatr** 1981 Jun;77(3):198–203 (Eng. Abstr.) (Cz

[Study of nomifensine in the treatment of depressive states (author's transl)] Zermatten A, et al. **Acta Psychiatr Belg** 1981 Jul-Aug; 81(4):379–98 (Eng. Abstr.) (Fr

[Comparative results of the treatment of anxiety in the depressive syndrome with Tolvon, Vivalan and Alival] Ivanov V, et al. **Agressologie** 1981 Nov;22(D):29–30 (Fr

[Demexiptiline in the treatment of melancholic states (reflections aft 3 years of use)] Martin A, et al. **Ann Med Psychol (Paris)** 1981 Nov; 139(9):1023–35 (Fr

[Unipolar periodic depressive psychosis and chronic tricyclic antidepressive treatment] Pascalis G. **Ann Med Psychol (Paris)** 1981 Nov;139(9):965–9 (Eng. Abstr.) (Fr

[Antidepressant monotherapy: efficacy and tolerability of mianseri (Athymil)] Pringuey D, et al. **Ann Med Psychol (Paris)** 1981 Nov; 139(9):1003–14 (Fr

[Therapists and therapeutic choice (author's transl)] Ayme J. **Encephale** 1981;7(4 Suppl):507–11 (Eng. Abstr.) (Fr

[Quantitative EEG in depression (author's transl)] Badr G, et al. **Encephale** 1981;7(4 Suppl):421–7 (Eng. Abstr.) (Fr

[Interactions between depression and anxiety (author's transl)] Ballus C. **Encephale** 1981;7(4 Suppl):335–7 (Eng. Abstr.) (Fr

[Analysis of controlled studies comparing mianserin and clomipramine (author's transl)] de Buck RP. **Encephale** 1981;7(4 Suppl):455–72 (Eng. Abstr.) (Fr

[Mianserin, presynaptic receptor and biochemical model of depressio of Tissot (author's transl)] Dereux JF. **Encephale** 1981; 7(4 Suppl):399–400 (Eng. Abstr.) (Fr

[An open study of Mianserin (author's transl)] Lemperiere T, et al. **Encephale** 1981;7(4 Suppl):445–54 (Eng. Abstr.) (Fr

[Therapeutic implications of the biochemical features about depressive illness (author's transl)] Lôo H. **Encephale** 1981;7(4 Suppl):429–40 (ref.) (Eng. Abstr.) (Fr

[Mianserin: review and discussion of its double-blind studies versus nomifensine] Montgomery SA, et al. **Encephale** 1981; 7(4 Suppl):485–94 (Eng. Abstr.) (Fr

[Prescription of antidepressants (author's transl)] Rainaut J. **Encephale** 1981;7(4 Suppl):513–22 (Eng. Abstr.) (Fr

[What to say to the family of a depressed patient?] Lempérière T, et al. **Rev Infirm** 1981 Oct;31(15):57–60 (Fr

[Depression: definition, evaluation, classification] Bobon DP. **Rev Med Liege** 1982 Jan 1;37(1):8–13 (Fr

[Depression. Treatment] Hougardy G. **Rev Med Liege** 1982 Jan 1; 37(1):14–6 (Fr

[Monoamines and endogenous depression. Biochemical and pharmacological aspects] Scuvée-Moreau J, et al. **Rev Med Liege** 1982 Jan 1;37(1):1–7 (Fr

[Depressions of the third age] Le Goues G. **Soins Psychiatr** 1982 Jan; (15):19–23 (Fr

[Antidepressive effect of partial sleep deprivation during the 1st half of the night] Goetze U, et al. **Psychiatr Clin (Basel)** 1981;14(3):129–49 (Eng. Abstr.) (Ge

[Depressions in old age] Fedortsov VI. **Med Sestra** 1982 Jan; 41(1):14–7 (Ru

[Catecholaminergic and serotoninergic systems in depression] Puzhin'skii S, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):66–8 (Eng. Abstr.) (Ru

DESIPRAMINE

Lorazepam and desipramine serum concentration [letter] Rosenblatt JE. **Am J Psychiatry** 1982 Apr;139(4):536–7

A study on the effect of chlorpromazine and desipramine on the activity of some adrenal enzymes. Chan MY, et al. **Biochem Pharmacol** 1981 Dec 15;30(24):3365–7

Cyclic AMP response to norepinephrine in the limbic forebrain of male and female rats: effect of desipramine. Mishra R, et al. **Biochem Pharmacol** 1981 Nov 15;30(22):3126–8

The effect of long-term chlorpromazine and desipramine treatment o adrenal corticosterone, cyclic AMP, and cholesterol distribution in rats. Hung F, et al. **Clin Exp Pharmacol Physiol** 1981 Dec;8(6):567-74

Active metabolites of imipramine and desipramine in man. Potter WZ, et al. **Clin Pharmacol Ther** 1982 Mar;31(3):393-401

Desipramine-induced agranulocytosis. A case report. Hardin TC, et al. **Drug Intell Clin Pharm** 1982 Jan;16(1):62-3

Behavioural evidence for supersensitivity of postsynaptic dopamine receptors in the mesolimbic system after chronic administration of desipramine. Spyraki C, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2-3):195-206

Determination of 2-hydroxydesipramine by high-performance liquid chromatography. Wong SH, et al. **J Chromatogr** 1981 Nov 13; 226(1):147-54

High-affinity binding of [3H]desipramine to rat brain: a presynaptic marker for noradrenergic uptake sites. Rehavi M, et al. **J Neurochem** 1982 Apr;38(4):889-95

Cerebral pharmacokinetics of imipramine in rats after single and multiple dosages. Daniel W, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):209-13

3H-Noradrenaline and 3H-5-hydroxytryptamine release from rat brain slices and its presynaptic alpha-adrenergic modulation after long-term desipramine pretreatment. Schoffelmeer AN, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):173-80

3H-WB 4101 binding in the rat vas deferens. Effects of chronic treatments with desipramine and prazosin. Wetzel HW, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):187-92

Depression, antidepressants, and plasma DBH. Mathew RJ, et al. **Psychiatry Res** 1981 Dec;5(3):331-4

The effects of desmethylimipramine and lithium on human sperm function. Amsterdam JD, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):359-63

A comparison of plasma and serum levels of two tricyclic antidepressants: imipramine and desipramine. Saady JJ, et al. **Psychopharmacology (Berlin)** 1981;75(2):173-4

[Decrease of paradoxical sleep in the rat under tricyclic antidepressant: the role of collateral inhibition (author's transl)] Justafre JC, et al. **Rev Electroencephalogr Neurophysiol Clin** 1981 Nov;11(2):228-35 (Eng. Abstr.) (Fre)

DESOXYCORTICOSTERONE

Identification of 19-hydroxydeoxycorticosterone, 19-oxo-deoxycorticosterone, and 19-oic-deoxycorticosterone as products of deoxycorticosterone metabolism by rat adrenals. Gomez-Sanchez CE, et al. **Endocrinology** 1982 Feb;110(2):384-9

DEXTROAMPHETAMINE

Effects of d-amphetamine on urinary metabolites of dopamine and norepinephrine in hyperactive boys. Shekim WO, et al. **Am J Psychiatry** 1982 Apr;139(4):485-8

Long-term decreases in striatal dopamine, 3,4-dihydroxyphenylacetic acid, and homovanillic acid after a single injection of amphetamine in iprindole-treated rats: time course and time-dependent interactions with amfonelic acid. Steranka LR. **Brain Res** 1982 Feb 18;234(1):123-36

Opposed stages of continuous amphetamine administration: parallel alterations in motor stereotypies and in vivo spiroperidol accumulation. Ellison G, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):207-14

D-Amphetamine at low doses suppresses noradrenergic functions. Huang YH, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):187-95

Drug preferences in humans. Johanson CE, et al. **Fed Proc** 1982 Feb; 41(2):228-33

A trial of dextroamphetamine in patients with involutional agitated depression. Ward NG, et al. **J Clin Psychiatry** 1982 Jan;43(1):35-6

Unstimulated and amphetamine-stimulated release of endogenous noradrenaline and dopamine from rat brain in vivo. Philips SR, et al. **J Neurochem** 1982 Apr;38(4):1106-10

Differential involvement of dopamine-containing tracts in 5-hydroxytryptamine-dependent behaviours caused by amphetamine in large doses. Andrews CD, et al. **Neuropharmacology** 1982 Jan; 21(1):63-8

Elevation of Met5-enkephalin and beta-endorphin hypothalamic content in rats receiving anorectic drugs: differences between D-fenfluramine and D-amphetamine. Harsing LG Jr, et al. **Neuropharmacology** 1982 Feb;21(2):141-5

Spinal modulation of acoustic startle: opposite effects of clonidine and d-amphetamine. Davis M, et al. **Psychopharmacology (Berlin)** 1981; 75(3):219-25

DIAZEPAM

Consumption of diazepam, nitrazepam and barbiturates in 5 large hospitals in Prague by defined daily doses per bed/day. Ivančová J, et al. **Act Nerv Super (Praha)** 1981;23(4):267-9

Diazepam adsorption to infusion sets and plastic syringes. Winsnes M, et al. **Acta Anaesthesiol Scand** 1981 Apr;25(2):93-6

Pharmacokinetics of diazepam administered rectally in geriatric patients: comparison of suppositories with rectal tubes in a cross-over study. Viukari M, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Jul; 49(1):59-64

The use of diazepam and of cocaine in combination with other drugs by Los Angeles County probationers. Budd RD. **Am J Drug Alcohol Abuse** 1981;8(2):249-55

Diazepam in schizophrenia: a preliminary double-blind trial. Jimerson DC, et al. **Am J Psychiatry** 1982 Apr;139(4):489-91

Pharmacokinetics of diazepam in the dog. Löscher W, et al. **Arch Int Pharmacodyn Ther** 1981 Dec;254(2):180-95

Biliary excretion of diazepam in rats: influence of the route of administration and dosage. Phillips R, et al. **Arch Int Pharmacodyn Ther** 1981;253(2):180-91

Sedation for upper gastrointestinal endoscopy [letter] Bardhan KD. **Br J Anaesth** 1981 Dec;53(12):1368

Effect of oral diazepam on lower oesophageal sphincter pressure. Cotton BR, et al. **Br J Anaesth** 1981 Nov;53(11):1147-50

Diazepam, propranolol and their combination in the management of chronic anxiety. Hallstrom C, et al. **Br J Psychiatry** 1981 Nov; 139:417-21

Diazepam and lidocaine plasma protein binding in renal disease. Grossman SH, et al. **Clin Pharmacol Ther** 1982 Mar;31(3):350-7

Steady-state plasma desmethyldiazepam during long-term clorazepate use: effects of antacids. Shader RI, et al. **Clin Pharmacol Ther** 1982 Feb;31(2):180-3

Diazepam dependency and withdrawal. Ayd FJ Jr. **Curr Psychiatr Ther** 1981;20:263-73

Pharmacokinetics of N-desmethyldiazepam after a single oral dose of clorazepate: the effect of smoking. Norman TR, et al. **Eur J Clin Pharmacol** 1981;21(3):229-33

Modification of diazepam's antileptazol activity by endogenous tryptophan-like compounds. Vellucci SV, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):255-9

3H-Diazepam binding sites in Roman high- and low-avoidance rats. Gentsch C, et al. **Experientia** 1981 Dec 15;37(12):1315-6

Drug preferences in humans. Johanson CE, et al. **Fed Proc** 1982 Feb; 41(2):228-33

The use of psychopharmacology to study reciprocal influences in parent-child interaction. Barkley RA. **J Abnorm Child Psychol** 1981 Sep;9(3):303-10

A safe method for repeatedly immobilizing seals. Geraci JR, et al. **J Am Vet Med Assoc** 1981 Dec 1;179(11):1192-3

A rapid procedure for the screening and quantitation of barbiturates, diazepam, desmethyldiazepam and methaqualone. McCurdy HH, et al. **J Anal Toxicol** 1981 Sep-Oct;5(5):253-7

Sedative-hypnotic tolerance testing and withdrawal comparing diazepam to barbiturates. Perry PJ, et al. **J Clin Psychopharmacol** 1981 Sep; 1(5):289-96

Assessment of pharmacodynamics of a new 'controlled release' form of diazepam (Valium CR Roche) by quantitative EEG and psychometric analysis in neurotic subjects. Saletu B, et al. **J Int Med Res** 1981; 9(6):408-33

[3H]Diazepam displacing activity in human cerebrospinal fluid. Kuhn W, et al. **J Neurochem** 1981 Oct;37(4):1045-7

Etomidate stereospecifically stimulates forebrain, but not cerebellar, 3H-diazepam binding. Ashton D, et al. **Life Sci** 1981 Dec 21; 29(25):2631-6

Impairment of diazepam metabolism by low-dose estrogen-containing oral-contraceptive steroids. Abernethy DR, et al. **N Engl J Med** 1982 Apr 1;306(13):791-2

The effects of acute administration of diazepam on the binding of [3H]-diazepam and [3H]-gaba to rat cortical membranes. Coupet J, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):965-8

Effect of parachlorophenylalanine on the incidence of abnormal behaviors observed following diazepam withdrawal. Suzuki T, et al. **Prog Neuropsychopharmacol** 1981;5(4):415-7

A dose response study of the hypnotic effectiveness of alprazolam and diazepam in normal subjects. Bonnet MH, et al. **Psychopharmacology (Berlin)** 1981;75(3):258-61

Two opposite effects of diazepam on fear by differential training in the CER-paradigm. Haug T, et al. **Psychopharmacology (Berlin)** 1981; 75(2):110-3

Anticonvulsant doses of inosine result in brain levels sufficient to inhibit [3H] diazepam binding. Marangos PJ, et al. **Psychopharmacology (Berlin)** 1981;75(2):175-8

Effect of age and sex on disposition of desmethyldiazepam formed from its precursor clorazepate. Shader RI, et al. **Psychopharmacology (Berlin)** 1981;75(2):193-7

Differential inhibition by diazepam and nitrazepam of UDP-glucuronyltransferase activities in rats. del Villar E, et al. **Res Commun Chem Pathol Pharmacol** 1981 Sep;33(3):433-47

The use of valium as a form of social control. Koumjian K. **Soc Sci Med [E]** 1981 Aug;15(3):245-9

[Comparative study of the effects of diazepam and fentanyl on the blink reflex threshold in the normal, conscious human (preliminary study)] Dauthier C, et al. **Ann Anesthesiol Fr** 1981;22(4):317-21 (Eng. Abstr.)

(Fre)

[Diazepam (Diazemuls Vitrum) and vein damages (letter)] Drøsdal S, et al. **Tidsskr Nor Laegeforen** 1981 Sep 20;101(26):1477-8 (Nor)

[Binding of 3H-diazepam by cerebral cortex synaptic membranes in the rat during conditioned reflex elaboration] Korotkov KO, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):695-6 (Eng. Abstr.) (Rus)

[Binding of 3H-serotonin, 3H-diazepam and lipid peroxidation in brain membranes] Libe ML, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):552-4 (Eng. Abstr.) (Rus)

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskiĭ Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) (Rus)

DIBENZAZEPINES

A suspected case of trimipramine-induced salivary adenitis. Ponte CD. **Drug Intell Clin Pharm** 1982 Mar;16(3):248-9

A controlled comparison of trimipramine and amitriptyline. Kline NS. **J Clin Psychiatry** 1981 Mar;43(3):100-4

Combined use of trimipramine and phenelzine in depression. Zetin M. **J Nerv Ment Dis** 1982 Apr;170(4):246-7

Serum concentration of pancreatic polypeptide after infusion of histamine and the effect of cimetidine, trimipramine, and atropine in man. Flaten O, et al. **Scand J Gastroenterol** 1981;16(8):989-91

Different synaptic location of mianserin and imipramine binding sites. Brunello N, et al. **Science** 1982 Feb 26;215(4536):1112-5

[Cloxazepine: neuropharmacological studies] Stefanova D. **Eksp Med Morfol** 1981;20(4):208-13 (Eng. Abstr.) (Bul)

[Agranulocytosis during treatment with mianserin (Tolvon)] Skallgård F. **Ugeskr Laeger** 1981 Nov 9;143(46):3057 (Eng. Abstr.) (Dan)

[Comparative results of the treatment of anxiety in the depressive syndrome with Tolvon, Vivalan and Alival] Ivanov V, et al. **Agressologie** 1981 Nov;22(D):29-30 (Fre)

[Antidepressant monotherapy: efficacy and tolerability of mianserin (Athymil)] Pringuey D, et al. **Ann Med Psychol (Paris)** 1981 Nov; 139(9):1003-14 (Fre)

[Analysis of controlled studies comparing mianserin and clomipramine (author's transl)] de Buck RP. **Encephale** 1981;7(4 Suppl):455-72 (Eng. Abstr.) (Fre)

[Mianserin, presynaptic receptor and biochemical model of depression of Tissot (author's transl)] Dereux JF. **Encephale** 1981; 7(4 Suppl):399-400 (Eng. Abstr.) (Fre)

[An open study of Mianserin (author's transl)] Lemperiere T, et al. **Encephale** 1981;7(4 Suppl):445-54 (Eng. Abstr.) (Fre)

[Mianserin: review and discussion of its double-blind studies versus nomifensine] Montgomery SA, et al. **Encephale** 1981; 7(4 Suppl):485-94 (Eng. Abstr.) (Fre)

[Agranulocytosis during treatment with mianserin (letter)] Lombrail P, et al. **Therapie** 1981 Sep-Oct;36(5):593-4 (Fre)

DIBENZOTHIEPINS

Further clinical experience with oxyprothepin-decanoate. Kalvach Z, et al. **Act Nerv Super (Praha)** 1981;23(4):271-2

Neuroleptics in neurotic anxiety. Boleloucky Z. **Agressologie** 1981 Nov; 22(D):15-7

Dothiepin, antianxiety effect in neurotic women. Boriová M, et al. **Agressologie** 1981 Nov;22(E):9-10

Anxiety in climax and its pharmacological treatment. Tondlova H, et al. **Agressologie** 1981 Nov;22(E):7-8

[Personality, antidepressant and neuroses] Boleloucký Z, et al. **Agressologie** 1981 Nov;22(E):3-5 (Fre)

[Comparison between the effectiveness of fluphenazine decanoate and oxyprothepin decanoate in schizophrenia (double-blind crossover study)] Balon R, et al. **Zh Nevropatol Psikhiatr** 1982;82(1):116-8 (Eng. Abstr.) (Rus)

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskiĭ Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) (Rus)

DIBENZOXAZEPINES

Physostigmine's use questioned for amoxapine overdose [letter] **Am J Hosp Pharm** 1981 Dec;38(12):1882, 1889

Case report of painful ejaculation as a side effect of amoxapine. Kulik FA, et al. **Am J Psychiatry** 1982 Feb;139(2):234-5

Case report of inhibition of ejaculation and retrograde ejaculation as side effects of amoxapine. Schwarcz G. **Am J Psychiatry** 1982 Feb; 139(2):233-4

The lipid-lowering profile in rodents. AZ-1355, a new dibenzoxazepine derivative. Wada S, et al. **Atherosclerosis** 1981 Nov-Dec; 40(3-4):263-71

Amoxapine (Asendin, Lederle Laboratories). Dugas JE, et al. **Drug Intell Clin Pharm** 1982 Mar;16(3):199-204 (34 ref.)

Amoxapine, an observation, and a perspective on MAOIs and their safety [editorial] Shader RI, et al. **J Clin Psychopharmacol** 1981 Sep; 1(5):263

DIETHYLAMINES

Toxicological testing of rats subjected to inhalation of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfide. Heicklen J, et al. **Environ Res** 1981 Dec;26(2):258-73

DISCRIMINATION (PSYCHOLOGY)

Hallucinogens as discriminative stimuli: a comparison of 4-OMe DMT and 5-OMe DMT with their methylthio counterparts. Glennon RA, et al. **Life Sci** 1982 Feb 1;30(5):465-7

Selective blockade of the discriminative stimulus effects of pentobarbital in pigeons. Herling S, et al. **Psychopharmacology (Berlin)** 1981; 75(3):321-3

DISCRIMINATION LEARNING

Behavioral properties of psychoactive phenylisopropylamines in rats. Glennon RA, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):353-60

Phencyclidine discrimination in the pigeon using color tracking under second-order schedule. McMillan DE, et al. **J Exp Anal Behav** 1982 Jan;37(1):143-7

Multiple drug training as a method for increasing the specificity of the drug discrimination procedure. Overton DA. **J Pharmacol Exp Ther** 1982 Apr;221(1):165-72

Environmental enrichment to alleviate maze performance deficits in rats with microcephaly induced by x-irradiation. Shibagaki M, et al. **Physiol Behav** 1981 Nov;27(5):797-802

The role of dopaminergic mechanisms in the rat hippocampus for the consolidation in a brightness discrimination. Grecksch G, et al. **Psychopharmacology (Berlin)** 1981;75(2):165-8

A repeated test procedure to assess onset and duration of the cue properties of (-) delta 9-THC, (-) delta 8-THC-DMH and (+) delta 8-THC. Järbe TU, et al. **Psychopharmacology (Berlin)** 1981; 75(2):152-7

DOPA

Renal handling of dopa, dopamine, norepinephrine, and epinephrine in the dog. Ball SG, et al. **Am J Physiol** 1982 Jan;242(1):F56-62

The increase of cardiac beta 1-subtype of beta-adrenergic receptors in adult rats following neonatal 6-hydroxydopa treatment. Kajiyama H, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):75-7

Simultaneous determination of 3,4-dihydroxyphenylalanine, 5-hydroxytryptophan, dopamine, 4-hydroxy-3-methoxyphenylalanine, norepinephrine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, serotonin, and 5-hydroxyindoleacetic acid in rat cerebrospinal fluid and brain by high-performance liquid chromatography with electrochemical detection. Wagner J, et al. **J Neurochem** 1982 May;38(5):1241-54

Use of liquid chromatography with electrochemistry to measure effects of varying intensities of white light on DOPA accumulation in rat retinas. Proll MA, et al. **Life Sci** 1982 Jan 4;30(1):11-9

[Spectrofluorometric determination of catecholamines and dihydroxyphenylalanine in 1 sample] Sominskiĭ VN, et al. **Lab Delo** 1982;(1):11-5 (Eng. Abstr.) (Rus)

DOPAMINE

Intestinal pharmacomanometry and glucose tolerance: two kinds of dopaminergic mechanisms in the human. Lechin F, et al. **Acta Gastroenterol Latinoam** 1981;11(2):247-59 (116 ref.)

Functional importance of nucleus accumbens noradrenaline in the rat. Svensson L, et al. **Acta Pharmacol Toxicol (Copenh)** 1982 Jan; 50(1):22-4

Interactions between GABA, dopamine, acetylcholine, and glutamate-containing neurons in the extrapyramidal and limbic systems. Bartholini G, et al. **Adv Biochem Psychopharmacol** 1981;30:119-28

Critical role of midbrain reticular formation in the expression of dopamine-mediated circling behaviour. Reavill C, et al. **Adv Biochem Psychopharmacol** 1981;30:187-204

Renal handling of dopa, dopamine, norepinephrine, and epinephrine in the dog. Ball SG, et al. **Am J Physiol** 1982 Jan;242(1):F56-62

Rapid fluctuations in plasma catecholamines in monkeys under undisturbed conditions. Hansen BC, et al. **Am J Physiol** 1982 Jan; 242(1):E40-6

Conditions for enhancement of renin release by isoproterenol, dopamine, and glucagon. Holdaas H, et al. **Am J Physiol** 1982 Mar; 242(3):F267-73

Neural and extraneural catecholamine production by rat kidneys. Stephenson RK, et al. **Am J Physiol** 1982 Mar;242(3):F261-6

Reduction of hypoxic ventilatory drive by dopamine. Ward DS, et al. **Anesth Analg (Cleve)** 1982 Apr;61(4):333-7

Comparison of dopamine and dobutamine following coronary artery bypass grafting. Salomon NW, et al. **Ann Thorac Surg** 1982 Jan; 33(1):48-54

Formation of 3H-dopamine and 3H-noradrenaline from 3H-tyrosine in the canine saphenous vein. Boels PJ, et al.

ch Int **Pharmacodyn Ther** 1981 Oct;253(2):315-16

ferences in the inhibitory effect of Cd2+, Mn2+ and Al3+ on the ptake of dopamine by synaptosomes from forebrain and from striatum f the rat. Lai JC, et al. **Biochem Pharmacol** 1981 Nov 15; 0(22):3123-5

zymology and subcellular localization of aldehyde oxidation in rat liver. Oxidation of 3,4-dihydroxyphenylacetaldehyde derived from dopamine o 3,4-dihydroxyphenylacetic acid. Tank AW, et al. **Biochem Pharmacol** 1981 Dec 15;30(24):3265-75

versible blockade of [3H]spiperone- but not [3H]dopamine-labeled dopamine receptors with phenoxybenzamine. Titeler M. **Biochem Pharmacol** 1981 Nov 15;30(22):3031-7

strogens, dopamine and mood [letter] Cookson J. **Br J Psychiatry** 1981 Oct;139:365-6

itive and negative schizophrenia symptoms and the role of dopamine. Crow TJ. **Br J Psychiatry** 1981 Sep;139:251-4

idence for dopamine autoreceptors controlling dopamine synthesis in the substantia nigra. Argiolas A, et al. **Brain Res** 1982 Feb 18; 234(1):177-81

perature regulation and dopaminergic systems in the brain: does the substantia nigra play a role? Brown SJ, et al. **Brain Res** 1982 Feb 25, 234(2):275-86

euronal localization of dopamine-sensitive adenylate cyclase within the rat olfactory tubercle. Church AC, et al. **Brain Res** 1982 Feb 25; 234(2):369-76

rebral circulatory response to hypercapnia: effects of lesions of central dopaminergic and serotoninergic neuron systems. Dahlgren N, et al. **Brain Res** 1981 Dec 28;230(1-2):221-33

CTH 1-24 and lysine vasopressin selectively activate dopamine synthesis in frontal cortex. Delanoy RL, et al. **Brain Res** 1982 Jan 7; 231(1):117-29

ltered neuronal responsiveness to biogenic amines in rat cerebral cortex after serotonin denervation or depletion. Ferron A, et al. **Brain Res** 1982 Jan 7;231(1):93-108

haracterization of high affinity dopamine uptake into the dopamine neurons of the hypothalamus. George SR, et al. **Brain Res** 1982 Feb 25;234(2):339-55

Evidence for dopamine as a transmitter in dorsal hippocampus. Ishikawa K, et al. **Brain Res** 1982 Jan 28;232(1):222-6

mygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst-motivated behavior. Lénárd L, et al. **Brain Res** 1982 Feb 4;233(1):115-32

volvement of GABA in the feedback action of estradiol on gonadotropin and prolactin release: hypothalamic GABA and catecholamine turnover rates. Mansky T, et al. **Brain Res** 1982 Jan 14;231(2):353-64

Long-term decreases in striatal dopamine, 3,4-dihydroxyphenylacetic acid, and homovanillic acid after a single injection of amphetamine in iprindole-treated rats: time course and time-dependent interactions with amfonelic acid. Steranka LR. **Brain Res** 1982 Feb 18;234(1):123-36

Effect of des-Tyr1-gamma-endorphin and des-Tyr1-alpha-endorphin on alpha-MPT-induced catecholamine disappearance in rat brain nuclei: a dose—response study. Versteeg DH, et al. **Brain Res** 1982 Jan 14; 231(2):343-51

Dopamine blocks carrier-mediated release of GABA from retinal horizontal cells. Yazulla S, et al. **Brain Res** 1982 Feb 4;233(1):211-5

Altered hypothalamic dopamine depletion rate and LHRH content in acyclic hamsters. Kumar MS, et al. **Brain Res Bull** 1982 Jan; 8(1):33-6

Aging of tuberoinfundibular (A-12) dopamine neurons in the C57Bl/6N male mouse. Selemon LD, et al. **Brain Res Bull** 1981 Nov; 7(5):585-94

The effects of catecholamines on hemorrhagic shock in dogs. Sakahira K, et al. **Bull Tokyo Med Dent Univ** 1981 Dec;28(4):125-34

Electrophysiological and mechanical studies of frog heart adrenoceptor stimulation by epinine. Soustre H, et al. **Cardiovasc Res** 1981 Dec; 15(12):700-10

Inhibition of reverse transcriptase by tyrosinase generated quinones related to levodopa and dopamine. Wick MM, et al. **Chem Biol Interact** 1981 Dec;38(1):99-107

Effect of inhibition of prostaglandin synthesis on urinary free dopamine excretion in women. Güllner HG, et al. **Clin Sci** 1982 Feb; 62(2):209-13

Role of dopamine in the regulation of blood pressure and the renin—angiotensin—aldosterone system in conscious rats. Kondo K, et al. **Clin Sci [Suppl]** 1981 Dec;61(7):235s-237s

Effects of age on dopaminergic supersensitivity induced by chronic fluphenazine. Misra CH, et al. **Commun Psychopharmacol** 1980; 4(5):411-5

Modification of the drug talking behavior in rats by interference in the metabolism of 5-hydroxytryptamine and catecholamines. Fuchs V, et al. **Drug Alcohol Depend** 1981 Nov;8(3):235-44

The decrease in hypothalamic dopamine secretion induced by suckling: comparison of voltammetric and radioisotopic methods of measurement. Plotsky PM, et al. **Endocrinology** 1982 Mar;110(3):691-6

Rat prolactin and hypothalamic catecholamine nerve terminal systems. Evidence for rapid and discrete increases in dopamine and noradrenaline turnover in the hypophysectomized male rat. Andersson K, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):261-5

Stereoselectivity of presynaptic autoreceptors modulating dopamine release. Arbilla S, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):345-51

The effect of some anti-epilepsy drugs on enhancement of the monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. Bhavsar VH, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):243-7

In vivo electrochemical detection of catechols in several dopaminergic brain regions of anaesthetized rats. Buda M, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):61-8

Benzodiazepines suppress the light response of retinal dopaminergic neurons in vivo. Kamp CW, et al. **Eur J Pharmacol** 1982 Feb 5; 77(4):343-6

Possible involvement of nigrostriatal dopamine system in the inhibition of thyrotropin secretion in the rat. Männistö P, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):403-9

Dopaminergic mechanisms in diet-induced thermogenesis and brown adipose tissue metabolism. Rothwell NJ, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):45-8

Dopamine neurones of the ventral tegmentum project to both medial and lateral habenula. Some implications for habenular function. Phillipson OT, et al. **Exp Brain Res** 1982;45(1-2):89-94

Dopamine-containing cells in rabbit nodose ganglia. Kojima H, et al. **Experientia** 1981 Dec 15;37(12):1332-3

Comparative effects of short- and long-term treatment with neuroleptics on behavioural activity as well as dopamine turnover in striatum. Rastogi RB, et al. **Gen Pharmacol** 1982;13(1):35-40

Effect of metoclopramide in guinea-pig ileum longitudinal muscle: evidence against dopamine-mediation. Zar MA, et al. **Gut** 1982 Jan; 23(1):66-70

Glial uptake of monoamines in primary cultures of rat median raphe nucleus and cerebellum. A combined monoamine fluorescence and glial fibrillary acidic protein immunofluorescence study. Liesi P, et al. **Histochemistry** 1981;73(2):239-50

Synaptic organization of the dopaminergic neurons in the retina of the cynomolgus monkey. Holmgren I. **Invest Ophthalmol Vis Sci** 1982 Jan; 22(1):8-24

Gas chromatographic method for the simultaneous determination of dopamine and norepinephrine metabolites. Chauhan MS, et al. **J Chromatogr** 1982 Feb 12;227(2):323-30

Future directions in dopaminergic nervous system and dopaminergic agonists. Cannon JG, et al. **J Med Chem** 1981 Oct;24(10):1113-8 (66 ref.)

Inhibitory effects of ascorbic acid on the binding of [3H]dopamine antagonists to neostriatal membrane preparations: relationship to lipid peroxidation. Heikkila RE, et al. **J Neurochem** 1982 Apr; 38(4):1000-6

Monoamine oxidase-catalyzed metabolism of 3,4-dihydroxyphenylethylamine in the dopaminergic synaptosomes from rat corpus striatum. Katz IR. **J Neurochem** 1982 Mar; 38(3):859-62

Catabolism of endogenous dopamine in peripheral tissues: is there an independent role for dopamine in peripheral neurotransmission? Lacković Z, et al. **J Neurochem** 1982 May;38(5):1453-8

The effects of chronic manganese chloride treatment expressed as age-dependent, transient changes in rat brain synaptosomal uptake of amines. Lai JC, et al. **J Neurochem** 1982 Mar;38(3):844-7

Biochemical evidence for alteration of neostriatal dopaminergic function by 5,7-dihydroxytryptamine. Liston DR, et al. **J Neurochem** 1982 May; 38(5):1329-35

Postmortem stability of dopamine-sensitive adenylate cyclase, guanylate cyclase, ATPase, and GTPase in rat striatum. Nicol SE, et al. **J Neurochem** 1981 Dec;37(6):1535-9

Unstimulated and amphetamine-stimulated release of endogenous noradrenaline and dopamine from rat brain in vivo. Philips SR, et al. **J Neurochem** 1982 Apr;38(4):1106-10

On the significance of endogenous 3-methoxytyramine for the effects of centrally acting drugs on dopamine release in the rat brain. Westerink BH, et al. **J Neurochem** 1982 Mar;38(3):680-6

Neuronal cell surfaces: distinctive glycoproteins of cultured adrenergic and cholinergic sympathetic neurons. Braun SJ, et al. **J Neurosci** 1981 Dec;1(12):1397-406

Collateralization of monoamine neurons: mesotelencephalic dopamine projections to caudate, septum, and frontal cortex. Fallon JH. **J Neurosci** 1981 Dec;1(12):1361-8

Dopamine and [D-ALA2, D-Leu5]enkephalin inhibit the electrically stimulated neurohypophyseal release of vasopressin in vitro: evidence for calcium-dependent opiate action. Lightman SL, et al. **J Neurosci** 1982 Jan;2(1):78-81

Specific uptake of norepinephrine and dopamine by homogenates of rat cerebral cortex after locus ceruleus lesion. Logan WJ, et al. **J Neurosci** 1982 Mar;2(3):394-8

Realization of a new multifiber electrochemical device allowing continuous in vivo measurements of neuromediators. Forni C. **J Neurosci Methods** 1982 Jan;5(1-2):167-71

Influence of dietary zinc on rat brain catecholamines. Wallwork JC, et al. **J Nutr** 1982 Mar;112(3):514-9

Gangrene in a neonate following dopamine therapy. Maggi JC, et al. **J Pediatr** 1982 Feb;100(2):323-5

Chronic treatment with haloperidol or fluphenazine decanoate: regional effects on dopamine and serotonin metabolism in primate brain. Bacopoulos NG, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):22-8

Effect of delta9-tetrahydrocannabinol on the synthesis of dopamine and norepinephrine in mouse brain synaptosomes. Bloom AS. **J Pharmacol Exp Ther** 1982 Apr;221(1):97-103

Differential dose- and time-dependent effects of molindone on dopamine neurons of rat brain: mediation by irreversible inhibition of monoamine oxidase. Meller E, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):609-15

gamma-Aminobutyric acid (GABA) receptor stimulation. III. Effect of progabide (SL 76002) on norepinephrine, dopamine and 5-hydroxytryptamine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):678-88

Catastrophe theory of dopaminergic transmission: a revised dopamine hypothesis of schizophrenia. King R, et al. **J Theor Biol** 1981 Oct 21; 92(4):373-400

Compared efficacy of dobutamine and dopamine in association with calcium chloride on termination of cardiopulmonary bypass. d'Hollander A, et al. **J Thorac Cardiovasc Surg** 1982 Feb; 83(2):264-71

Dopaminergic inhibition from substantia nigra of caudate neurons activated by cortical stimulation. Fujimoto S, et al. **Jpn J Pharmacol** 1981 Dec;31(6):1037-42

Acute changes in the state of dopamine receptors: in vitro monitoring with 3H-dopamine. Bacopoulos NG. **Life Sci** 1981 Dec 7; 29(23):2407-14

The convulsive effects of dopamine sulfate conjugates in rat brain. Buu NT, et al. **Life Sci** 1981 Nov 30;29(22):2311-6

Biphasic influence of a 8 alpha-amino ergoline, CU 32-085, on striatal dopamine synthesis and turnover in vivo in the rat. Enz A. **Life Sci** 1981 Nov 23;29(21):2227-34

Forebrain catecholamine concentrations in the rat after neocortical and hippocampal lesions. Woodruff ML, et al. **Life Sci** 1981 Dec 21; 29(25):2603-7

Dopamine- and serotonin-sensitive adenylate cyclase in the gill of Aplysia californica. Weiss S, et al. **Mol Pharmacol** 1981 Nov;20(3):592-7

Unique response to antipsychotic drugs is due to absence of terminal autoreceptors in mesocortical dopamine neurones. Bannon MJ, et al. **Nature** 1982 Apr 1;296(5856):444-6

Non-dopaminergic fibres may regulate dopamine-sensitive adenylate cyclase in the prefrontal cortex and nucleus accumbens. Tassin JP, et al. **Nature** 1982 Feb 25;295(5851):696-8

Motor effects following application of putative excitatory amino acid antagonists to the region of the mesencephalic dopamine cell bodies in the rat. Dawbarn D, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(2):100-4

Analysis of the effects of dopamine and noradrenaline in relation to the proposed postsynaptic dopamine receptor in rat vas deferens. Langeloh A, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb; 318(3):202-9

Effects of piracetam on the central dopaminergic transmission. Rägo LK, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(1):36-7

Tissue specificity of dopamine effects on brain ATPases. Antonelli de Gómez de Lima M, et al. **Neurochem Res** 1981 Sep;6(9):969-77

Central effects of dopamine and bromocriptine on vasopressin release and blood pressure. Kimura T, et al. **Neuroendocrinology** 1981 Dec; 33(6):347-51

Neuroleptic malignant syndrome caused by dopamine depleting drugs [letter] Login IS, et al. **Neurology (NY)** 1982 Feb;32(2):218-9

Antiestrogen-induced alterations of hypothalamic dopamine and norepinephrine levels in the female rat. Baksi SN, et al. **Neuropharmacology** 1981 Dec;20(12A):1163-7

The use of dopamine agonists in the treatment of schizophrenia. Corsini GU, et al. **Neuropharmacology** 1981 Dec;20(12B):1309-13

Repeated administration of triiodothyronine (T3) to rats enhances nigrostriatal and mesolimbic dopaminergic behavioural responses. Heal DJ, et al. **Neuropharmacology** 1982 Feb;21(2):159-62

Correlation between the rate of avoidance conditioning and the brain catecholamine level in rats. Saul'skaya NB. **Neurosci Behav Physiol** 1981 May-Jun;11(3):221-6

Differential effects of certain dopaminergic drugs on the striatal concentration of dopamine metabolites, with special reference to 3-methoxytramine. Ponzio F, et al. **Neurosci Lett** 1981 Nov 18; 27(1):61-7

Involvement of the thalamus in the reciprocal regulation of the two nigrostriatal dopaminergic pathways. Chéramy A, et al. **Neuroscience** 1981;6(12):2657-68

Origin, course and termination of dopaminergic substantia nigra neurons projecting to the amygdaloid complex in the cat. Meibach RC, et al. **Neuroscience** 1981;6(11):2159-71

Dopaminergic dendrites in the pars reticulata of the rat substantia nigra and their striatal input. Combined immunocytochemical localization of tyrosine hydroxylase and anterograde degeneration. Wassef M, et al. **Neuroscience** 1981;6(11):2125-39

The influence of ingested aluminum upon norepinephrine and dopamine levels in the rat brain. Wenk GL, et al. **Neurotoxicology (Park Forest II)** 1981 Oct;2(2):347-53

Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Brown OM, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):911-4

Measurement of metabolites of dopamine and 5-hydroxytryptamine in cerebroventricular perfusates of unanesthetized, freely-moving rats: selective effects of drugs. Nielsen JA, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):131-7

Infant rat hyperactivity elicited by home cage bedding is unaffected by neonatal telencephalic dopamine or norepinephrine depletion. Pappas BA, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):151-4

Substituted dopamine quinazolones as potent antiparkinsonian agents. Kumar P, et al. **Pharmazie** 1981 Nov;36(11):780

Effects of nootropic drugs on dopaminergic systems in the CNS. Westermann KH, et al. **Pol J Pharmacol Pharm** 1981;33(4):431-6

Role of the dopaminergic system in luteinizing hormone release and ovulation in the hen. Johnson PA, et al. **Poult Sci** 1981 Nov; 60(11):2551-6

Isolated horizontal cells from carp retina demonstrate dopamine-dependent accumulation of cyclic AMP. Van Buskirk R, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7825-9

Phenothiazine biphasic effect on dopamine concentrations in the basal ganglia of subhuman primates. Bird ED, et al. **Psychiatry Res** 1982 Feb;6(1):1-6

A comparison of some behavioural effects of amphetamine and electrical brain stimulation of the mesolimbic dopamine system in rats. D'Mello GD. **Psychopharmacology (Berlin)** 1981;75(2):184-92

Differential reversal of various dopamine antagonists by anticholinergics in Sidman avoidance: possible relationship to adrenergic blockade. Liebman JM, et al. **Psychopharmacology (Berlin)** 1981;75(3):248-53

Differential inhibitory effects of ascorbic acid on the binding of dopamine agonists and antagonists to neostriatal membrane preparations: correlations with behavioral effects. Heikkila RE, et al. **Res Commun Chem Pathol Pharmacol** 1981 Dec;34(3):409-21

Evidence for the existence of a dopamine-sensitive adenylate cyclase in chick optic tectum. Nisticò G, et al. **Res Commun Chem Pathol Pharmacol** 1981 Sep;33(3):387-93

Evidence for endogenous dopaminergic control of GH release in man. Hanew K, et al. **Tohoku J Exp Med** 1981 Sep;135(1):103-8

[Rate of cerebral dopamine synthesis in rats] Vamvakides A. **Agressologie** 1981;22(3):117-28 (Eng. Abstr.) (Fre)

[Biochemical analysis of dopaminergic nerve terminals of post-mortem brain from schizophrenic patients (author's transl)] Toru M, et al. **Seishin Shinkeigaku Zasshi** 1981;83(7):430-47 (Eng. Abstr.) (Jpn)

[Effect of dopamine on the contractility of isolated blood vessels of the human placenta] Urban J, et al. **Ginekol Pol** 1981;52(9):757-62 (Eng. Abstr.) (Pol)

[Effect of intracaudate administration of kainic acid on the activity of the dopaminergic system] Zharkovskiĭ AM, et al. **Fiziol Zh SSSR** 1981 Nov;67(11):1606-10 (Eng. Abstr.) (Rus)

[Various features of dopamine metabolism in schizophrenia] Anokhina IP, et al. **Zh Nevropatol Psikhiatr** 1981;81(9):1343-7 (Eng. Abstr.) (Rus)

[Ligand-dopaminergic receptor bond in the guinea pig bladder] Idoate Tomás C, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):123-4 (Spa)

[Respiratory effects of intracerebroventricular dopamine in the rat] Mediavilla A, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):73-6 (Spa)

DOPAMINE BETA-HYDROXYLASE

Plasma dopamine-beta-hydroxylase activity during labour in women. Wasilewska E, et al. **Acta Physiol Pol** 1981;32(4):399-405

Biochemical differences in children with conduct disorder socialized and undersocialized. Rogeness GA, et al. **Am J Psychiatry** 1982 Mar; 139(3):307-11

Dopamine beta-hydroxylase: activity and inhibition in the presence of beta-substituted phenethylamines. Klinman JP, et al. **Biochemistry** 1982 Jan 5;21(1):67-75

Purification and characterization of avian dopamine beta-hydroxylase. Long RA, et al. **Biochemistry** 1981 Dec 22;20(26):7423-31

Plasma copper and dopamine-beta-hydroxylase in schizophrenia. Baron M, et al. **Biol Psychiatry** 1982 Jan;17(1):115-20

Oxygen dependence of dopamine-beta-hydoxylase activity and lactate metabolism in synaptosomes from rat brain. Katz IR. **Brain Res** 1982 Jan 14;231(2):399-409

Nitriphenol compound induces Ca-dependent exocytotic secretion of catecholamines by a direct effect on the plasma membranes of the adrenal medullary cells. Sorimachi M, et al. **Brain Res** 1982 Jan 28; 232(1):242-6

Assay for dopamine beta-hydroxylase in rat serum and adrenal medulla by high-performance liquid chromatography with fluorescence detection. Nohta H, et al. **J Chromatogr** 1982 Feb 12;227(2):415-22

Dopamine beta-hydroxylase and other glycoproteins from the soluble content and the membranes of adrenal chromaffin granules: isolation and carbohydrate analysis. Fischer-Colbrie R, et al. **J Neurochem** 1982 Mar;38(3):725-32

Immunochemical evidence for exocytosis in isolated chromaffin cells after stimulation with depolarizing agents. Wildmann J, et al. **J Neuroimmunol** 1981 Sep;1(3):353-64

Catecholamine and dopamine-beta-hydroxylase in anxiety. Mathew RJ, et al. **J Psychosom Res** 1981;25(6):499-504

Radioimmunoassay and immunotitration of human serum dopamine beta-hydroxylase. Dunnette J, et al. **Methods Enzymol** 1981; 74 Pt C:370-80

Effects of aging on the activity of hypothalamic dopamine-beta-hydroxylase during various stages of the estrous cycle in C57BL/6 mice. Banerji TK, et al. **Neuroendocrinology** 1982 Jan; 34(1):14-9

Depression, antidepressants, and plasma DBH. Mathew RJ, et al. **Psychiatry Res** 1981 Dec;5(3):331-4

DOXEPIN

Solubility and ionization characteristics of doxepin and desmethyldoxepin. Embil K, et al. **J Pharm Sci** 1982 Feb;71(2):191-3

DRUG EVALUATION

Guidelines for the evaluation of drugs in the elderly neuropsychiatric patient (demented and non-demented). **Pharmacopsychiatria** 1981 Nov; 14(6):217-22

DRUG INTERACTIONS

Digitalis toxicity mistaken for jaundice. Dickstein ES. **Geriatrics** 1982 Apr;37(4):133, 137-8

Drug interactions at excretory mechanisms. Offerhaus L. **Pharmacol Ther** 1981;15(1):69-78 (64 ref.)

DRUG SCREENING

[Predicted pharmacology of an antidepressant] Pinder RM. **Encephale** (Fre) 1981;7(4 Suppl):371-80 (Eng. Abstr.)

ELECTROCONVULSIVE THERAPY

Lithium continuation therapy following electroconvulsive therapy. Coppen A, et al. **Br J Psychiatry** 1981 Oct;139:284-7

Electroconvulsive shock results in a functional activation of endorphin systems. Holaday JW, et al. **Mod Probl Pharmacopsychiatry** 1981; 17:142-57

ELECTROENCEPHALOGRAPHY

EEG changes in the limbic system after the administration of leu5-enkephalin. Herink J, et al. **Act Nerv Super (Praha)** 1981; 23(4):290-2

An electroencephalographic study of 4-aminopyridine. Sia RL, et al. **Anesth Analg (Cleve)** 1982 Apr;61(4):354-7

EEG spectral analysis in vital depression: ultradian cycles. Lange H. **Biol Psychiatry** 1982 Jan;17(1):3-21

A reliable multichannel commutator for making electrical contact with conscious, freely moving rats. Andrews CD, et al. **J Neurosci Methods** 1982 Jan;5(1-2):73-6

Effect of serotonin injected into the amygdala on conditioned and unconditioned food reflexes and the EEG in cats. Gasanov GG, et al. **Neurosci Behav Physiol** 1981 May-Jun;11(3):207-12

Inverse relationship between onset and duration of EEG effects of six peripherally administered peptides. Miller LH, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):845-8

Quantitative EEG and behavioral effects in volunteers of a new benzodiazepine (SAS 643) in relation to drug plasma concentration. Sannita WG, et al. **Ther Drug Monit** 1981;3(4):341-9

[Quantitative EEG in depression (author's transl)] Badr G, et al. (Fre) **Encephale** 1981;7(4 Suppl):421-7 (Eng. Abstr.)

ELECTROLYTES

Divalent cation, ATP-dependent [3H]leu-enkephalin uptake by synaptic vesicle fraction isolated from bovine caudate nucleus. Takeda M, et al. **Brain Res** 1982 Feb 25;234(2):319-26

Neurohumoral control of ileal electrolyte transport. II. Neurotensin and substance P. Kachur JF, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):456-63

Lithium delays biochemical circadian rhythms in rats. McEachron DL, et al. **Neuropsychobiology** 1982 Jan-Feb;8(1):12-29

Lithium-induced polydipsia in birds: a comparative study and analysis of electrolyte excretion. Hardy WT, et al. **Physiol Behav** 1981 Oct; 27(4):575-83

ELECTROSHOCK

The effect of some anti-epilepsy drugs on enhancement of the monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. Bhavsar VH, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):243-7

Enhancement of responsiveness of the central serotonergic system and serotonin-2 receptor density in rat frontal cortex by electroconvulsive treatment. Vetulani J, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):81-5

Electroconvulsive shock and reserpine: effects on beta-adrenergic receptors in rat brain. Kellar KJ, et al. **J Neurochem** 1981 Oct; 37(4):830-6

Chronic electroconvulsive shock and chronic haloperidol administration are not additive in effects on dopamine receptors. Globus M, et al. **Neuropharmacology** 1981 Nov;20(11):1125-8

EMOTIONS

The effects of imipramine on socio-emotional and alimentary motivated behavior in dogs. Zagrodzka J, et al. **Acta Neurobiol Exp (Warsz)** 1981; 41(4):363-72

Drug preferences in humans. Johanson CE, et al. **Fed Proc** 1982 Feb; 41(2):228-33

[Effects of afloqualone, a new centrally acting muscle relaxant, on DRL response and CER in rats (author's transl)] Yamamura M, et al. (Jpn) **Nippon Yakurigaku Zasshi** 1981 Oct;78(4):381-92 (Eng. Abstr.)

[Characteristics of the psychoemotional state of children undergoing dental treatment] Solov'ev MM, et al. **Stomatologiia (Mosk)** 1982 (Rus) Jan-Feb;61(1):77-82 (Eng. Abstr.)

[Learning in rats with differing emotional responsiveness and its relation to brain monoamines] Gromova EA, et al. **Zh Vyssh Nerv Deiat** 1981 (Rus) Nov-Dec;31(6):1238-46 (Eng. Abstr.)

[Psychological component of human stress (author's transl)] Vargas Fernández L. **Rev Med Chil** 1981 May;109(5):441-51 (Eng. Abstr.) (Spa)

ENDORPHINS

EEG changes in the limbic system after the administration of leu5-enkephalin. Herink J, et al. **Act Nerv Super (Praha)** 1981; 23(4):290-2

Physiological role of endorphins in neuroendocrinology. Dupont A, et al. **Acta Physiol Pol** 1981;32(5 Suppl 23):37-57 (45 ref.)

Inhibition of salivary and lacrimal secretion by an enkephalin analogue [letter] Sullivan SN. **Am J Psychiatry** 1982 Mar;139(3):385-6

Endorphins and behavior. Bolles RC, et al. **Annu Rev Psychol** 1982; 33:87-101

Identification of the octapeptide [Met]enkephalin -Arg6-Gly7-Leu8 in extracts of bovine adrenal medulla. Kilpatrick DL, et al. **Biochem Biophys Res Commun** 1981 Nov 30;103(2):698-705

Solution conformations of the pituitary opioid peptide dynorphin-(1-13). Maroun R, et al. **Biochem Biophys Res Commun** 1981 Nov 30; 103(2):442-6

Acetylated and nonacetylated forms of beta-endorphin in rat brain and pituitary. Weber E, et al. **Biochem Biophys Res Commun** 1981 Dec 15; 103(3):982-9

Colocalization of alpha-neo-endorphin and dynorphin immunoreactivity in hypothalamic neurons. Weber E, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):951-8

Fast-atom-bombardment mass spectra of enkephalins. Barber M, et al. **Biochem J** 1981 Aug 1;197(2):401-4

Effects of metenkephalin on the formation and fixation of defensive temporal associations and on the incorporation of C14-leucine in brain proteins of the rat. Kruglikov RI, et al. **Biol Bull Acad Sci USSR** 1980 Sep-Oct;7(5):432-4

The treatment of schizophrenic psychoses with gamma-type endorphins. van Praag HM, et al. **Biol Psychiatry** 1982 Jan;17(1):83-98

Neostriatal enkephalin-immunoreactive neurones project to the globus pallidus. Del Fiacco M, et al. **Brain Res** 1982 Jan 7;231(1):1-17

Immunoreactive dynorphin in human brain and pituitary. Gramsch C, et al. **Brain Res** 1982 Feb 4;233(1):65-74

Immunocytochemical localization of beta-endorphin (lipotropin C-fragment) in the developing rat spinal cord and hypothalamus. Haynes LW, et al. **Brain Res** 1982 Jan 28;232(1):115-28

Beta-endorphin concentrations in serum, hypothalamus and central gray of hypophysectomized and mediobasal hypothalamus lesioned rats. Kerdelhué B, et al. **Brain Res** 1982 Jan 7;231(1):85-91

The actions of neuropeptides on dorsal horn neurons in the rat spinal cord slice preparation: an intracellular study. Murase K, et al. **Brain Res** 1982 Feb 18;234(1):170-6

Divalent cation, ATP-dependent [3H]leu-enkephalin uptake by synaptic vesicle fraction isolated from bovine caudate nucleus. Takeda M, et al. **Brain Res** 1982 Feb 25;234(2):319-26

Analgesic dipeptide, kyotorphin (Tyr-Arg), is highly concentrated in the synaptosomal fraction of the rat brain. Ueda H, et al. **Brain Res** 1982 Jan 7;231(1):222-4

Regional distribution of alpha- and gamma-type endorphins in rat brain. Verhoef J, et al. **Brain Res** 1982 Jan 14;231(2):454-60

Effect of des-Tyr1-gamma-endorphin and des-Tyr1-alpha-endorphin on alpha-MPT-induced catecholamine disappearance in rat brain nuclei: a dose--response study. Versteeg DH, et al. **Brain Res** 1982 Jan 14; 231(2):343-51

Endogenous opioid peptides. Goedert M, et al. **Bull Soc Sci Med Grand Duche Luxemb** 1981;118(1):7-17

Distribution of neuropeptides in the dorsal pontine tegmental area of the rat. Matsuzaki T, et al. **Cell Mol Biol** 1981;27(5):499-508

Central peptidergic stimulation in blood pressure control: role of enkephalins in rats. Yukimura T, et al. **Clin Sci [Suppl]** 1981 Dec; 61(7):347s-350s

Inhibition of the enzymatic degradation of Met-enkephalin by catecholamines. Caffrey JL, et al. **Endocrinology** 1982 Jan; 110(1):291-3

Dopaminergic inhibition of pituitary beta-endorphin-like immunoreactivity secretion in the rat. Farah JM Jr, et al. **Endocrinology** 1982 Feb;110(2):657-9

Evidence for independent secretion of beta-endorphin immunoreactivity from rat pars distalis in vivo. Pettibone DJ, et al. **Endocrinology** 1982 Feb;110(2):469-73

Characterization of an early inhibitory effect of glucocorticoids on stimulated adrenocorticotropin and endorphin release from a clonal strain of mouse pituitary cells. Phillips M, et al. **Endocrinology** 1982 Mar;110(3):892-900

In vivo corticotropin-releasing factor-induced secretion of adrenocorticotropin, beta-endorphin, and corticosterone. Rivier C, et al. **Endocrinology** 1982 Jan;110(1):272-8

A puberty-related attenuation of opiate peptide-induced inhibition of LH secretion. Wilkinson M, et al. **Endocrinology** 1982 Mar;110(3):1046-8

Biosynthesis of pairs of peptides related to melanotropin, corticotropin and endorphin in the pars intermedia of the amphibian pituitary gland. Martens GJ, et al. **Eur J Biochem** 1982 Feb;122(1):1-10

270-MHz 1H nuclear-magnetic-resonance study of met-enkephalin in solvent mixtures. Conformational transition from dimethylsulphoxide to water. Zetta L, et al. **Eur J Biochem** 1982 Feb;122(1):215-22

In vivo potentiation of [D-Ala2]Met-enkephalin amide central effects after administration of an enkephalinase inhibitor. Algeri S, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):261-2

Phosphoryl-Leu-Phe: a potent inhibitor of the degradation of enkephalin by enkephalinase. Altstein M, et al. **Eur J Pharmacol** 1981 Dec 3; 76(2-3):299-300

Opiate agonists inhibit neurogenic plasma extravasation in the rat. Barthó L, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):101-4

Interaction of p-nitrophenylalanine enkephalins with mu-, delta- and kappa-subtypes of the opiate receptor. Fauchère JL, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):339-42

Opiate receptor-binding activity of [D-Thr2,Thz5]-and [D-Met2,Thz5]-enkephalinamides. Ferrara P, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):69-73

ACTH1-24 counteracts the prolactin-releasing effect of an opioid. Ferri S, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):143-5

Calcium-opiate antagonism in the periaqueductal grey (PGA) region. Guerrero-Muñoz F, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):417-9

Excitability of beta-endorphin, morphine and catecholamines of the vas deferens of the rat at different stages of development. Huidobro-Toro JP, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):115-8

Des-tyr-gamma-endorphin (DT gamma E) and pineal levels of melatonin and arginine vasopressin (AVP). King MG, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):271-4

Mixed type inhibition of [D-Ala2, D-Leu5]enkephalin binding to mu-opiate binding sites by mu-, but not by kappa-opiate ligands. Pfeiffer A, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):359-61

Dynorphins: similar relative potencies on mu, delta- and kappa-opiate receptors. Quirion R, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):467-8

A characterization of dynorphin-(1-13) on the guinea pig ileal longitudinal muscle. Vaught JL. **Eur J Pharmacol** 1981 Dec 17;76(4):453-6

Effect of enkephalins in the presence of the antibiotic bacitracin in the longitudinal muscle strip preparation from guinea-pig ileum. Aleixandre A, et al. **Experientia** 1981 Dec 15;37(12):1318-20

Biogenic amines and beta-endorphin responses in the rat vas deferens. Miranda H, et al. **Gen Pharmacol** 1982;13(1):45-8

Comparative immunocytochemical localization of putative opioid ligands in the central nervous system. Stengaard-Pedersen K, et al. **Histochemistry** 1981;73(1):89-114 (50 ref.)

Lipolytic and enkephalinase inhibitory activities of polypeptides from placental autolysate prepared for therapeutic purposes. Nencini P, et al. **Int J Tissue React** 1981 Dec;3(3-4):167-72

beta-Endorphin and deletion peptides. A correlation of opiate receptor affinity with helix potential. Hammonds RG Jr, et al. **J Biol Chem** 1982 Mar 25;257(6):2990-5

Opioid peptides in human plasma: evidence for multiple forms. Boarder MR, et al. **J Clin Endocrinol Metab** 1982 Apr;54(4):715-20

Presence of immunoreactive gamma-melanocyte-stimulating hormone, adrenocorticotropin, and beta-endorphin in human gastric antral mucosa. Tanaka I, et al. **J Clin Endocrinol Metab** 1982 Feb; 54(2):392-6

Localization of methionine-enkephalin, substance P, and somatostatin immunoreactivities in the main olfactory bulb of the hamster. Davis BJ, et al. **J Comp Neurol** 1982 Feb 1;204(4):377-83

Beta-lipotropin and beta-endorphin in physiological and surgical menopause. Genazzani AR, et al. **J Endocrinol Invest** 1981 Oct-Dec; 4(4):375-8

Degradation and oxidation of methionine enkephalin by human neutrophils. Turkall RM, et al. **J Lab Clin Med** 1982 Mar; 99(3):418-27

Endorphins and legal issues. Harrison J. **J Leg Med (Chicago)** 1981 Dec; 2(4):543-68

Serotonin and gamma-aminobutyric acid turnover after injection into the median raphe of substance P and D-ala-met-enkephalin amide. Forchetti CM, et al. **J Neurochem** 1982 May;38(5):1336-41

Light and electron microscopic localization of immunoreactive Leu-enkephalin in the monkey basal ganglia. DiFiglia M, et al. **J Neurosci** 1982 Mar;2(3):303-20

Dopamine and [D-ALA2, D-Leu5]enkephalin inhibit the electrically stimulated neurohypophyseal release of vasopressin in vitro: evidence for calcium-dependent opiate action. Lightman SL, et al. **J Neurosci** 1982 Jan;2(1):78-81

Degradation of exogenous enkephalin in the guinea-pig ileum: relative importance of aminopeptidase, enkephalinase and angiotensin converting enzyme activity. Geary LE, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):104-11

Evidence for a gamma-aminobutyric acid (GABA) mediation in the benzodiazepine inhibition of the release of Met5-enkephalin elicited by depolarization. Harsing LG Jr, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):616-20

The effect of acute opioid administration on the phosphorylation of rat striatal synaptic membrane proteins. Williams N, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):278-86

Endorphin-mental illness link far from proved [news] Check WA. **JAMA** 1982 Feb 5;247(5):570-1, 575-7

Beta-adrenergic stimulation induces an increase of the plasma levels of immunoreactive alpha-MSH, beta-endorphin, ACTH and of corticosterone. Berkenbosch F, et al. **Life Sci** 1981 Nov 30; 29(22):2249-56

Age-related changes in central nervous system enkephalins and substance P. Dupont A, et al. **Life Sci** 1981 Nov 30;29(22):2317-22

The role of endorphins in neuropsychiatry. **Mod Probl Pharmacopsychiatry** 1981;17:1-290

Stress, endorphins and psychosis. A hypothesis. Amir S, et al. **Mod Probl Pharmacopsychiatry** 1981;17:192-201

Action of [Des-Tyr1]-gamma-endorphin in schizophrenia. Emrich HM, et al. **Mod Probl Pharmacopsychiatry** 1981;17:279-86

beta-Endorphin studies in psychiatric patients. Gorelick DA, et al. **Mod Probl Pharmacopsychiatry** 1981;17:236-45

Electroconvulsive shock results in a functional activation of endorphin systems. Holaday JW, et al. **Mod Probl Pharmacopsychiatry** 1981; 17:142-57

Effects of neuroleptic drugs on endogenous opioid peptides in the rat. Höllt V. **Mod Probl Pharmacopsychiatry** 1981;17:1-18

Role of endorphins in endogenous pain control systems. Mayer DJ, et al. **Mod Probl Pharmacopsychiatry** 1981;17:68-96

Anxiolytic properties of opiates and endogenous opioid peptides and their relationship to the actions of benzodiazepines. Millan MJ, et al. **Mod Probl Pharmacopsychiatry** 1981;17:123-41

Stress and endogenous opioid peptides: a review. Millan MJ. **Mod Probl Pharmacopsychiatry** 1981;17:49-67

Detoxication treatment of schizophrenic patients: a possible role of endorphins? Nedopil N, et al. **Mod Probl Pharmacopsychiatry** 1981; 17:263-5

Measurement of endorphins in CSF. Relationship to psychiatric diagnosis. Pickar D, et al. **Mod Probl Pharmacopsychiatry** 1981;17:246-62

Localization and modulation of enkephalins, endorphins and opiate receptors in the CNS and the pituitary gland. Simantov R. **Mod Probl Pharmacopsychiatry** 1981;17:38-48

Neuroleptic-like and antipsychotic effects of gamma-type endorphins. Van Ree JM, et al. **Mod Probl Pharmacopsychiatry** 1981;17:266-78

Primary structure of the human Met- and Leu-enkephalin precursor and its mRNA. Comb M, et al. **Nature** 1982 Feb 25;295(5851):663-6

Co-occurrence of substance P-like and Leu-enkephalin-like immunoreactivities in neurones and fibres of avian nervous system. Erichsen JT, et al. **Nature** 1982 Feb 4;295(5848):407-10

Molecular cloning establishes proenkephalin as precursor of enkephalin-containing peptides. Gubler U, et al. **Nature** 1982 Jan 21; 295(5846):206-8

A carboxypeptidase processing enzyme for enkephalin precursors. Hook VY, et al. **Nature** 1982 Jan 28;295(5847):341-2

Identification of a beta-endorphin-like peptide in cultured human placental cells. Liotta AS, et al. **Nature** 1982 Feb 18;

295(5850):593-5

Cloning and sequence analysis of cDNA for bovine adrenal preproenkephalin. Noda M, et al. **Nature** 1982 Jan 21; 295(5846):202-6

Isolation and structure of dynorphin, an opioid peptide, from porcine duodenum. Tachibana S, et al. **Nature** 1982 Jan 28;295(5847):339-40

O-sulphated Leu-enkephalin in brain. Unsworth CD, et al. **Nature** 1982 Feb 11;295(5849):519-22

beta-Endorphin is processed differently in specific regions of rat pituitary and brain. Zakarian S, et al. **Nature** 1982 Mar 18;296(5854):250-2

Analgesic activity of enkephalin analogues containing aminophosphonic acid residues at C-terminal position. Mastalerz P, et al. **Naturwissenschaften** 1982 Jan;69(1):46-7

Immunoreactive beta-endorphin in the plasma, pituitary and hypothalamus of young and old male rats. Forman LJ, et al. **Neurobiol Aging** 1981 Winter;2(4):281-4

Elevation of Met5-enkephalin and beta-endorphin hypothalamic content in rats receiving anorectic drugs: differences between D-fenfluramine and D-amphetamine. Harsing LG Jr, et al. **Neuropharmacology** 1982 Feb;21(2):141-5

Effects of acute and chronic haloperidol treatment on the concentrations of immunoreactive beta-endorphin in plasma, pituitary and brain of rats. Höllt V, et al. **Neuropharmacology** 1982 Feb;21(2):147-54

Endorphins in schizophrenia. van Ree JM, et al. **Neuropharmacology** 1981 Dec;20(12B):1271-7 (93 ref.)

Ultrastructural immunocytochemical localization of enkephalin in the goldfish preoptic nucleus. Cumming R, et al. **Neurosci Lett** 1981 Dec 23;27(3):313-8

Dramatic increase in pineal melatonin levels in the rat after subcutaneous injection of Des-tyrosine1-gamma-endorphin. Geffard M, et al. **Neurosci Lett** 1981 Dec 23;27(3):329-34

Evidence for analgesic activity of beta-casomorphin in rats. Grecksch G, et al. **Neurosci Lett** 1981 Dec 23;27(3):325-8

Enkephalin-like immunoreactivity in the gustatory lobes and visceral nuclei in the brains of goldfish and catfish. Finger TE. **Neuroscience** 1981;6(12):2747-58

Enkephalin-like immunoreactivity in the mossy fiber pathway of the hippocampal formation of the tree shrew (Tupaia glis). Fitzpatrick D, et al. **Neuroscience** 1981;6(12):2485-94

Enkephalin immunoreactivity in Golgi cells and mossy fibers of mammalian, avian, amphibian and teleost cerebellum. Schulman JA, et al. **Neuroscience** 1981;6(11):2407-16

Endorphins, opiate receptors and their evolving biology. Smith JR, et al. **Pathobiol Annu** 1981;11:87-126 (212 ref.)

Plasma opioids in the first hours of life. Facchinetti F, et al. **Pediatr Res** 1982 Feb;16(2):95-8

Effect of beta-endorphin on the thermal excitability of preoptic neurons in the unanesthetized rabbit. Gordon CJ, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):397-401

Cardiopulmonary pharmacology of enkephalins in the conscious dog. Sander GE, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):403-7

The correlation between swim-stress induced antinociception and [3H] leu-enkephalin binding to brain homogenates in mice. Christie MJ, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):853-7

Method of sacrifice influences leucine enkephalin binding to mouse brain. Christie MJ, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):849-51

Kyotorphins affect aversive pecking in chicks. Kastin AJ, et al. **Physiol Behav** 1981 Dec;27(6):1073-6

beta-Endorphin: demonstration of a tertiary structure in aqueous solution. Nicolas P, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7290-3

Human lymphocyte production of corticotropin and endorphin-like substances: association with leukocyte interferon. Smith EM, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7530-4

Tetraethylammonium facilitates the stimulation-evoked loss of the enkephalins from the myenteric plexus of guinea-pig ileum. Corbett AD, et al. **Proc R Soc Lond [Biol]** 1981 Oct 14;213(1191):171-82

Differential effects of warm- and cold-ambient temperature on blood levels of beta-endorphin and prolactin in the rat. Deeter WT 3d, et al. **Proc Soc Exp Biol Med** 1981 Dec;168(3):369-72

Running elevates plasma beta-endorphin immunoreactivity and ACTH in untrained human subjects. Gambert SR, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):1-4

(Des-tyrosine1)-gamma-endorphin in schizophrenia: clinical, biochemical, and hormonal aspects. Verhoeven WM, et al. **Psychiatry Res** 1981 Dec;5(3):293-309

beta-Endorphin and beta-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. Brambilla F, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):321-30

The effect of a synthetic met-enkephalin analogue (FK 33-824) on gastric acid secretion and serum gastrin in man. Skov Olsen P, et al. **Scand J Gastroenterol** 1981;16(4):531-3

Dynorphin and vasopressin: common localization in magnocellular neurons. Watson SJ, et al. **Science** 1982 Apr 2;216(4541):85-7

[Opioid peptides] Neuzil E, et al. **Expos Annu Biochim Med** 1982; 35:161-214 (287 ref.) (Fre)

[Effect of cold stress on the concentrations in the hypothalamus, pituitary, and blood of beta-lipotropin and beta-endorphin in the rabbit] Petraglia F, et al. **Boll Soc Ital Biol Sper** 1981 Sep 30;57(18):1862-8 (Eng. Abstr.) (Ita)

[Effects of intrathecal beta-endorphin and morphine on post-operative pain (author's transl)] Taniguchi K, et al. **Masui** 1981 Oct; 30(10):1105-11 (Eng. Abstr.) (Jpn)

[Neuropeptides in the rabbit eye. I. RIA for beta-endorphin, substance P and neurotensin in the aqueous humor, iris-ciliary body and retina (author's transl)] Baba S, et al. **Nippon Ganka Gakkai Zasshi** 1981 Sep 10;85(9):1267-72 (Eng. Abstr.) (Jpn)

[Comparative action of met-enkephalin and gamma-endorphin on the neuronal reactions of the rabbit dorsomedial hypothalamus to electrocutaneous and acupuncture stimulation] Iasnetsov VV, et al. **Dokl Akad Nauk SSSR** 1981;260(6):1502-8 (Rus)

[Enkephalin inhibition of the electrical activity of the visual cortex of the left and right hemispheres] Pivovarov AS, et al. **Dokl Akad Nauk SSSR** 1981;261(1):240-4 (Rus)

[Reaction between methionine enkephalin and human lymphocytes] Zozulia AA, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):28-33 (Eng. Abstr.) (Rus)

ENURESIS

Treatment of enuresis with sydnocarb. Polák L, et al. **Act Nerv Super (Praha)** 1981;23(4):261-4

Nocturnal enuresis: an update on treatment. Schmitt BD. **Pediatr Clin North Am** 1982 Feb;29(1):21-36

EPHEDRINE

A study of the thermic responses to a meal and to a sympathomimetic drug (ephedrine) in relation to energy balance in man. Morgan JB, et al. **Br J Nutr** 1982 Jan;47(1):21-32

Selected cardiac and metabolic responses to pseudoephedrine with exercise. Bright TP, et al. **J Clin Pharmacol** 1981 Nov-Dec; 21(11-12 Pt 1):488-92

EPINEPHRINE

Effect of insulin and epinephrine on some early oestrogenic responses in the rat uterus. Steinsapir J, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):263-71

Role of some biogenic amines in the pathomechanism of glomerulonephritis. II. Adrenaline, noradrenaline and serotonin in acute serum sickness in rabbits. Gębala A, et al. **Acta Physiol Pol** 1981; 32(4):363-73

Role of some biogenic amines in the pathomechanism of glomerulonephritis. Zajączkowska M, et al. **Acta Physiol Pol** 1981; 32(4):375-82

Epinephrine potentiation of arachidonate-induced aggregation of cyclooxygenase-deficient platelets. Rao GH, et al. **Am J Hematol** 1981; 11(4):355-66

Renal handling of dopa, dopamine, norepinephrine, and epinephrine in the dog. Ball SG, et al. **Am J Physiol** 1982 Jan;242(1):F56-62

Rapid fluctuations in plasma catecholamines in monkeys under undisturbed conditions. Hansen BC, et al. **Am J Physiol** 1982 Jan; 242(1):E40-6

Parathyroid gland response to epinephrine: a rate-sensitivity mechanism. Jung A, et al. **Am J Physiol** 1982 Jan;242(1):R151-6

Catecholamine release and blood pressure changes induced by exercise in dogfish. Opdyke DF, et al. **Am J Physiol** 1982 Mar; 242(3):R306-10

Neural and extraneural catecholamine production by rat kidneys. Stephenson RK, et al. **Am J Physiol** 1982 Mar;242(3):F261-6

Urinary excretion of catecholamines in the night monkey (Aotus trivirgatus) (Primates, Cebidae). Peyrin L, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):345-56

The effect of echothiophate on the biphasic response of rabbit ocular pressure to dipivefrin. Mindel JS, et al. **Arch Ophthalmol** 1982 Jan; 100(1):147-51

Activation of hormone-sensitive lipase: disparity between evaluations in intact and disrupted fat cells. Salers P, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):813-8

In vitro desensitization of human lymphocytes by epinephrine. Krall JF, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):117-9

Catecholamine-stimulation of Cl- secretion in MDCK cell epithelium. Brown CD, et al. **Biochim Biophys Acta** 1981 Dec 7;649(2):427-35

Catecholamine content of chromaffin granule 'ghosts' isolated from bovine adrenal glands. Deupree JD, et al. **Biochim Biophys Acta** 1982 Feb 25; 714(3):471-8

The reversible inhibition by carbonyl cyanide m-chlorophenyl hydrazone of epinephrine-stimulated lipolysis in perifused isolated fat cells. Huber CT, et al. **Biochim Biophys Acta** 1981 Dec 23;666(3):462-7

Regulation of adrenergic stimulation of hepatic adenylate cyclase by divalent cations. Jackowski MM, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):74-83

Nitriphenol compound induces Ca-dependent exocytotic secretion of catecholamines by a direct effect on the plasma membranes of the adrenal medullary cells. Sorimachi M, et al. **Brain Res** 1982 Jan 28; 232(1):242-6

2,4-Dinitrophenol—mechanism of action. El-Guindy MM, et al. **Cell Mol Biol** 1981;27(5):399-402

Influence of somatostatin on plasma cyclic AMP and metabolic substrate responses to i.v. adrenaline and glucagon in humans. Nistrup Madsen S, et al. **Clin Endocrinol (Oxf)** 1981 Nov;15(5):431-7

Evidence for the involvement of central epinephrine systems in the regulation of luteinizing hormone, prolactin, and growth hormone release in female rats. Crowley WR, et al. **Endocrinology** 1982 Apr; 110(4):1102-7

Specific inhibition by glucocorticoids of the alpha 2-adrenergic stimulation of adrenocorticotropin release in rat anterior pituitary cells. Giguère V, et al. **Endocrinology** 1982 Apr;110(4):1225-30

Epinephrine-sensitive adenylyl cyclase activity in rabbit ovarian tissues. Hunzicker-Dunn M. **Endocrinology** 1982 Jan;110(1):233-40

Abnormalities of insulin secretory and lipolytic response to epinephrine produced by a high fat diet and electric stress in rats. Yamaguchi K, et al. **Endokrinologie** 1981 Dec;78(2-3):253-61

Discrepancy in the regulatory effects of sodium and guanine nucleotides on adrenaline and clonidine binding to alpha 2-adrenoceptors in human fat cell membranes. Gonzalez JL, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):289-93

Desensitization of the beta-adrenergic receptor-adenylate cyclase complex in rabbit iris-ciliary body induced by topical epinephrine. Mittag T, et al. **Exp Eye Res** 1981 Nov;33(5):497-503

Close relationship of mitochondria with intercellular junctions in the adrenaline cells of the mouse adrenal gland. Grynszpan-Winograd O. **Experientia** 1982 Feb 15;38(2):270-1

Chronic exercise does not alter the chronotropic response of isolated rat atria to catecholamines. Smith DC, et al. **Experientia** 1982 Feb 15; 38(2):260-1

Associations between rates of urinary catecholamine excretion and aspects of lifestyle among adult women in some Oxfordshire villages. Harrison GA, et al. **Hum Biol** 1981 Dec;53(4):617-33

Plasma catecholamines in trained and untrained volunteers during graduated exercise. Lehmann M, et al. **Int J Sports Med** 1981 Aug; 2(3):143-7

Studies of the interaction between glucagon and alpha-adrenergic agonists in the control of hepatic glucose output. Assimacopoulos-Jeannet FD, et al. **J Biol Chem** 1982 Apr 10;257(7):3759-65

The effects of age on the plasma catecholamine response to mental stress in man. Barnes RF, et al. **J Clin Endocrinol Metab** 1982 Jan; 54(1):64-9

Regulation of episodic growth hormone secretion by the central epinephrine system. Studies in the chronically cannulated rat. Terry LC, et al. **J Clin Invest** 1982 Jan;69(1):104-12

Effects of catecholamines on free fatty acid release from bone marrow adipose tissue. Tran MA, et al. **J Lipid Res** 1981 Nov;22(8):1271-6

(alpha S)-erythro-alpha-methylepinephrine: preparation and stereoselective binding to adrenergic receptors in rat forebrain. Taylor CA Jr, et al. **J Med Chem** 1981 Oct;24(10):1261-3

Changes in plasma noradrenaline and adrenaline associated with central and peripheral thermal stimuli in the pig. Barrand MA, et al. **J Physiol (Lond)** 1981 Jul;316:139-52

Calcium and the alpha-action of catecholamines on guinea-pig taenia caeci. Den Hertog A. **J Physiol (Lond)** 1981 Jul;316:109-25

Cimetidine alters plasma catecholamine levels and cortisol and aldosterone excretion [letter] Feely J, et al. **N Engl J Med** 1982 Apr 29; 306(17):1054

Neonatal adaptation: sympatho-adrenal response to umbilical cord cutting. Padbury JF, et al. **Pediatr Res** 1981 Dec;15(12):1483-7

Effect of epinephrine on glucose metabolism in kid liver slices. Machaňová L, et al. **Physiol Bohemoslov** 1981;30(6):573-6

Epinephrine induced myocardial necrosis: effects of aminophylline and adrenergic blockade. Blaiklock RG, et al. **Res Commun Chem Pathol Pharmacol** 1981 Nov;34(2):179-92

[Effects of adrenaline, noradrenaline and isoprenaline administration on carbohydrate and lipid metabolism parameters in swine blood plasma] Brenner KV, et al. **Arch Exp Veterinarmed** 1981;35(5):697-706 (Eng. Abstr.) (Ger)

[The aerobic and anaerobic capacity of adolescents and catecholamine excretion during prolonged submaximal exercise (author's transl)] Lehmann M, et al. **Eur J Applied Physiol** 1982;48(1):135-45 (Eng. Abstr.) (Ger)

[On the National Institute of Hygienic Sciences Standard (Japanese Pharmacopoeia Standard) 'Epinephrine Bitartrate Reference Standard (Control 781)' and 'Norepinephrine Bitartrate Reference Standard (Control 791)' (author's transl)] Kimura T, et al. **Eisei Shikenjo Hokoku** 1981;99:118-21 (Eng. Abstr.) (Jpn)

[Effects of adrenaline, noradrenaline and pilocarpine on the oxygen uptake in rat submandibular gland (author's transl)] Sakamoto S, et al. **Nippon Seirigaku Zasshi** 1981;43(10):469-78 (Eng. Abstr.) (Jpn)

[Effect of catecholamines on the morphological picture of the peripheral autonomic nervous system of the digestive tract of rats—light-microscopical study] Jędrzejewska A, et al. **Patol Pol** 1981; 32(2):233-42 (Eng. Abstr.) (Pol)

[Effect of adrenaline administration on the interrelation between free fatty acid concentration in the blood and platelet accumulation in the circulatory bed of the myocardium] Gereliuk IP. **Biull Eksp Biol Med** 1981 Dec;92(12):661-3 (Eng. Abstr.) (Rus)

[Morphologic changes in the hematopoietic organs of rats in response to adrenaline] Khil'ko AS, et al. **Fiziol Zh** 1982 Jan-Feb;28(1):40-5 (Eng. Abstr.) (Rus)

[Changes in intraocular pressure following local injection of catecholamines into the hypothalamus] Danilov GE, et al. **Fiziol Zh SSSR** 1981 Oct;67(10):1487-92 (Eng. Abstr.) (Rus)

[Determination of the adrenaline concentration in human saliva] Semenkova GN, et al. **Lab Delo** 1982;(1):15-7 (Eng. Abstr.) (Rus)

[Changes in the catecholamine content in adrenaline-synthetizing structures of the medulla oblongata in rats with different reactions to long-term immobilization] Kvetnansky R, et al. **Probl Endokrinol (Mosk)** 1981;27(6):58-63 (Eng. Abstr.) (Rus)

[Action of propranolol, nifenalol, and pindolol on the lipolytic effect of adrenaline in the rat epididymis] Sánchez-Cuadrado MC, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):181-2 (Spa)

ESCAPE REACTION

Increased serotonin level via augmented tryptophan diet and its effect on escape learning. Yehuda S, et al. **Int J Neurosci** 1981; 15(4):193-6

ESTRADIOL

Effect of 2-substituted oestrogens in vivo on the metabolism of noradrenaline in rat brain. Köster G, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):1-8

Effect of insulin and epinephrine on some early oestrogenic responses in the rat uterus. Steinsapir J, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):263-71

Release of LH in vitro from anterior pituitary glands of ovariectomized rats by LRH or elevated potassium concentration after pre-treatment with oestradiol benzoate in vivo. Tijssen AM, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):206-10

The effect of gonadotropin-releasing hormone on ovarian estradiol secretion. Kletzky OA, et al. **Am J Obstet Gynecol** 1982 Feb 15; 142(4):427-31

Involvement of GABA in the feedback action of estradiol on gonadotropin and prolactin release: hypothalamic GABA and catecholamine turnover rates. Mansky T, et al. **Brain Res** 1982 Jan 14;231(2):353-64

Comparative effects of estrogens and prolactin on nigral and striatal GAD activity. Nicoletti F, et al. **Brain Res** 1982 Jan 28;232(1):238-41

Effects of ovarian steroids on serotonin metabolism within grossly dissected and microdissected brain regions of the ovariectomized rat. Cone RI, et al. **Brain Res Bull** 1981 Dec;7(6):639-44

The luteinizing hormone-releasing hormone (LHRH) system in normal and estrogenized neonatal rats. Elkind-Hirsch K, et al. **Brain Res Bull** 1981 Dec;7(6):645-54

Somatostatin inhibits prolactin secretion in the estradiol primed male rat. Cooper GR, et al. **Can J Physiol Pharmacol** 1981 Oct;59(10):1082-8

Studies on the microheterogeneity of follicle-stimulating hormone present within the anterior pituitary gland of ovariectomized hamsters. Chappel SC, et al. **Endocrinology** 1982 Mar;110(3):847-54

Pituitary receptor sites for gonadotropin-releasing hormone: effect of castration and substitutive therapy with sex steroids in the male rat. Conne BS, et al. **Endocrinology** 1982 Jan;110(1):70-9

Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **Endocrinology** 1982 Mar;110(3):717-21

Estrogen in high doses inhibits perphenazine-induced prolactin release. Sinha YN, et al. **Endocrinology** 1982 Jan;110(1):126-30

Evaluation of Delestrogen and Parlodel as a luteolytic agent in humans. Blackwell RE, et al. **Fertil Steril** 1982 Feb;37(2):213-7

The luteolytic and abortifacient potential of an estrogen-bromergocryptine regimen in the baboon. Castracane VD, et al. **Fertil Steril** 1982 Feb;37(2):258-62

Inhibin-like activity and steroid content in human follicular fluid during the periovulatory period. Lefevre B, et al. **Int J Fertil** 1981; 26(4):295-6

Effect of oestrogen on gonadotrophin release in stumptailed monkeys (Macaca arctoides) treated chronically with an agonist analogue of luteinizing hormone releasing hormone. Fraser HM. **J Endocrinol** 1981 Dec;91(3):525-30

Effects of estradiol on norepinephrine and prostaglandin efflux in medial basal hypothalamus of ovariectomized rats. Cardinali DP, et al. **J Neural Transm** 1982;53(1):39-47

Modulation by estradiol of serotonin receptors in brain. Biegon A, et al. **J Neurosci** 1982 Feb;2(2):199-205

Motor activity of the human Fallopian tube in vitro in relation to plasma concentration of oestradiol and progesterone, and the influence of noradrenaline. Heim G, et al. **J Reprod Fertil** 1982 Jan;64(1):233–42

Comparison of steroid and LH-RH effects on the responsiveness of hemipituitary glands and dispersed pituitary cells. Speight A, et al. **Mol Cell Endocrinol** 1981 Dec;24(3):267–81

Dissociation of the effects of gonadal steroids on brain serotonin metabolism and sexual behavior in the male rat. Bradshaw WG, et al. **Neuroendocrinology** 1982 Jan;34(1):38–45

Differential effects of low serum levels of estradiol-17 beta on hypothalamic LHRH levels and LH secretion in castrated male rats. Kalra PS, et al. **Neuroendocrinology** 1981 Dec;33(6):340–6

Temporal and other effects of catechol estrogens on prolactin secretion in the rat. Shin SH, et al. **Neuroendocrinology** 1981 Dec;33(6):352–7

Prepuberal ontogeny of responsiveness to estradiol in female rat central nervous system. Dudley SD. **Neurosci Biobehav Rev** 1981 Winter; 5(4):421–35 (238 ref.)

[Ureteral response, through adrenergic stimulation, to the action of progesterone and estradiol] García Sacristán A, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):129–32 **(Spa)**

EXPLORATORY BEHAVIOR

Behavior during hippocampal microinfusions. I. Norepinephrine and diversive exploration. Flicker C, et al. **Brain Res** 1982 Mar; 237(1):79–103

Arginine vasotocin: effects on open field behavior, whole brain monoamines and plasma corticosterone. Golus P, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):437–40

Cholecystokinin reduces exploratory behavior in mice. Crawley JN, et al. **Physiol Behav** 1981 Sep;27(3):407–11

EXTINCTION (PSYCHOLOGY)

Failure to obtain functional equivalence between dopamine receptor blockade and extinction: evidence supporting a sensory-motor conditioning hypothesis. Tombaugh TN, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):67–72

FEAR

Two opposite effects of diazepam on fear by differential training in the CER-paradigm. Haug T, et al. **Psychopharmacology (Berlin)** 1981; 75(2):110–3

[Role of corticosteroids in the development of fear and aggression reactions] Malyshenko NM. **Zh Vyssh Nerv Deiat** 1982 Jan–Feb; 32(1):144–51 (Eng. Abstr.) **(Rus)**

FENFLURAMINE

Kinetics of fenfluramine isomers in the rat. Caccia S, et al. **Eur J Drug Metab Pharmacokinet** 1981;6(4):297–301

Drug preferences in humans. Johanson CE, et al. **Fed Proc** 1982 Feb; 41(2):228–3?

Central mechanisms of fenfluramine and related anorectic drugs. Garattini S. **Jpn J Pharmacol** 1981;31 Suppl:29P–35P (26 ref.)

Elevation of Met5-enkephalin and beta-endorphin hypothalamic content in rats receiving anorectic drugs: differences between D-fenfluramine and D-amphetamine. Harsing LG Jr, et al. **Neuropharmacology** 1982 Feb;21(2):141–5

Ontogeny of fenfluramine and amphetamine anorexia compared in rat pups. Leshem M. **Pharmacol Biochem Behav** 1981 Dec;15(6):?59–63

The effects of quipazine, fenfluramine and apomorphine on the morphine potentiation of tonic immobility. Wallnau LB. **Pharmacol Biochem Behav** 1981 Dec;15(6):895–901

FLUPHENAZINE

Fluphenazine and flupenthixol decanoate in psychiatric outpatients practice. Coufal J, et al. **Act Nerv Super (Praha)** 1981;23(4):269–71

Plasma imipramine concentrations in patients receiving concomitant fluphenazine decanoate. Siris SG, et al. **Am J Psychiatry** 1982 Jan; 139(1):104–6

Fluphenazine vs placebo in patients with remitted, acute first-episode schizophrenia. Kane JM, et al. **Arch Gen Psychiatry** 1982 Jan; 39(1):70–3

Calmodulin is involved in the first step of oocyte maturation: effects of the antipsychotic drug fluphenazine and of anticalmodulin antibodies on the progesterone-induced maturation of xenopus laevis oocyte. Cartaud A, et al. **Cell Differ** 1981 Dec;10(6):357–63

Effects of age on dopaminergic supersensitivity induced by chronic fluphenazine. Misra CH, et al. **Commun Psychopharmacol** 1980; 4(5):411–5

Influence of age on the effects of chronic fluphenazine on receptor binding in rat brain. Misra CH, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):317–24

Chronic treatment with haloperidol or fluphenazine decanoate: regional effects on dopamine and serotonin metabolism in primate brain. Bacopoulos NG, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):22–8

Treatment of unstable detrusor (irritable bladder) using fluphenazine and nortriptyline: progress report. Martin MR, et al. **Prog Clin Biol Res** 1981;78:335–8

The use of fluphenazine decanoate (Modecate)depot therapy in outpatient schizophrenics-a retrospective study. Tan CT, et al. **Singapore Med J** 1981 Aug;22(4):214–8

[Clinical observation on the effect of domestic fluphenazine decanoate in the treatment of schizophrenia---report of 431 cases (author's transl)] Zhang YF. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1981 Aug; 14(3):182–5 **(Chi)**

[Treatment of schizophrenic psychoses by sustained-action neuroleptics in psychiatric outpatients' treatment (author's transl)] Poláček J. **Cesk Psychiatr** 1982 Feb;78(1):49–55 (Eng. Abstr.) **(Cze)**

[Comparison between the effectiveness of fluphenazine decanoate and oxyprothepin decanoate in schizophrenia (double-blind crossover study)] Balon R, et al. **Zh Nevropatol Psikhiatr** 1982;82(1):116–8 (Eng. Abstr.) **(Rus)**

[Follow-up study of patients treated with depot phenothiazines in Valparaiso, Chile] Michel G, et al. **Bol Of Sanit Panam** 1981 Nov; 91(5):418–27 (Eng. Abstr.) **(Spa)**

FLURAZEPAM

Assay of flunitrazepam, temazepam and desalkylflurazepam in plasma by capillary gas chromatography with electron-capture detection. Jochemsen R, et al. **J Chromatogr** 1982 Jan 8;227(1):199–206

GLC-ECD determination of 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1,3-dihydro-5-(O-fluorophe (SAS 643) in plasma and urine and identification of its main biotransformation products. Mardente S, et al. **Ther Drug Monit** 1981; 3(4):351–6

Quantitative EEG and behavioral effects in volunteers of a new benzodiazepine (SAS 643) in relation to drug plasma concentration. Sannita WG, et al. **Ther Drug Monit** 1981;3(4):341–9

FOOD DEPRIVATION

Effect of food deprivation on rat gastric somatostatin and gastrin release. Koop H, et al. **Gastroenterology** 1982 May;82(5 Pt 1):871–6

Mild zinc deficiency and undernutrition during the prenatal and postnatal periods in rats: effects on weight, food consumption, and brain catecholamine concentrations. Halas ES, et al. **J Nutr** 1982 Mar; 112(3):542–51

Effects of early overnutrition and undernutrition in rats on the metabolic responses to overnutrition in later life. Rothwell NJ, et al. **J Nutr** 1982 Mar;112(3):426–35

FSH

Gonadotrophin releasing hormone causes a biphasic secretion of luteinizing hormone and follicle stimulating hormone by cultures of rat anterior pituitary cells. Eddie LW, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):44–9

The role of catecholamines in the regulation of pituitary luteinizing hormone and follicle-stimulating hormone secretion. Barraclough CA, et al. **Endocr Rev** 1982 Winter;3(1):91–119 (268 ref.)

Norepinephrine in Graafian follicles is depleted by follicle-stimulating hormone. Ben-Jonathan N, et al. **Endocrinology** 1982 Feb; 110(2):457–61

Studies on the microheterogeneity of follicle-stimulating hormone present within the anterior pituitary gland of ovariectomized hamsters. Chappel SC, et al. **Endocrinology** 1982 Mar;110(3):847–54

Intraventricular injection of follicle-stimulating hormone (FSH) during proestrus stimulates the rise in serum FSH on estrus in phenobarbital-treated hamsters through a central nervous system-dependent mechanism. Coutifaris C, et al. **Endocrinology** 1982 Jan;110(1):105–13

Melatonin directly inhibits rat gonadotroph cells. Martin JE, et al. **Endocrinology** 1982 Apr;110(4):1079–84

Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **Endocrinology** 1982 Mar;110(3):717–21

Effect of pulsatile gonadotropin-releasing hormone on the release of luteinizing hormone and follicle-stimulating hormone in vitro by anterior pituitaries from lactating and cycling rats. Smith MS. **Endocrinology** 1982 Mar;110(3):882–91

Regulation of tonic gonadotropin release in prepubertal female hamsters. Smith SG 3d, et al. **Endocrinology** 1982 Apr;110(4):1262–7

Basal and GnRH-induced release and synthesis of LH and FSH from incubated pituitary glands throughout the 4-day estrous cycle of the rat. Apfelbaum ME. **Horm Res** 1981;15(2):109–21

Further studies of the effects of intravenous infusion or intramuscular injection of gonadotropin-releasing hormone during childhood and adolescence. Reiter EO, et al. **J Adolesc Health Care** 1981 Jun; 1(4):275–81

Development of a homologous radioimmunoassay for ovine follicle stimulating hormone: studies after estrus, ovariectomy, estradiol and releasing hormone. Bolt DJ. **J Anim Sci** 1981 Sep;53(3):730–41

Effects of porcine follicular fluid on gonadotropin concentrations in rhesus monkeys. Rettori V, et al. **J Clin Endocrinol Metab** 1982 Mar; 54(3):500–3

Effects of LHRH and long–acting LHRH on serum LH and FSH levels of healthy women. Bartfai G, et al. **J Endocrinol Invest** 1981 Jul–Sep; 4(3):359–62

Pituitary cell cultures as a tool for the studies on the GnRH–induced release and biosynthesis of gonadotropins. Jutisz M, et al. **Mater Med Pol** 1980 Jan–Jun;12(1–2):53–62

[Studies on the feedback regulation of gonadotropin concentrations in male rats (I). The effects of hypothalamic implantation of testosterone and its metabolites on gonadotropin release in castrated male rats (author's transl)] Noguchi K. **Nippon Naibunpi Gakkai Zasshi** 1981 Aug 20;57(8):1139–47 (Eng. Abstr.) **(Jpn)**

GABA

The action of putative neurotransmitter substances in the cat labyrinth. Felix D, et al. **Acta Otolaryngol (Stockh)** 1982 Jan–Feb; 93(1–2):101–5

GABA and the basal ganglia. **Adv Biochem Psychopharmacol** 1981; 30:1–241

Interactions between GABA, dopamine, acetylcholine, and glutamate–containing neurons in the extrapyramidal and limbic systems. Bartholini G, et al. **Adv Biochem Psychopharmacol** 1981;30:119–28

Evidence in favour of GABA as an inhibitory transmitter in the rat striatum. Bernardi G, et al. **Adv Biochem Psychopharmacol** 1981; 30:69–77

In vivo release of 3H–GABA synthesized from 3H–Glutamine in the substantia nigra and the pallido entopeduncular nuclei in the cat. Besson MJ, et al. **Adv Biochem Psychopharmacol** 1981;30:95–103

Role of GABA neurons in the expression of striatal motor functions. Di Chiara G, et al. **Adv Biochem Psychopharmacol** 1981;30:129–63 (77 ref.)

Electrophysiological studies of GABAergic neurons in the basal ganglia: nigro–collicular, nigro–thalamic, and pallido–subthalamic neurons. Feger J. **Adv Biochem Psychopharmacol** 1981;30:53–68

Evidence for the involvement of nigrothalamic GABA neurons in circling behaviour in the rat. Kilpatrick IC, et al. **Adv Biochem Psychopharmacol** 1981;30:205–24

Distribution and release of GABA in the basal ganglia. Korf J, et al. **Adv Biochem Psychopharmacol** 1981;30:105–17

The GABAergic neurons of the extrapyramidal system as revealed by immunocytochemistry. Ribak CE. **Adv Biochem Psychopharmacol** 1981; 30:23–36

Role of GABA in the striatal output system: globus pallidus, nucleus entopeduncularis, substantia nigra and nucleus subthalamicus. Scheel–Krüger J, et al. **Adv Biochem Psychopharmacol** 1981; 30:165–86 (92 ref.)

Single unit responses of substantia nigra and globus pallidus neurons to GABA agonist and antagonist drugs. Waszczak BL, et al. **Adv Biochem Psychopharmacol** 1981;30:79–94

The GABAergic systems and the role of basal ganglia in motor control. Yoshida M. **Adv Biochem Psychopharmacol** 1981;30:37–52

Differential effects of light and dark adaptations on function and metabolism of retinal taurine and gamma–aminobutyric acid (GABA). Kuriyama K, et al. **Adv Exp Med Biol** 1981;139:221–38

CSF levels of gamma–aminobutyric acid in schizophrenia. Low values in recently ill patients. van Kammen DP, et al. **Arch Gen Psychiatry** 1982 Jan;39(1):91–7

Inhibition of neuronal GABA uptake and glial beta–alanine uptake by synthetic GABA analogues. Breckenridge RJ, et al. **Biochem Pharmacol** 1981 Nov 15;30(22):3045–9

Inhibition by apomorphine of the potassium–evoked release of [3H]–gamma–aminobutyric acid from the rat substantia nigra in vitro. Arbilla S, et al. **Br J Pharmacol** 1981 Oct;74(2):389–97

Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Glickman RD, et al. **Brain Res** 1982 Feb 18;234(1):81–99

GABA uptake and release in purified neuronal and nonneuronal cultures from chick embryo retina. Hyndman AG, et al. **Brain Res** 1982 Feb; 255(2):167–80

Involvement of GABA in the feedback action of estradiol on gonadotropin and prolactin release: hypothalamic GABA and catecholamine turnover rates. Mansky T, et al. **Brain Res** 1982 Jan 14;231(2):353–64

Release of GABA from the guinea–pig neocortex induced by electrical stimulation of the 'locus coeruleus' or by norepinephrine. Moroni F, et al. **Brain Res** 1982 Jan 28;232(1):216–21

Dopamine blocks carrier–mediated release of GABA from retinal horizontal cells. Yazulla S, et al. **Brain Res** 1982 Feb 4;233(1):211–5

Chemoreceptors for serotonin (5–HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma–aminobutyric acid (GABA) on rabbit visceral afferent neurons. Higashi H, et al. **Brain Res Bull** 1982 Jan; 8(1):23–32

Ontogeny of 3H–diazepam binding sites in different rat brain area. Effect of GABA. Aldinio C, et al. **Dev Neurosci** 1981;4(6):461–6

Affinity of thiocolchicoside and thiocolchicoside analogues for the postsynaptic GABA receptor site. Biziere K, et al. **Eur J Pharmacol** 1981 Oct 22;75(2–3):167–8

Endogenous GABA determines the characteristics of [3H]GABA–binding. Gardner CR, et al. **Eur J Pharmacol** 1981 Oct 22;75(2–3):83–92

The effect of GABA antagonism on propulsive activity of the guinea–pig large intestine. Krantis A, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):111–4

Depolarizing IPSPs and Depolarization by GABA of rat neostriatum cells in vitro. Misgeld U, et al. **Exp Brain Res** 1982;45(1–2):108–14

K+–stimulated release of endogenous glutamate, GABA and other amino acids from neuron– and glia–enriched cultures of the rat cerebellum. Pearce BR, et al. **FEBS Lett** 1981 Nov 30;135(1):215–8

Liposome–induced changes in the uptake of GABA and glutamate in mouse brain in vitro. Dam M, et al. **Ital J Neurol Sci** 1981 Dec; 2(4):375–7

Plasma GABA in affective illness. A preliminary investigation. Petty F, et al. **J Affective Disord** 1981 Dec;3(4):339–43

Determination of gamma–aminobutyric acid by liquid chromatography with electrochemical detection. Caudill WL, et al. **J Chromatogr** 1982 Feb 12;227(2):331–9

Possible inhibitory influence of gamma–aminobutyric acid on growth hormone secretion in the rat. Fiók J, et al. **J Endocrinol** 1981 Dec; 91(3):391–7

Inhibition of [3H]GABA binding to postsynaptic receptors in human cerebellar synaptic membranes by carboxyl and amino derivatives of GABA. Breckenridge RJ, et al. **J Neurochem** 1981 Oct;37(4):837–44

Pyrrolines as prodrugs of gamma–aminobutyric acid analogues. Callery PS, et al. **J Neurochem** 1982 Apr;38(4):1063–7

Phosphatidylserine enhancement of [3H]gamma–aminobutyric acid uptake by rat whole brain synaptosomes. Chweh AY, et al. **J Neurochem** 1982 Mar;38(3):691–5

In vitro effect of tetanus toxin on GABA release form rat hippocampal slices. Collingridge GL, et al. **J Neurochem** 1981 Oct;37(4):1039–41

Higher GABA concentrations in fallopian tube than in brain of the rat. Erdö SL, et al. **J Neurochem** 1982 Apr;38(4):1174–6

The binding of the GABA agonist [3H]THIP to rat brain synaptic membranes. Falch E, et al. **J Neurochem** 1982 Apr;38(4):1123–9

A regional study of 4–aminobutyrate metabolism and amino acid levels in rat brain following chronic oral administration of ethanolamine O–sulphate. Fletcher A, et al. **J Neurochem** 1982 Apr;38(4):1022–8

The topographical distribution of alanine, aspartate, gamma–aminobutyric acid, glutamate, glutamine, and glycine in the pigeon optic tectum and the effect of retinal ablation. Fonnum F, et al. **J Neurochem** 1982 Apr; 38(4):1130–4

Serotonin and gamma–aminobutyric acid turnover after injection into the median raphe of substance P and D–ala–met–enkephalin amide. Forchetti CM, et al. **J Neurochem** 1982 May;38(5):1336–41

Neuronal and glial release of [3H]GABA from the rat olfactory bulb. Jaffé EH, et al. **J Neurochem** 1981 Dec;37(6):1457–66

Effect of homo–beta–proline and other heterocyclic GABA analogues on GABA uptake in neurons and astroglial cells and on GABA receptor binding. Larsson OM, et al. **J Neurochem** 1981 Dec;37(6):1509–16

Ethylenediamine as a specific releasing agent of gamma–aminobutyric acid in rat striatal slices. Lloyd HG, et al. **J Neurochem** 1982 Apr; 38(4):1168–9

Transport of GABA at the blood–CSF interface. Löscher W, et al. **J Neurochem** 1982 Apr;38(4):1072–9

Comparative effects of chronic haloperidol and sulpiride treatment on nigral and striatal GABA content. Nicoletti F, et al. **J Neurochem** 1981 Oct;37(4):1048–51

Effects of anticonvulsants on the formation of gamma–hydroxybutyrate from gamma–aminobutyrate in rat brain. Whittle SR, et al. **J Neurochem** 1982 Mar;38(3):848–51

Interactions of di–n–propylacetate, gabaculine, and aminooxyacetic acid: anticonvulsant activity and the gamma–aminobutyrate system. Wood JD, et al. **J Neurochem** 1981 Dec;37(6):1440–7

The uptake of [3H]gamma–aminobutyric acid by isolated glial (Müller) cells from the mouse retina. Sarthy PV. **J Neurosci Methods** 1982 Jan; 5(1–2):77–82

Evidence for a gamma–aminobutyric acid (GABA) mediation in the benzodiazepine inhibition of the release of Met5–enkephalin elicited by depolarization. Harsing LG Jr, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):616–20

gamma–Aminobutyric acid (GABA) receptor stimulation. II. Specificity of progabide (SL 76002) and SL 75102 for the GABA receptor. Lloyd KG, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):672–7

Valproic acid: brain and plasma levels of the drug and its metabolites, anticonvulsant effects and gamma–aminobutyric acid (GABA) metabolism in the mouse. Nau H, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):654–9

gamma–Aminobutyric acid (GABA) receptor stimulation. IV. Effect of progabide (SL 76002) and other GABAergic agents on acetylcholine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):689–95

gamma–Aminobutyric acid (GABA) receptor stimulation. III. Effect of progabide (SL 76002) on norepinephrine, dopamine and

5-hydroxytryptamine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):678–88

Comparison of the effects of GABA and chloride ion on the affinities of ligands for the benzodiazepine receptor. Fujimoto M, et al. **Life Sci** 1982 Jan 4;30(1):51–7

Sodium valproate exerts anti-conflict activity in rats without any concomitant rise in forebrain GABA level. Rasmussen KJ, et al. **Life Sci** 1981 Nov 23;29(21):2163–70

Comparison of content with synthesis, uptake and breakdown of GABA in substantia nigra of unoperated, hemitransected and kainate-treated rats. Starr M, et al. **Life Sci** 1981 Nov 30;29(22):2281–7

Halide- and gamma-aminobutyric acid-induced enhancement of diazepam receptors in rat brain. Reversal by disulfonic stilbene blockers of anion channels. Costa T, et al. **Mol Pharmacol** 1981 Nov;20(3):470–6

gamma-Aminobutyric acid enhancement of CL 218,872 affinity and evidence of benzodiazepine receptor heterogeneity. Regan JW, et al. **Mol Pharmacol** 1981 Nov;20(3):477–83

Effects of intraventricular gamma-acetylenic-GABA on GABA concentrations, GABA-T and GAD in several areas of the chick brain. Nisticò G, et al. **Monogr Neural Sci** 1981;5:34–9

Vertical organization of neurones accumulating 3H-GABA in visual cortex of rhesus monkey. Somogyi P, et al. **Nature** 1981 Dec 24; 294(5843):761–3

GABA-ergic mechanisms in central respiratory control in the anesthetized rat. Hedner J, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981; 317(4):315–20

Gaba induced excitatory responses in the guinea-pig small intestine are antagonized by bicuculline, picrotoxinin and chloride ion blockers. Krantis A, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov; 317(3):257–61

Functional interaction between benzodiazepine and GABA recognition sites in aged rats. Calderini G, et al. **Neurobiol Aging** 1981 Winter; 2(4):309–13

Neurochemical effects of kojic amine, a GABAmimetic and its interaction with benzylamine oxidase. Ferkany JW, et al. **Neuropharmacology** 1981 Dec;20(12A):1177–82

The activity of cis and trans -2- (aminomethyl) cyclopropane carboxylic acids on GABA - related mechanisms in the central nervous system of Limulus and Periplanata and of mammals. Gardner CR, et al. **Neuropharmacology** 1982 Feb;21(2):197–200

Effect of metabolites of valproic acid on the metabolism of GABA in brain and brain nerve endings. Löscher W, et al. **Neuropharmacology** 1981 Dec;20(12A):1187–92

Simultaneous reduction in the turnover rates of septal gamma-aminobutyric acid and hippocampal acetylcholine following administration of nabilone. Revuelta AV, et al. **Neuropharmacology** 1981 Nov;20(11):1111–4

Further evidence for GABA-like action on kojic amine. Martin GE, et al. **Neurosci Lett** 1981 Nov 18;27(1):37–40

Desensitization-like changes in GABA receptor binding of rat fascia dentata after entorhinal lesion. Nadler JV. **Neurosci Lett** 1981 Nov 4; 26(3):275–81

Inhibitory conductance changes and action of gamma-aminobutyrate in rat hippocampus. Ben-Ari Y, et al. **Neuroscience** 1981;6(12):2445–63

Primary monolayer cultures of the rat corpus striatum: morphology and properties related to acetylcholine and gamma-aminobutyrate. Messer A. **Neuroscience** 1981;6(12):2677–87

Decreased uptake of GABA by dorsal ganglia in methylmercury-treated rats. Araki K, et al. **Neurotoxicology (Park Forest II)** 1981 Nov; 2(3):557–66

The effects of acute administration of diazepam on the binding of [3H]-diazepam and [3H]-gaba to rat cortical membranes. Coupet J, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):965–8

gamma-Aminobutyric acid in brain areas of isolated aggressive or non-aggressive inbred strains of mice. Simler S, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):57–61

Evidence of a role for GABA in benzodiazepine effects on food preference in rats. Hodges HM, et al. **Psychopharmacology (Berlin)** 1981; 75(3):305–10

Gnawing and changes in reactivity produced by microinjections of picrotoxin into the superior colliculus of rats. Redgrave P, et al. **Psychopharmacology (Berlin)** 1981;75(2):198–203

Involvement of GABA in ganglion cell receptive field organization in the frog retina. Bonaventure N, et al. **Vision Res** 1981;21(11):1653–5

Effect of synaptic transmitter drugs on receptive fields of rabbit retinal ganglion cells. Daw NW, et al. **Vision Res** 1981;21(11):1643–7

[The effects of phenobarbitone on the inhibitory action of GABA (author's transl)] Kaneko S, et al. **No To Shinkei** 1982 Jan;34(1):77–84 (Eng. Abstr.) **(Jpn)**

[Function of gamma-aminobutyric acid in central nervous system (author's transl)] Matsuda M. **Seikagaku** 1981;53(7):517–22 (24 ref.) **(Jpn)**

[Atypical antidepressants: effect on synaptosomal uptake of serotonin and GABA] Avdulov NA, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):564–6 (Eng. Abstr.) **(Rus)**

[Primary afferent depolarization induced by gamma-aminobutyric acid injected into the central canal of the spinal cord in the cat] Kozhechkin SN, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):703–5 (Eng. Abstr.) **(Rus)**

[Effect of GABA isonicotinoylamide on cerebral circulation] Mirzoian RS, et al. **Biull Eksp Biol Med** 1981 Nov;92(11):573–4 (Eng. Abstr.) **(Rus)**

[Effect of intrahypothalamic administration of gamma-aminobutyric acid on hypothalamic temperature and overall body-heat production] Arutunian RA. **Fiziol Zh SSSR** 1981 Oct;67(10):1480–6 (Eng. Abstr.) **(Rus)**

[Effect of hydrocortisone on gamma-aminobutyric acid content and glutamate decarboxylase activity in various areas of the rat brain] Kononenko VIa, et al. **Ukr Biokhim Zh** 1982;54(1):31–5 (Eng. Abstr.) **(Rus)**

[Seasonal changes in the gamma-aminobutyric acid system of the mouse brain] Rozanov VA. **Ukr Biokhim Zh** 1982;54(1):36–40 (Eng. Abstr.) **(Rus)**

[Physicochemical heterogeneity of the GABA receptors and the detection of the differences in their structural relation with benzodiazepine receptors] Korneev AIa, et al. **Zh Nevropatol Psikhiatr** 1981; 81(11):1661–2 (Eng. Abstr.) **(Rus)**

[Effect of GABA on motor activity in the rat during the early postnatal period] Malakhovskaia DB, et al. **Zh Vyssh Nerv Deiat** 1982 Jan–Feb; 32(1):115–21 (Eng. Abstr.) **(Rus)**

GLUCURONIDASE

The beta-glucuronidase catalyzed hydrolysis of a glucopyranosiduronamide and a glucopyranoside: evidence for the oxocarbonium ion mechanism for bovine liver beta-glucuronidase. Parker A, et al. **Biochem Biophys Res Commun** 1981 Dec 31; 103(4):1390–4

Sequential hydrolysis of hyaluronate by beta-glucuronidase and beta-N-acetylhexosaminidase. Longas MO, et al. **Biochem J** 1981 Aug 1;197(2):275–82

O-and C-D-glucosyluronic acid derivatives of delta 1-tetrahydrocannabinol: synthesis and differential behavior to beta-glucuronidase. Zehavi U, et al. **Carbohydr Res** 1981 Dec 1; 98(1):143–7

Morphine glucuronide hydrolysis: superiority of beta-glucuronidase from Patella vulgata. Combie J, et al. **Clin Chem** 1982 Jan;28(1):83–6

The antiandrogenic action of gonadotropin-releasing hormone and its agonists on the mouse kidney. Lecomte P, et al. **Endocrinology** 1982 Jan;110(1):1–6

Studies on the possible involvement of complement component C3 in the initiation of acid hydrolase secretion by macrophages. Riches DW, et al. **Immunology** 1982 Mar;45(3):473–81

The selective polymorphonuclear neutrophils (PMN) degranulation as the probable additional mechanism of the hemodialysis (HD)-induced complement activation. Wysocki H, et al. **Int J Artif Organs** 1981 Jul; 4(4):174–7

Separation and properties of two enzyme forms of beta-glucuronidase from the mollusc Helicella ericetorum. Reglero A, et al. **Int J Biochem** 1981;13(11):1185–9

Cloning and endonuclease restriction analysis of uidA and uidR genes in Escherichia coli K-12: determination of transcription direction for the uidA gene. Blanco C, et al. **J Bacteriol** 1982 Feb;149(2):587–94

Reactivity of epidermal Langerhans cells to a histochemical method for demonstration of beta-glucuronidase. Mackenzie IC, et al. **J Invest Dermatol** 1982 Mar;78(3):239–42

Acid mucopolysaccharide and one of its glomerular degrading enzymes beta-glucuronidase in experimental and human glomerulonephritis. Matsuo E, et al. **Renal Physiol** 1980;3(1–6):97–105

GONADOTROPINS, PITUITARY

Ultrastructural evidence of gonadotrophin release from castration cells following injection of LHRH in the rat. Shiino M. **Cell Tissue Res** 1982 Jan;222(1):213–22

Effect of oestrogen on gonadotrophin release in stumptailed monkeys (Macaca arctoides) treated chronically with an agonist analogue of luteinizing hormone releasing hormone Fraser HM. **J Endocrinol** 1981 Dec;91(3):525–30

Effect of passive immunization against LH-RH on gonadotropin secretion in the ferret. Gledhill B, et al. **J Reprod Fertil** 1982 Jan;64(1):19–23

GUANETHIDINE

Impairment of trophic response of brown fat to cold in guanethidine-treated rats. Mory G, et al. **Am J Physiol** 1982 Mar; 242(3):C159–65

Comparative studies of (—)-, (+/-)-propranolol, atenolol, guanethidine, bretylium and tetracaine on adrenergic transmission. Kaiho M, et al. **Br J Pharmacol** 1981 Oct;74(2):365–70

Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Brown OM, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):911–4

HABITUATION (PSYCHOPHYSIOLOGY)

Enhanced responsiveness of alpha-noradrenergic receptors following discrete electrolytic lesions of the nucleus locus coeruleus: a behavioral demonstration. De Carvalho LP, et al. **J Neural Transm** 1982; 53(1):23-37

HALOPERIDOL

Stability of haloperidol in 5% dextrose injection. Das Gupta V, et al. **Am J Hosp Pharm** 1982 Feb;39(2):292-4

Physostigmine and haloperidol treatment of acute phencyclidine intoxication. Castellani S, et al. **Am J Psychiatry** 1982 Apr; 139(4):508-10

Unintentional haloperidol abuse [letter] Jack RA. **Am J Psychiatry** 1982 Feb;139(2):258

Questions about combined lithium and haloperidol treatment [letter] Rudorfer MV, et al. **Am J Psychiatry** 1982 Apr;139(4):537-8

High doses of haloperidol in schizophrenia. A clinical, biochemical, and pharmacokinetic study. Zarifian E, et al. **Arch Gen Psychiatry** 1982 Feb; 39(2):212-5

Subsensitivity of the presynaptic dopamine receptors in cat heart after the termination of chronic haloperidol treatment. Verimer T, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):233-40

Effect of haloperidol on adrenal ornithine decarboxylase activity of the rat. Almazan G, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):131-6

Long-term effects of nigro-striatal denervation of striatal [3H]haloperidol binding. Feuerstein C, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):457-60

Lithium dissociates haloperidol-induced behavioral supersensitivity from reduced dopac increase in rat striatum. Meller E, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):25-9

Treatment of pregnant rats with haloperidol delays the onset of sexual maturation in female offspring. Bhanot R, et al. **Experientia** 1982 Jan 15;38(1):137-9

The haloperidol effect on the histofluorescence in the caudate nucleus of the rat brain treated with agonistic and antagonistic acetylcholine compounds. Wawrzyniak M, et al. **Folia Histochem Cytochem (Krakow)** 1981;19(3):143-8

Interaction of antacids with psychotropics. Goldstein BJ. **Hosp Community Psychiatry** 1982 Feb;33(2):96

Haloperidol concentrations in saliva and serum: determination by the radioimmunoassay method. Yamazumi S, et al. **Int Pharmacopsychiatry** 1981;16(3):174-83

Measurement of haloperidol in human plasma using reversed-phase high-performance liquid chromatography. Jatlow PI, et al. **J Chromatogr** 1982 Jan 8;227(1):233-8

Comparative effects of chronic haloperidol and sulpiride treatment on nigral and striatal GABA content. Nicoletti F, et al. **J Neurochem** 1981 Oct;37(4):1048-51

GLC determination of bromperidol in tablets. Martin RP, et al. **J Pharm Sci** 1982 Jan;71(1):112-4

Chronic treatment with haloperidol or fluphenazine decanoate: regional effects on dopamine and serotonin metabolism in primate brain. Bacopoulos NG, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):22-8

Haloperidol pharmacokinetics: a preliminary study in rhesus monkeys using a new radioimmunoassay procedure. Stafford JE, et al. **J Pharmacol Methods** 1981 Dec;6(4):261-79

Chronic haloperidol treatment increased calcium-dependent phosphorylation in rat striatum. Lau YS, et al. **Life Sci** 1982 Jan 4; 30(1):21-8

Unique response to antipsychotic drugs is due to absence of terminal autoreceptors in mesocortical dopamine neurones. Bannon MJ, et al. **Nature** 1982 Apr 1;296(5856):444-6

Differential time- and dose-dependent effects in the haloperidol blockade of luteinizing hormone release and ovulation. Krieg RJ Jr, et al. **Neuroendocrinology** 1981 Dec;33(6):372-5

Chronic electroconvulsive shock and chronic haloperidol administration are not additive in effects on dopamine receptors. Globus M, et al. **Neuropharmacology** 1981 Nov;20(11):1125-8

Effects of acute and chronic haloperidol treatment on the concentrations of immunoreactive beta-endorphin in plasma, pituitary and brain of rats. Höllt V, et al. **Neuropharmacology** 1982 Feb;21(2):147-54

Substance P levels in the rat forebrain after apomorphine and haloperidol treatment. Janicki P, et al. **Pol J Pharmacol Pharm** 1981; 33(5):499-502

Red blood cell/plasma haloperidol ratios and antipsychotic efficacy [letter] Neborsky RJ, et al. **Psychiatry Res** 1982 Feb;6(1):123-4

Antiemetic effect of haloperidol in the dog as related to plasma level and dose. Niemegeers CJ, et al. **Psychopharmacology (Berlin)** 1981; 75(3):240-4

Haloperidol and clonidine increase, and apomorphine decreases ultrasonic vocalizations by gerbils. Thiessen DD, et al. **Psychopharmacology (Berlin)** 1981;75(3):287-90

[Effect of phenamine and haloperidol on stereotyped behavior in response to electric stimulation of the substantia nigra in cats] Arushanian EB, et al. **Biull Eksp Biol Med** 1981 Oct;91(10):444-7 (Eng. Abstr.) (Rus)

HEXOBARBITAL

Induction of hexobarbital and antipyrine metabolism by rifampicin treatment in the pig. van den Broek JM, et al. **Drug Metab Dispos** 1981 Nov-Dec;9(6):541-4

HISTAMINE

On the interaction of histamine with the tryptaminergic smooth-muscle receptors. Todorov S, et al. **Acta Physiol Pharmacol Bulg** 1980; 6(4):47-54

Histamine, cAMP, and activation of piglet gastric mucosa. Machen TE, et al. **Am J Physiol** 1982 Feb;242(2):G79-84

The influence of some cardiodepressant drugs on the histamine-induced restoration of contractility in potassium-depolarized heart preparations. Mantelli L, et al. **Arch Int Pharmacodyn Ther** 1981 Nov; 254(1):99-108

Chemoreceptors for serotonin (5-HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma-aminobutyric acid (GABA) on rabbit visceral afferent neurons. Higashi H, et al. **Brain Res Bull** 1982 Jan; 8(1):23-32

Histamine synthesis by intact mast cells from canine fundic mucosa and liver. Beaven MA, et al. **Gastroenterology** 1982 Feb;82(2):254-62

Histamine concentration and its effect on ovarian contractility in humans. Morikawa H, et al. **Int J Fertil** 1981;26(4):283-6

Pharmacology of arterioles: some aspects of variability in response to norepinephrine, histamine, and 5-hydroxytryptamine. Burrows ME, et al. **J Cardiovasc Pharmacol** 1981 Nov-Dec;3(6):1370-80

Histamine: correlative studies in nucleus accumbens. Chronister RB, et al. **J Neurobiol** 1982 Jan;13(1):23-37

Studies on isolated smooth muscle cells. VII. Response to agonists and the contraction velocity of taenia coli of guinea pig and the single smooth muscle cells. Momose K, et al. **J Pharmacobiodyn** 1981 Sep; 4(9):670-6

Use of 125I-labeled human serum albumin for quantitation of microvascular permeability in rat skin: reevaluation of an old method for studies on substances with an enhancing effect on microvascular permeability. Gerdin B. **J Pharmacol Methods** 1981 Nov;6(3):167-75

Serum concentration of pancreatic polypeptide after infusion of histamine and the effect of cimetidine, trimipramine, and atropine in man. Flaten O, et al. **Scand J Gastroenterol** 1981;16(8):989-91

[Effects of cigarette smoking on pulmonary functions and on plasma levels of serotonin, histamine and serum angiotensin I converting enzyme activity (author's transl)] Ishihara Y, et al. **Nippon Kyobu Shikkan Gakkai Zasshi** 1981 Oct;19(10):721-7 (Eng. Abstr.) (Jpn)

[Serotonin and histamine liberation in experimental skin wounds] Lipshits RU, et al. **Fiziol Zh** 1982 Jan-Feb;28(1):107-9 (Rus)

[Study of serotonin and histamine metabolism in cosmonauts] Dolgun ZS, et al. **Kosm Biol Aviakosm Med** 1982 Jan-Feb;16(1):89-91 (Rus)

[Fluorimetric determination of serotonin and histamine in one sample] Sominskiĭ VN, et al. **Lab Delo** 1982;(2):104-7 (Eng. Abstr.) (Rus)

HUNGER

Amygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst-motivated behavior. Lénárd L, et al. **Brain Res** 1982 Feb 4;233(1):115-32

HYDANTOINS

Biopharmaceutical studies on hydantoin derivatives. I. Physico-chemical properties of hydantoin derivatives and their intestinal absorption. Fujioka H, et al. **J Pharmacobiodyn** 1981 Oct;4(10):759-70

Relation of in vivo drug metabolism to stereoselective fetal hydantoin toxicology in mouse: evaluation of mephenytoin and its metabolite, nirvanol. Wells PG, et al. **J Pharmacol Exp Ther** 1982 Apr; 221(1):228-34

HYDRAZINES

Chemical modification of peptides by hydrazine. Honegger A, et al. **Biochem J** 1981 Oct 1;199(1):53-9

Temperature effects on hydraziine toxicity to bluegills. Hunt TP, et al. **Bull Environ Contam Toxicol** 1981 Nov;27(5):588-95

Cerebral protective effect and radical scavenging action. Yasuda H, et al. **J Neurochem** 1981 Oct;37(4):934-8

Metabolic fate of hydrazine. Springer DL, et al. **J Toxicol Environ Health** 1981 Jul-Aug;8(1-2):21-9

Blockade of 5-HTp reduction of ethanol drinking with the decarboxylase inhibitor, ro 4-4602. Geller I, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):871-4

[Antiestrogens and antiandrogens based on acylhydrazines] Tret'iakov AV. **Dokl Akad Nauk SSSR** 1981;261(1):247-51 (Rus)

[Hydrazine derivative modification of the activity of brain mitochondrial monoamine oxidases] Kalninia IE, et al. **Vopr Med Khim** 1981 Nov-Dec;

27(6):773-9 (Eng. Abstr.) (Rus)

HYDRAZONES

Studies on benzhydrazone, a specific inhibitor of herpesvirus glycoprotein synthesis. Size distribution of glycopeptides and endo-beta-N-acetylglucosaminidase-H treatment. Serafini-Cessi F, et al. **Arch Virol** 1981;70(4):331-43

HYDROXYBUTYRATES

Cellular glycogen, beta-1,2,-glucan, poly beta-hydroxybutyric acid and extracellular polysaccharides in fast-growing species of Rhizobium. Zevenhuizen LP. **Antonie Van Leeuwenhoek** 1981;47(6):481-97

Mapping of a new pan mutation in Escherichia coli K-12. Manch JN. **Can J Microbiol** 1981 Nov;27(11):1231-3

Effects of anticonvulsants on the formation of gamma-hydroxybutyrate from gamma-aminobutyrate in rat brain. Whittle SR, et al. **J Neurochem** 1982 Mar;38(3):848-51

[The effects of butoctamide hydrogen succinate (BAHS) on the sleep of the aged people (author's transl)] Hayashi Y, et al. **No To Shinkei** 1981 Dec;33(12):1243-50 (Eng. Abstr.) (Jpn)

[Effect of hydrocortisone on the respiration of rat cerebral cortex slices in media containing pyruvic or beta-hydroxybutyric acid] Emel'ianov NA, et al. **Fiziol Zh SSSR** 1981 Oct;67(10):1468-71 (Eng. Abstr.) (Rus)

[Changes in the 11-hydroxycorticosteroid content of patients receiving droperidol and sodium oxybutyrate and undergoing electrostimulation] Sergeenko NI, et al. **Vestn Khir** 1981 Nov;127(11):114-6 (Rus)

HYDROXYDOPAMINES

The structure of cerebral cortex in the rat following prenatal administration of 6-hydroxydopamine. Lidov HG, et al. **Brain Res** 1982 Jan;255(1):81-108

Further studies on the effects of intravenously administered 6-hydroxydopamine on the median eminence of the rat. Smith GC, et al. **Brain Res** 1982 Feb 18;234(1):101-10

Selective chemical hepatic sympathectomy in the dog. Allman FD, et al. **Crit Care Med** 1982 Feb;10(2):100-3

Ultrastructural changes after intracisternal injection of 6-hydroxydopamine in the intermediolateral nucleus of the monkey (Macaca fascicularis). Wong WC, et al. **J Anat** 1981 Oct;133(Pt 3):321-31

Experimental studies on cerebellar foliation. II. A morphometric analysis of cerebellar fissuration defects and growth retardation after neonatal treatment with 6-OHDA in the rat. Allen C, et al. **J Comp Neurol** 1981 Dec 20;203(4):771-83

Experimental studies on cerebellar foliation. I. A qualitative morphological analysis of cerebellar fissuration defects after neonatal treatment with 6-OHDA in the rat. Sievers J, et al. **J Comp Neurol** 1981 Dec 20;203(4):751-69

Drug-induced circling after unilateral 6-hydroxydopamine lesions of the nigro-striatal pathway is mediated via the midbrain periaqueductal grey and adjacent reticular formation (angular complex). Reavill C, et al. **Life Sci** 1981 Dec 7;29(23):2357-65

6-Hydroxydopamine decreases benzodiazepine but not GABA receptor binding in rat cerebellum. Doble A, et al. **Neurosci Lett** 1981 Dec 11;27(2):199-204

Effects of 5,7-dihydroxytryptamine and 6-hydroxydopamine on fever response in conscious rats. Matuszek M, et al. **Pol J Pharmacol Pharm** 1981;33(3):305-12

Collicular picrotoxin alleviates akinesia but not sensory neglect in rats with bilateral 6-hydroxydopamine lesions of ventral midbrain. Redgrave P, et al. **Psychopharmacology (Berlin)** 1981;75(2):204-9

HYDROXYINDOLEACETIC ACID

Determination of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in rat and human brain and biological fluids by reversed-phase high-performance liquid chromatography with electrochemical detection. Semerdjian-Rouquier L, et al. **J Chromatogr** 1981 Nov 20;218:663-70

Simultaneous determination of serotonin, 5-hydroxindoleacetic acid, 3,4-dihydroxyphenylacetic acid and homovanillic acid by high performance liquid chromatography with electrochemical detection. Sperk G. **J Neurochem** 1982 Mar;38(3):840-3

Gradients of monoamine metabolites and cortisol in cerebrospinal fluid of psychiatric patients and healthy controls. Bertilsson L, et al. **Psychiatry Res** 1982 Feb;6(1):77-83

[5-Hydroxyindoleacetic acid excretion in patients with the glossalgia syndrome] Dychko EN, et al. **Stomatologiia (Mosk)** 1982 Jan-Feb;61(1):34-5 (Eng. Abstr.) (Rus)

HYDROXYTRYPTOPHAN

Plasma accumulation of metabolism of orally administered single dose L-5-hydroxytryptophan in man. Magnussen I, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):184-9

Comparison of the cardiovascular responses to intracerebroventricular administration of tryptamine, 5-hydroxytryptamine, tryptophan and 5-hydroxytryptophan in rats. Krstić MK, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):385-91

Contrasting effects of clonidine and 5-hydroxytryptophan on spinal sympathetic pathways. Madsen PW, et al. **Clin Exp Hypertens** 1981;3(6):1151-63

Determination of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in rat and human brain and biological fluids by reversed-phase high-performance liquid chromatography with electrochemical detection. Semerdjian-Rouquier L, et al. **J Chromatogr** 1981 Nov 20;218:663-70

Long-term infusion of L-5-hydroxytryptophan increases brain serotonin turnover and decreases blood pressure in normotensive rats. Echizen H, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):579-84

Evidence that the effects of 5-hydroxytryptophan on the secretion of ACTH and growth hormone in dogs are not mediated by central release of serotonin. Zimmermann H, et al. **Neuroendocrinology** 1982 Jan;34(1):27-31

Antagonism by methysergide of the effects of L-5-hydroxytryptophan and quipazine on schedule-controlled responding. Leander JD. **Neuropharmacology** 1981 Dec;20(12A):1141-3

Blockade of 5-HTp reduction of ethanol drinking with the decarboxylase inhibitor, ro 4-4602. Geller I, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):871-4

HYPERKINESIS

Growth hormone and prolactin secretion in adults and hyperactive children: relation to methylphenidate serum levels. Gualtieri CT, et al. **Psychoneuroendocrinology** 1981 Dec;6(4):331-9

[Effect of alpua-methyl-para-tyrosine on 'methamphetamine-induced sterotype and hypermotility' of reserpinized rats (author's transl)] Nakajima H, et al. **Nippon Yakurigaku Zasshi** 1981 Dec;78(6):557-69 (Eng. Abstr.) (Jpn)

HYPERKINETIC SYNDROME

Effects of d-amphetamine on urinary metabolites of dopamine and norepinephrine in hyperactive boys. Shekim WO, et al. **Am J Psychiatry** 1982 Apr;139(4):485-8

Food additives and developmental disorders: the case of erythrosin (FD&C Red 3), or guilty until proven innocent? Mailman RB, et al. **Appl Res Ment Retard** 1981;2(4):297-305

The use of psychopharmacology to study reciprocal influences in parent-child interaction. Barkley RA. **J Abnorm Child Psychol** 1981 Sep;9(3):303-10

A four-year follow-up study of the effects of methylphenidate on the behavior and academic achievement of hyperactive children. Charles L, et al. **J Abnorm Child Psychol** 1981 Dec;9(4):495-505

Medication effects in the classroom: three naturalistic indicators. Whalen CK, et al. **J Abnorm Child Psychol** 1981 Dec;9(4):419-33

Methylphenidate compared with behavioral self-control in attention deficit disorder: preliminary report. Anderson EE, et al. **JDBP** 1981 Dec;2(4):137-41

Effects of levodopa on attention deficit disorder, residual type. Wood D, et al. **Psychiatry Res** 1982 Feb;6(1):13-20

IMIPRAMINE

The effects of imipramine on socio-emotional and alimentary motivated behavior in dogs. Zagrodzka J, et al. **Acta Neurobiol Exp (Warsz)** 1981;41(4):363-72

Relationship between plasma antidepressant levels and clinical outcome for inpatients receiving imipramine. Simpson GM, et al. **Am J Psychiatry** 1982 Mar;139(3):358-60

Plasma imipramine concentrations in patients receiving concomitant fluphenazine decanoate. Siris SG, et al. **Am J Psychiatry** 1982 Jan;139(1):104-6

Steady-state plasma imipramine levels in prepubertal depressed children. Weller EB, et al. **Am J Psychiatry** 1982 Apr;139(4):506-8

Level of ego development and psychotherapy outcome in phobic patients. Rock MH, et al. **Br J Med Psychol** 1981 Dec;54(Pt 4):319-28

Active metabolites of imipramine and desipramine in man. Potter WZ, et al. **Clin Pharmacol Ther** 1982 Mar;31(3):393-401

Decreased 3H-imipramine binding in depressed males and females. Asarch KB, et al. **Commun Psychopharmacol** 1980;4(5):425-32

Toward a biochemical classification of depressive disorders IV: Pretreatment urinary MHPG levels as predictors of antidepressant response to imipramine. Schatzberg AF, et al. **Commun Psychopharmacol** 1980;4(5):441-5

Autoradiographic localization of imipramine binding in rat brain. Rainbow TC, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):363-4

Changes in saliva secretion and accommodation width during short-term administration of imipramine and zimelidine in healthy volunteers. von Knorring L. **Int Pharmacopsychiatry** 1981;16(2):69-78

Viloxazine HCl in the treatment of endogenous depression: a standard (imipramine) controlled clinical study. McEvoy JP, et al. **J Clin Psychiatry** 1981 Mar;43(3):111–2

Maprotiline versus imipramine [letter] Rifkin A. **J Clin Psychiatry** 1981 Mar;43(3):122

The influence of amitriptyline, imipramine and chlorpromazine on activity of arginase in rat's brain and liver. Grabowska-Hibner J, et al. **Mater Med Pol** 1981 Jan–Mar;13(1):54–7

Cerebral pharmacokinetics of imipramine in rats after single and multiple dosages. Daniel W, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):209–13

3H-Imipramine binding sites in the rat brain. Selective localization on serotoninergic neurones. Gross G, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981;317(4):310–4 ·

Beta-adrenergic receptors in rat cerebellum after neonatal X-irradiation: effect of prolonged imipramine and lithium treatment. Türck M, et al. **Neurosci Lett** 1981 Dec 23;27(3):357–62

Human platelet imipramine recognition sites: biochemical and pharmacological characterization. Wennogle LP, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):975–82

High-affinity 3H-imipramine binding: a new biological marker in depression. Langer SZ, et al. **Pharmacopsychiatria** 1982 Jan; 15(1):4–10 (57 ref.)

A comparison of plasma and serum levels of two tricyclic antidepressants: imipramine and desipramine. Saady JJ, et al. **Psychopharmacology (Berlin)** 1981;75(2):173–4

Different synaptic location of mianserin and imipramine binding sites. Brunello N, et al. **Science** 1982 Feb 26;215(4536):1112–5

ISOCARBOXAZID

Monoamine oxidase inhibitor-responsive depression. Giller E, et al. **Psychiatry Res** 1982 Feb;6(1):41–8

LACTATES

Oxygen dependence of dopamine-beta-hydoxylase activity and lactate metabolism in synaptosomes from rat brain. Katz IR. **Brain Res** 1982 Jan 14;231(2):399–409

Steroidogenic and glycolytic responses to nucleotides, nucleosides and steroids in rodent adrenal glands: opposing, species-dependent effects of cyclic GMP. Hum WT, et al. **J Endocrinol** 1981 Dec; 91(3):447–56

Comparative utilization of the isomers of phenylalanine and phenyllactic acid by chicks and rats. Boebel KP, et al. **J Nutr** 1982 Feb; 112(2):367–76

[The aerobic and anaerobic capacity of adolescents and catecholamine excretion during prolonged submaximal exercise (author's transl)] Lehmann M, et al. **Eur J Applied Physiol** 1982;48(1):135–45 (Eng. Abstr.) **(Ger)**

LEARNING

An attempt to use central dopaminergic stimulation as a reinforcement for T-maze learning in rats. Jurkowlaniec E, et al. **Acta Neurobiol Exp (Warsz)** 1981;41(4):357–62

Behavioral and neurochemical changes in rats simultaneously exposed to manganese and lead. Chandra AV, et al. **Arch Toxicol** 1981 NOV; 49(1):49–56

Time-dependent environmentally-induced changes in cerebral and extra-cerebral morphology and chemistry--the basis of learning, memory and behavior. DeFeudis FV. **Gen Pharmacol** 1982;13(1):1–9 (97 ref.)

Selective associations in one-day-old rats: taste-toxicosis and texture-shock aversion learning. Gemberling GA, et al. **J Comp Physiol Psychol** 1982 Feb;96(1):105–13

[Duration of the normalizing effect of substance P in disturbances of the learning process after long-term exposure to noise] Hecht K, et al. **Pharmazie** 1981 Dec;36(12):859–60 **(Ger)**

LEARNING DISORDERS

DOes the child with a learning disability have a biochemical defect? Leary PM. **S Afr Med J** 1982 Jan 2;61(1):14–6

LEVODOPA

Study of the neural basis of circling behavior induced by L-dopa in lesioned entopeduncular cats. Pazo JH, et al. **Brain Res** 1982 Feb 11; 233(2):337–45

The regulation of striatal DOPA synthesis by alpha 2-adrenoreceptors. Rabey JM, et al. **Brain Res** 1981 Dec 28;230(1–2):422–6

Inhibition of reverse transcriptase by tyrosinase generated quinones related to levodopa and dopamine. Wick MM, et al. **Chem Biol Interact** 1981 Dec;38(1):99–107

Suppressive action of cholecystokinin octapeptide on the behavioral effects of L-DOPA in the rat. Itoh S, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):313–6

Levodopa and aspirin pretreatment beneficial in experimental decompression sickness. Popovic P, et al. **Proc Soc Exp Biol Med** 1982 Jan;169(1):140–3

Effects of levodopa on attention deficit disorder, residual type. Wood D, et al. **Psychiatry Res** 1982 Feb;6(1):13–20

LH

Gonadotrophin releasing hormone causes a biphasic secretion of luteinizing hormone and follicle stimulating hormone by cultures of rat anterior pituitary cells. Eddie LW, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):44–9

Long-lasting desensitizing effect of short-term LRH exposure on the pituitary responsiveness to LRH in the ovariectomized rat. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):200–5

Kinetics of LRH-induced LH-release in vivo: influence of LRH pre-treatment. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):195–9

Short-term kinetics of LRH-induced LH-release in the long-term ovariectomized rat. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):187–94

Release of LH in vitro from anterior pituitary glands of ovariectomized rats by LRH or elevated potassium concentration after pre-treatment with oestradiol benzoate in vivo. Tijssen AM, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):206–10

Electrophysiologic correlates of steroid modulation of luteinizing hormone release. Leung PC, et al. **Am J Physiol** 1982 Mar; 242(3):E164–70

Immunohistochemical study of the responsiveness of LH cells of fetal rats to synthetic LHRH in vitro. Watanabe YG. **Cell Tissue Res** 1981; 221(1):59–66

The role of catecholamines in the regulation of pituitary luteinizing hormone and follicle-stimulating hormone secretion. Barraclough CA, et al. **Endocr Rev** 1982 Winter;3(1):91–119 (268 ref.)

Intraventricular injection of follicle-stimulating hormone (FSH) during proestrus stimulates the rise in serum FSH on estrus in phenobarbital-treated hamsters through a central nervous system-dependent mechanism. Coutifaris C, et al. **Endocrinology** 1982 Jan;110(1):105–13

Evidence for the involvement of central epinephrine systems in the regulation of luteinizing hormone, prolactin, and growth hormone release in female rats. Crowley WR, et al. **Endocrinology** 1982 Apr; 110(4):1102–7

Melatonin directly inhibits rat gonadotroph cells. Martin JE, et al. **Endocrinology** 1982 Apr;110(4):1079–84

Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **Endocrinology** 1982 Mar;110(3):717–21

Catecholestrogens and release of anterior pituitary gland hormones. I. Luteinizing hormone. Rodriguez-Sierra JF, et al. **Endocrinology** 1982 Feb;110(2):318–24

Study of the direct action of luteinizing hormone-releasing hormone agonists at the testicular level in intact rats treated with an antiluteinizing hormone serum. Séguin C, et al. **Endocrinology** 1982 Feb; 110(2):524–30

Effect of pulsatile gonadotropin-releasing hormone on the release of luteinizing hormone and follicle-stimulating hormone in vitro by anterior pituitaries from lactating and cycling rats. Smith MS. **Endocrinology** 1982 Mar;110(3):882–91

Regulation of tonic gonadotropin release in prepubertal female hamsters. Smith SG 3d, et al. **Endocrinology** 1982 Apr;110(4):1262–7

A puberty-related attenuation of opiate peptide-induced inhibition of LH secretion. Wilkinson M, et al. **Endocrinology** 1982 Mar;110(3):1046–8

Adaptation of the pituitary gland to prolonged LRH stimulation. Koiter TR, et al. **Experientia** 1981 Dec 15;37(12):1349–51

Differential effects of bromocriptine treatment on LH release and copulatory behavior in hyperprolactinemic male rats. Doherty PC, et al. **Horm Behav** 1981 Dec;15(4):436–50

Basal and GnRH-induced release and synthesis of LH and FSH from incubated pituitary glands throughout the 4-day estrous cycle of the rat. Apfelbaum ME. **Horm Res** 1981;15(2):109–21

Further studies of the effects of intravenous infusion or intramuscular injection of gonadotropin-releasing hormone during childhood and adolescence. Reiter EO, et al. **J Adolesc Health Care** 1981 Jun; 1(4):275–81

Diminution of the in vitro response to luteinizing hormone by corpora lutea induced by gonadotropin releasing hormone treatment of postpartum suckled beef cows. Kesler DJ, et al. **J Anim Sci** 1981 Sep; 53(3):749–54

Effects of porcine follicular fluid on gonadotropin concentrations in rhesus monkeys. Rettori V, et al. **J Clin Endocrinol Metab** 1982 Mar; 54(3):500–3

Effects of an intermittent lighting schedule on the time of egg-laying and the levels of luteinizing hormone, progesterone and corticosterone in the plasma of the domestic hen. Duplaix M, et al. **J Endocrinol** 1981 Dec;91(3):375–83

Drug-induced hyperprolactinaemia and discharges of luteinizing hormone voked by oestrogen in ovariectomized rhesus monkeys. Martensz ND, et al. **J Endocrinol** 1982 Jan;92(1):111-22

Effect of cortisol or adrenocorticotrophin on release of luteinizing hormone induced by luteinizing hormone releasing hormone in the diary heifer. Matteri RL, et al. **J Endocrinol** 1982 Jan;92(1):141-6

Effects of LHRH and long-acting LHRH on serum LH and FSH levels of healthy women. Bartfai G, et al. **J Endocrinol Invest** 1981 Jul-Sep; 4(3):359-62

Plasma LH and testosterone responses to synthetic gonadotrophin-releasing hormone (GnRH) or dexamethasone-GnRH combined treatment and their relationship to semen output in bulls. Abdel Malak G, et al. **J Reprod Fertil** 1982 Jan;64(1):107-13

In-vivo and in-vitro effects of domperidone on the release of prolactin and LH in male and female rats. Carter DA, et al. **J Reprod Fertil** 1982 Jan;64(1):191-7

Lack of effect of melatonin on the pituitary response to LH-RH in the ewe. Symons AM, et al. **J Reprod Fertil** 1982 Jan;64(1):103-6

Direct in vitro stimulation of pituitary LH release by alpha melanocyte stimulating hormone. Miyake A, et al. **Life Sci** 1981 Dec 21; 29(25):2637-40

Pituitary cell cultures as a tool for the studies on the GnRH-induced release and biosynthesis of gonadotropins. Jutisz M, et al. **Mater Med Pol** 1980 Jan-Jun;12(1-2):53-62

Patterns of pituitary LH release during sustained stimulation by synthetic LED in cycling female rats. Lu KH, et al. **Mater Med Pol** 1980 Jan-Jun; 12(1-2):63-9

Effects of aging on the activity of hypothalamic dopamine-beta-hydroxylase during various stages of the estrous cycle in C57BL/6 mice. Banerji TK, et al. **Neuroendocrinology** 1982 Jan; 34(1):14-9

Differential effects of low serum levels of estradiol-17 beta on hypothalamic LHRH levels and LH secretion in castrated male rats. Kalra PS, et al. **Neuroendocrinology** 1981 Dec;33(6):340-6

Differential time- and dose-dependent effects in the haloperidol blockade of luteinizing hormone release and ovulation. Krieg RJ Jr, et al. **Neuroendocrinology** 1981 Dec;33(6):372-5

Influence of adrenocorticotropin and adrenalectomy on gonadotropin secretion in immature rats. Mann DR, et al. **Neuroendocrinology** 1982 Jan;34(1):20-6

Role of the dopaminergic system in luteinizing hormone release and ovulation in the hen. Johnson PA, et al. **Poult Sci** 1981 Nov; 60(11):2551-6

Neurotensin inhibits LH release. Motta M, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):62-4

Effects of hypothalamic arcuate nucleus lesions on pulsatile luteinizing hormone concentration in ovariectomized rats. Sridaran R, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):38-44

[Neural origin and modulation by hypothalamic catecholamines of pulsatile secretion of luteinizing hormone in ovariectomized rats (author's transl)] Endo M. **Hokkaido Igaku Zasshi** 1981 Mar; 56(2):185-98 (Eng. Abstr.) **(Jpn)**

[Studies on the feedback regulation of gonadotropin concentrations in male rats (I). The effects of hypothalamic implantation of testosterone and its metabolites on gonadotropin release in castrated male rats (author's transl)] Noguchi K. **Nippon Naibunpi Gakkai Zasshi** 1981 Aug 20;57(8):1139-47 (Eng. Abstr.) **(Jpn)**

[Role of the hypothalamus in the regulation of luteinizing hormone secretion and in the ovulation process] Przekop F. **Acta Physiol Pol** 1981;32(5 Suppl 23):87-128 (117 ref.) **(Pol)**

[Immunoreactive luteinizing hormone in the CNS and peripheral tissues of hypophysectomized rats] Krivosheev OG, et al. **Probl Endokrinol (Mosk)** 1982 Jan-Feb;28(1):58-64 **(Rus)**

LH-FSH RELEASING HORMONE

Short-term kinetics of LRH-induced LH-release in the long-term ovariectomized rat. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):187-94

Pattern of prolactin secretion and pituitary responsiveness to LRH in pseudopregnant rats maintained in constant light. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):31-8

Long-lasting desensitizing effect of short-term LRH exposure on the pituitary responsiveness to LRH in the ovariectomized rat. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):200-5

Kinetics of LRH-induced LH-release in vivo: influence of LRH pre-treatment. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):195-9

Release of LH in vitro from anterior pituitary glands of ovariectomized rats by LRH or elevated potassium concentration after pre-treatment with oestradiol benzoate in vivo. Tijssen AM, et al. **Acta Endocrinol (Copenh)** 1982 Feb;99(2):206-10

LH-RH induced changes in cAMP content of the anterior pituitary gland in male and female rats in vivo and in vitro. Szabó G, et al. **Acta Physiol Acad Sci Hung** 1981;57(4):343-53

Chymotryptic-like hydrolysis of luliberin (LH-RF) by an adenohypophyseal enzyme of high molecular weight. Horsthemke B, et al. **Biochem Biophys Res Commun** 1981 Dec 31;103(4):1322-8

Lack of luteolytic effect of D-Trp-6-LH-RH in hypophysectomized rhesus monkeys (Macaca mulatta). Asch RH, et al. **Biol Reprod** 1981 Dec;25(5):963-8

Temporal relationship between the development of the self-priming effect of LHRH and changes in serum concentrations of testosterone and androstenedione during the sexual maturation of the male rat. Nazian SJ. **Biol Reprod** 1981 Dec;25(5):977-82

A new systematic treatment for infertile women with abnormal hormone profiles. Fleming R, et al. **Br J Obstet Gynaecol** 1982 Jan; 89(1):80-3

The luteinizing hormone-releasing hormone (LHRH) system in normal and estrogenized neonatal rats. Elkind-Hirsch K, et al. **Brain Res Bull** 1981 Dec;7(6):645-54

Altered hypothalamic dopamine depletion rate and LHRH content in noncyclic hamsters. Kumar MS, et al. **Brain Res Bull** 1982 Jan; 8(1):33-6

Immunocytochemical distribution of LHRH neurons and processes in the rat: hypothalamic and extrahypothalamic locations. Bennett-Clarke C, et al. **Cell Tissue Res** 1982;221(3):493-504

Immunohistochemical study of the responsiveness of LH cells of fetal rats to synthetic LHRH in vitro. Watanabe YG. **Cell Tissue Res** 1981; 221(1):59-66

Effects of chronic LHRH agonist treatment on the endometrium and ovaries of the stumptailed macaque. Kerr-Wilson RH, et al. **Contraception** 1981 Dec;24(6):647-55

Early follicular phase luteinizing hormone-releasing hormone agonist administration - effects on follicular maturation and corpus luteum function in women. Skarin G, et al. **Contraception** 1982 Jan; 25(1):31-9

Luteinizing hormone-releasing hormone peptidase activities in discrete hypothalamic regions and anterior pituitary of the rat: apparent regulation during the prepubertal period and first estrous cycle at puberty. Advis JP, et al. **Endocrinology** 1982 Apr;110(4):1238-45

Induction of testicular gonadotropin-releasing hormone (GnRH) receptors by GnRH: effects of pituitary hormones and relationship to inhibition of testosterone production. Bourne GA, et al. **Endocrinology** 1982 Mar;110(3):727-33

Copper stimulates the release of luteinizing hormone releasing hormone from isolated hypothalamic granules. Burrows GH, et al. **Endocrinology** 1982 Apr;110(4):1456-8

Stimulation of progesterone and prostaglandin E accumulation by luteinizing hormone-releasing hormone (LHRH) and LHRH analogs in rat granulosa cells. Clark MR. **Endocrinology** 1982 Jan; 110(1):146-52

Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of gonadotropin-releasing hormone immunoneutralization. Clayton RN, et al. **Endocrinology** 1982 Apr; 110(4):1116-22

Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of hypothalamic lesions and a gonadotropin-releasing hormone antagonist. Clayton RN, et al. **Endocrinology** 1982 Apr; 110(4):1108-15

Pituitary receptor sites for gonadotropin-releasing hormone: effect of castration and substitutive therapy with sex steroids in the male rat. Conne BS, et al. **Endocrinology** 1982 Jan;110(1):70-9

Peptide antagonists of LH-RH: large increases in antiovulatory activities produced by basic D-amino acids in the six position. Coy DH, et al. **Endocrinology** 1982 Apr;110(4):1445-7

A sex difference in the activation of hypothalamic catecholaminergic and luteinizing hormone-releasing hormone peptidergic neurons after acute castration. DePaolo LV, et al. **Endocrinology** 1982 Feb;110(2):531-9

Neonatal monosodium glutamate treatment alters the response of median eminence luteinizing hormone-releasing hormone nerve terminals to potassium and prostaglandin E2. DePaolo LV, et al. **Endocrinology** 1982 Mar;110(3):835-41

Ovulation induced by a gonadotropin releasing hormone analog in hypophysectomized rats involves prostaglandins. Ekholm C, et al. **Endocrinology** 1982 Jan;110(1):288-90

Inhibition of granulosa cell differentiation by gonadotropin-releasing hormone. Knecht M, et al. **Endocrinology** 1982 Mar;110(3):865-72

The antiandrogenic action of gonadotropin-releasing hormone and its agonists on the mouse kidney. Lecomte P, et al. **Endocrinology** 1982 Jan;110(1):1-6

Evidence for involvement of alpha-adrenergic receptors in norepinephrine-induced prostaglandin E2 and luteinizing hormone-releasing hormone release from the median eminence. Ojeda SR, et al. **Endocrinology** 1982 Feb;110(2):409-12

Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **Endocrinology** 1982 Mar;110(3):717-21

Dependence of pituitary gonadotropin-releasing hormone (GnRH) receptors on GnRH secretion from the hypothalamus. Pieper DR, et al. **Endocrinology** 1982 Mar;110(3):749-53

Study of the direct action of luteinizing hormone-releasing hormone agonists at the testicular level in intact rats treated with an antiluteinizing hormone serum. Séguin C, et al. **Endocrinology** 1982 Feb;

110(2):524-30

Effect of pulsatile gonadotropin-releasing hormone on the release of luteinizing hormone and follicle-stimulating hormone in vitro by anterior pituitaries from lactating and cycling rats. Smith MS. **Endocrinology** 1982 Mar;110(3):882-91

Regulation of tonic gonadotropin release in prepubertal female hamsters. Smith SG 3d, et al. **Endocrinology** 1982 Apr;110(4):1262-7

Inhibition of pituitary-testicular function with [D-Trp6] luteinizing hormone-releasing hormone in rhesus monkeys. Sundaram K, et al. **Endocrinology** 1982 Apr;110(4):1308-14

Adaptation of the pituitary gland to prolonged LRH stimulation. Koiter TR, et al. **Experientia** 1981 Dec 15;37(12):1349-51

The effect of luteinizing hormone-releasing factor and its agonist on cultured human granulosa cells. Casper RF, et al. **Fertil Steril** 1982 Mar;37(3):406-9

Sensitivity of pituitary and corpus luteum responses to single intranasal administration of (D-ser[TBU]6-des-gly-NH2(10)) luteinizing hormone-releasing hormone ethylamide (Buserelin) in normal women. Lemay A, et al. **Fertil Steril** 1982 Feb;37(2):193-200

Induction of luteolysis by luteinizing hormone-releasing factor (LRF) agonist: sensitivity, reproducibility, and reversibility. Sheehan KL, et al. **Fertil Steril** 1982 Feb;37(2):209-12

Basal and GnRH-induced release and synthesis of LH and FSH from incubated pituitary glands throughout the 4-day estrous cycle of the rat. Apfelbaum ME. **Horm Res** 1981;15(2):109-21

Effects of castration, sex steroids, LHRH and glucocorticoids on LHRH binding in the anterior pituitary of male rats. Naess O, et al. **Int J Androl** 1981 Dec;4(6):685-90

Further studies of the effects of intravenous infusion or intramuscular injection of gonadotropin-releasing hormone during childhood and adolescence. Reiter EO, et al. **J Adolesc Health Care** 1981 Jun; 1(4):275-81

Inhibition of human granulosa cell progesterone secretion by a gonadotropin-releasing hormone agonist. Tureck RW, et al. **J Clin Endocrinol Metab** 1982 May;54(5):1078-80

Effect of oestrogen on gonadotrophin release in stumptailed monkeys (Macaca arctoides) treated chronically with an agonist analogue of luteinizing hormone releasing hormone. Fraser HM. **J Endocrinol** 1981 Dec;91(3):525-30

Decapeptide luteinizing hormone releasing hormone in ovine pineal gland. King JA, et al. **J Endocrinol** 1981 Dec;91(3):405-14

Effects of LHRH and long-acting LHRH on serum LH and FSH levels of healthy women. Bartfai G, et al. **J Endocrinol Invest** 1981 Jul-Sep; 4(3):359-62

Immunocytochemical analysis of the rat pineal gland using antisera generated against analogs of luteinizing hormone-releasing hormone (LHRH). Piekut DT, et al. **J Histochem Cytochem** 1982 Feb; 30(2):106-10

Effect of passive immunization against LH-RH on gonadotropin secretion in the ferret. Gledhill B, et al. **J Reprod Fertil** 1982 Jan;64(1):19-23

Lack of effect of melatonin on the pituitary response to LH-RH in the ewe. Symons AM, et al. **J Reprod Fertil** 1982 Jan;64(1):103-6

A direct effect on LHRH on anterior pituitary estrogen receptors in the female rat. Singh P, et al. **J Steroid Biochem** 1982 Jan;16(1):31-7

Recent immunohistological findings on the LH-RH neuron system of the rat. Flerkó B, et al. **Mater Med Pol** 1980 Jan-Jun; 12(1-2):119-23

Pituitary cell cultures as a tool for the studies on the GnRH-induced release and biosynthesis of gonadotropins. Jutisz M, et al. **Mater Med Pol** 1980 Jan-Jun;12(1-2):53-62

Degradation of luteinizing hormone releasing hormone LH-RH by the hypothalamic and pituitary tissue in the presence of its analogs and TRH. Kochman K, et al. **Mater Med Pol** 1980 Jan-Jun; 12(1-2):114-8

Patterns of pituitary LH release during sustained stimulation by synthetic LED in cycling female rats. Lu KH, et al. **Mater Med Pol** 1980 Jan-Jun; 12(1-2):63-9

Occurrence of higher molecular forms cf LHRH in fractionated extracts from rat hypothalamus, cortex and placenta. Gautron JP, et al. **Mol Cell Endocrinol** 1981 Oct;24(1):1-15

Comparison of steroid and LH-RH effects on the responsiveness of hemipituitary glands and dispersed pituitary cells. Speight A, et al. **Mol Cell Endocrinol** 1981 Dec;24(3):267-81

A new class of contraceptives? [news] Fraser HM. **Nature** 1982 Apr 1; 296(5856):391-2

Differential effects of low serum levels of estradiol-17 beta on hypothalamic LHRH levels and LH secretion in castrated male rats. Kalra PS, et al. **Neuroendocrinology** 1981 Dec;33(6):340-6

Presence and localization of immunoreactive luteinizing hormone-releasing hormone (LHRH) within the olfactory bulbs of adult male and female rats. Dluzen DE, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):493-6

The effect of LHRH antagonist analogs and an antibody to LHRH on mating behavior in female rats. Dudley CA, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):393-6

Tritium labeling of gonadotropin releasing hormone in its proline and histidine residues. Klauschenz E, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):445-52

Facilitation of sexual receptivity in the rat by an ovulation-inhibiting analog of LHRH. Zadina JE, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):961-4

Regulation of gonadotropin secretion in the anterior pituitary. Hopkins CR, et al. **Philos Trans R Soc Lond [Biol]** 1981 Dec 18; 296(1080):73-81

Rostral medial preoptic area lesions' influence on female estrous processes and LHRH distribution. Popolow HB, et al. **Physiol Behav** 1981 Nov; 27(5):855-61

Antifertility effects of luteinizing hormone-releasing hormone (LHRH) agonists. Labrie F, et al. **Prog Clin Biol Res** 1981;74:273-91 (70 ref.)

Effects of dibutyryl cAMP, LHRH, and aromatase inhibitor on simultaneous outputs of prostaglandin F2 alpha, and 13,14-dihydro-15-keto-prostaglandin F2 alpha by term placental explants. Haning RV Jr, et al. **Prostaglandins** 1982 Jan;23(1):29-40

Contraception with LHRH agonists, a new physiological approach. Labrie F, et al. **Reproduccion** 1981 Oct-Dec;5(4):229-41 (48 ref.)

Mid-cycle contraception with LHRH in women. Maia H Jr, et al. **Reproduccion** 1981 Oct-Dec;5(4):251-60

[The regulation of the hypothalamo-hypophyso-ovarian fuction during the menstrual cycle in the normal woman. A scheme to explain the coordination and control of the secretion and release of gonadotrophins by LH-RH and oestrogens (author's transl)] Buvat J, et al. **J Gynecol Obstet Biol Reprod (Paris)** 1981;10(5):415-23 (55 ref.) (Eng. Abstr.) (Fre)

[The influence of long-term medication with the LH-RH analogue buserelin on the regulation of the menstrual cycle (author's transl)] Hardt W, et al. **Geburtshilfe Frauenheilkd** 1981 Nov;41(11):791-6 (Eng. Abstr.) (Ger)

[Effects of a GnRH analog (Hoe 766) administered in the puerperium on the fertility of dairy cows] Küpfer U, et al. **Schweiz Arch Tierheilkd** 1981;123(7):355-62 (Eng. Abstr.) (Ger)

[Hypophyseal reaction state during oral contraceptiva (author's transl)] Gitsch E, et al. **Wien Klin Wochenschr** 1981 Oct 16;93(19):599-601 (Eng. Abstr.) (Ger)

[Accumulation of hormones in the hypothalamic neurons] Kochman K. **Acta Physiol Pol** 1981;32(5 Suppl 23):79-85 (37 ref.) (Pol)

[Role of the hypothalamus in the regulation of luteinizing hormone secretion and in the ovulation process] Przekop F. **Acta Physiol Pol** 1981;32(5 Suppl 23):87-128 (117 ref.) (Pol)

[Peptid contraception--new principles for family planning] Nilius SJ. **Lakartidningen** 1981 Aug 19;78(34):2845-8 (Eng. Abstr.) (Swe)

LIPOTROPIN

Effect of beta-lipotropin on aldosterone production in the isolated rat adrenal cell preparation. Washburn DD, et al. **J Clin Endocrinol Metab** 1982 Mar;54(3):613-8

Beta-lipotropin and beta-endorphin in physiological and surgical menopause. Genazzani AR, et al. **J Endocrinol Invest** 1981 Oct-Dec; 4(4):375-8

Plasma opioids in the first hours of life. Facchinetti F, et al. **Pediatr Res** 1982 Feb;16(2):95-8

beta-Endorphin and beta-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. Brambilla F, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):321-30

[Effect of cold stress on the concentrations in the hypothalamus, pituitary, and blood of beta-lipotropin and beta-endorphin in the rabbit] Petraglia F, et al. **Boll Soc Ital Biol Sper** 1981 Sep 30;57(18):1862-8 (Eng. Abstr.) (Ita)

LITHIUM

Comparison of the dosage schedules during the administration of retarded lithium carbonate. Balon R, et al. **Act Nerv Super (Praha)** 1981; 23(4):278-80

Lithium levels in the ejaculate, spermiogram and adjuvant psychopharmacological therapy. Kolomaznik M, et al. **Act Nerv Super (Praha)** 1981;23(4):275-6

Spermiologic findings during longterm lithium therapy. Raboch J Jr, et al. **Act Nerv Super (Praha)** 1981;23(4):274-5

Study of lithium levels in the serum and sex organs of female rats. Suva J, et al. **Act Nerv Super (Praha)** 1981;23(4):280-1

The influence of LiCL on animal halves isolated from ascidian eggs. Ferruzza N, et al. **Acta Embryol Morphol Exp** 1981 Aug;2(1):57-67

Effects of lithium and neuroleptics and combinations of the two on renal function and structure in rats. Christensen S, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):161-7

A comparison between the natriuretic response to potassium in lithium- and amiloride-treated rats. Olesen OV, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 May;48(5):382-9

On the mechanism of inhibition of rat fat cell adenylate cyclase by lithium. Thams P, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 May; 48(5):397-403

Flupenthixol decanoate in recurrent manic–depressive illness. A comparison with lithium. Ahlfors UG, et al. **Acta Psychiatr Scand** 1981 Sep;64(3):226–37

Serum lithium concentrations around the clock with different treatment regimens and the diurnal variation of the renal lithium clearance. Lauritsen BJ, et al. **Acta Psychiatr Scand** 1981 Oct;64(4):314–9

Lithium kinetics in single daily dosing. Perry PJ, et al. **Acta Psychiatr Scand** 1981 Oct;64(4):281–94

Lithium therapy in China. Brief communication. Shanming Y. **Acta Psychiatr Scand** 1981 Sep;64(3):270–2

Treatment of childhood aggressivity with lithium. Vetro A, et al. **Agressologie** 1981 Nov;22(E):27–30

Human leukocyte interferon–mediated granulopoietic differentiation arrest and its abrogation by lithium carbonate. Verma DS, et al. **Am J Hematol** 1982 Feb;12(1):39–46

Studies of the urinary acidification defect induced by lithium. Bank N, et al. **Am J Physiol** 1982 Jan;242(1):F23–9

Lithium and amino acids [letter] Goodnick PJ, et al. **Am J Psychiatry** 1982 Apr;139(4):538–9

Lithium and glycine levels [letter] Prakash R. **Am J Psychiatry** 1982 Jan; 139(1):132

Questions about combined lithium and haloperidol treatment [letter] Rudorfer MV, et al. **Am J Psychiatry** 1982 Apr;139(4):537–8

Lithium and neuromuscular transmission. Waud BE, et al. **Anesth Analg (Cleve)** 1982 May;61(5):399–402

Blockade of 5–hydroxytryptamine–induced responses of rat seminal vesicle by lithium–possible meciation through calcium exchange.. Gandhi DN, et al. **Arch Int Pharmacodyn Ther** 1981 Oct; 253(2):220–32

Lithium dosage regimen design by the repeated one–point method. Ritschel WA, et al. **Arzneimittelforsch** 1982;32(2):98–102

A study of Li+–selective permeation through lipid bilayer membranes mediated by a new ionophore (AS701). Margalit R, et al. **Biochim Biophys Acta** 1981 Dec 7;649(2):441–8

A new method for the use of salivary lithium concentrations as an indicator of plasma lithium levels. Selinger D, et al. **Biol Psychiatry** 1982 Jan;17(1):99–102

The biological disposition and kinetics of lithium. Thornhill DP. **Biopharm Drug Dispos** 1981 Oct–Dec;2(4):305–22 (121 ref.)

Oscillation of the electrical potential of the frog skin under the effect of Li+: theoretical formulation. Lassalles JP, et al. **Biophys Chem** 1981 Sep;14(1):65–80

Cyclic hematopoiesis: effects of lithium on colony–forming cells and colony–stimulating activity in grey collie dogs. Hammond WP, et al. **Blood** 1982 Jan;59(1):179–84

Aplastic anaemia treated with lithium carbonate [letter] Ricevuti G, et al. **Br J Haematol** 1982 Jan;50(1):173–4

Lithium continuation therapy following electroconvulsive therapy. Coppen A, et al. **Br J Psychiatry** 1981 Oct;139:284–7

Lithium withdrawal triggers psychotic states [letter] Klein HE, et al. **Br J Psychiatry** 1981 Sep;139:255–6

Dietary sodium, erythrocyte sodium concentration, sodium–stimulated lithium efflux and blood pressure. Trevisan M, et al. **Clin Sci [Suppl]** 1981 Dec;61(7):29s–32s

Cerebral fluoride in mania and the effect of lithium: a hypothesis. Gal EM. **Commun Psychopharmacol** 1980;4(5):405–9

Mechanism of lithium–induced elevation in red blood cell choline content: an in vitro analysis. Hanin I, et al. **Commun Psychopharmacol** 1980; 4(5):345–55

A mechanism for the accumulation of choline in erythrocytes during treatment with lithium. Jenden DJ, et al. **Commun Psychopharmacol** 1980;4(5):339–44

Renal toxicity of lithium. Hansen HE. **Drugs** 1981 Dec;22(6):461–76 (96 ref.)

Lithium nephrotoxicity: is there cause for concern? Walker RG, et al. **Drugs** 1981 Dec;22(6):421–2

Distribution of lithium elimination rates in a selected population of psychiatric patients. Thornhill DP, et al. **Eur J Clin Pharmacol** 1982; 21(4):351–4

The effect of lithium on rat brain and erythrocyte glycine levels. Deutsch SI, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):75–6

Lithium dissociates haloperidol–induced behavioral supersensitivity from reduced dopac increase in rat striatum. Meller E, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):25–9

Does protein synthesis decline in lithium–treated sea urchin embryos because RNA synthesis is inhibited? Wolcott DL. **Exp Cell Res** 1982 Feb;137(2):427–31

Influence of lithium on proliferation of hematopoietic stem cells. Gallicchio VS, et al. **Exp Hematol** 1981 Aug;9(7):804–10

Comparison of colony stimulating activities secreted into mouse lung conditioned medium in the presence and absence of lithium chloride. Horak H, et al. **Exp Hematol** 1982 Jan;10(1):123–9

Reversal of in vitro drug induced myeloid suppression by lithium. Miller AM, et al. **Exp Hematol** 1981 Aug;9(7):775–80

Effect of Na+, K+ and Li+ on pH dependence of in situ beta–galactosidase from E. coli. de Arriaga D, et al. **Int J Biochem** 1982;14(1):47–52

Effects of lithium on rat tail nerve conduction velocity. Ebara T, et al. **Int Pharmacopsychiatry** 1981;16(3):129–37

Poor prophylactic lithium response due to antidepressants. Reginaldi D, et al. **Int Pharmacopsychiatry** 1981;16(2):124–8

Adverse effects of lithium therapy in the acutely ill elderly patient. Smith RE, et al. **J Clin Psychiatry** 1981 Mar;43(3):94–9

Bioavailability of lithium carbonate: single versus multiple daily dosing. Bone S, et al. **J Clin Psychopharmacol** 1981 Nov;1(6):390–1

A double–blind controlled trial of lithium carbonate primary anorexia nervosa. Gross HA, et al. **J Clin Psychopharmacol** 1981 Nov; 1(6):376–81

A clarification of 'some hazards of lithium use' [letter] Jefferson JW. **J Clin Psychopharmacol** 1981 Nov;1(6):409

Slowed release lithium: a review and a comparative study. Lyskowski J, et al. **J Clin Psychopharmacol** 1981 Nov;1(6):406–8

Early changes in renal distal convoluted tubules and collecting ducts of lithium–treated rats: light microscopy, enzyme histochemistry, and 3H–thymidine autoradiography. Jacobsen NO, et al. **Lab Invest** 1982 Mar;46(3):298–305

Albumin and beta 2–microglobulin excretion in patients on long–term lithium treatment. Hansen HE, et al. **Nephron** 1981;29(5–6):229–32

Effect of lithium on circadian neurotransmitter receptor rhythms. Kafka MS, et al. **Neuropsychobiology** 1982 Jan–Feb;8(1):41–50

Lithium delays biochemical circadian rhythms in rats. McEachron DL, et al. **Neuropsychobiology** 1982 Jan–Feb;8(1):12–29

Lack of benefit from magnesium in lithium toxicity. Zohar J, et al. **Neuropsychobiology** 1982 Jan–Feb;8(1):10–1

Beta–adrenergic receptors in rat cerebellum after neonatal X–irradiation: effect of prolonged imipramine and lithium treatment. Türck M, et al. **Neurosci Lett** 1981 Dec 23;27(3):357–62

Biological factors in affective disorders and their relevance to lithium prophylaxis. Mendlewicz J. **Pharmacopsychiatria** 1982 Jan;15(1):11–8

Effects of lithium administration on central and peripheral nervous system in rats. Biochemical and morphological findings. Scelsi R, et al. **Pharmacopsychiatria** 1981 Nov;14(6):213–6

Lithium–induced polydipsia in birds: a comparative study and analysis of electrolyte excretion. Hardy WT, et al. **Physiol Behav** 1981 Oct; 27(4):575–83

Period lengthening and disruption of socially facilitated circadian activity rhythms of goldfish by lithium. Kavaliers M. **Physiol Behav** 1981 Oct; 27(4):625–8

Establishing lithium clinics in office practice. Hasan MK, et al. **Postgrad Med** 1982 Feb;71(2):182, 186, 190

Lithium's effects on the kidney. Lippmann S. **Postgrad Med** 1982 Mar; 71(3):99–104, 107–8

Lithium stimulates thromboxane B2 formation in human platelets. Imandt L, et al. **Prostaglandins Med** 1981 Nov;7(5):421–9

Course and relationship of lithium side effects to plasma lithium levels. Peselow ED, et al. **Psychiatr Clin (Basel)** 1981;14(3):178–83

The effects of desmethylimipramine and lithium on human sperm function. Amsterdam JD, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):359–63

Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Phillips RH. **Psychosomatics** 1982 Jan;23(1):81–7

Effect of lithium chloride on the circadian rhythm in the flight activity of the microchiropteran bat, Taphozous melanopogon. Subbaraj R. **Z Naturforsch [C]** 1981 Nov–Dec;36(11–12):1068–71

[Effect of diuretics on the distribution and renal excretion of lithium in rats of different ages] Kersten L, et al. **Acta Biol Med Ger** 1981; 40(6):837–48 (Eng. Abstr.) **(Ger)**

[Recurrence prophylaxis of affective diseases with lithium and their results] Felber W. **Psychiatr Clin (Basel)** 1981;14(3):161–6 (Eng. Abstr.) **(Ger)**

[Lithium in the prophylaxis of recurrent affective disorders. Effectiveness of low plasma levels and predictors to clinical response (author's transl)] Faravelli C, et al. **Riv Patol Nerv Ment** 1980 Nov–Dec; 101(6):261–71 (Eng. Abstr.) **(Ita)**

[Effect of chronic administration of lithium chloride on the development of dopamine receptor sensitivity during morphine withdrawal in rats] Allikmets LKh, et al. **Biull Eksp Biol Med** 1981 Nov;92(11):571–2 (Eng. Abstr.) **(Rus)**

[Effect of lithium on the renal excretory function and Na, K–ATPase activity in rats] Vasil'eva VF, et al. **Fiziol Zh SSSR** 1981 Dec; 67(12):1866–72 (Eng. Abstr.) **(Rus)**

[Effect of the structural integrity of Na,K–ATPase preparations on the ability of lithium to substitute for sodium in enzyme activation] Skul'skil IA, et al. **Tsitologiia** 1982 Jan;24(1):95–8 (Eng. Abstr.) **(Rus)**

MEMORY

Pharmacological modulation of memory: trends and problems. Mondadori C. **Acta Neurol Scand [Suppl]** 1981;89:129–43

The effects of nutritional factors on memory. Wurtman RJ. **Acta Neurol Scand [Suppl]** 1981;89:145–54

Time–dependent environmentally–induced changes in cerebral and extra–cerebral morphology and chemistry—the basis of learning, memory and behavior. DeFeudis FV. **Gen Pharmacol** 1982;13(1):1-9 (97 ref.)

Correlation between retention of defensive conditioned reflexes and brain acetylcholinesterase activity in rats. Dish TN. **Neurosci Behav Physiol** 1981 May-Jun;11(3):230-3

Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Brown OM, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):911-4

The role of dopaminergic mechanisms in the rat hippocampus for the consolidation in a brightness discrimination. Grecksch G, et al. **Psychopharmacology (Berlin)** 1981;75(2):165-8

MEMORY, SHORT-TERM

Effects of chemicals on delayed matching behavior in pigeons I: acute effects of drugs. McMillan DE. **Neurotoxicology (Park Forest II)** 1981 Nov;2(3):485-98

MENTAL DISORDERS

Comparison of the dosage schedules during the administration of retarded lithium carbonate. Balon R, et al. **Act Nerv Super (Praha)** 1981; 23(4):278-80

Patterns of psychotropic drug prescriptions in two psychiatric hospitals and two out-patient clinics. Hošek K, et al. **Act Nerv Super (Praha)** 1981;23(4):261-3

Lithium therapy in China. Brief communication. Shanming Y. **Acta Psychiatr Scand** 1981 Sep;64(3):270-2

Problems of psychiatric practice in community mental health centers. Donovan CM. **Am J Psychiatry** 1982 Apr;139(4):456-60

The Boston State Hospital case: a conflict of civil liberties and true liberalism. Schultz S. **Am J Psychiatry** 1982 Feb;139(2):183-8

Hypnotizability and psychopathology. Spiegel D, et al. **Am J Psychiatry** 1982 Apr;139(4):431-7

A program for late twentieth-century psychiatry. Unger RM. **Am J Psychiatry** 1982 Feb;139(2):155-64

Realism and drug refusal: a reply to Appelbaum and Gutheil. Dix GE. **Bull Am Acad Psychiatry Law** 1981;9(3):180-98

Polypsychopharmacy revisited. Rapp MS, et al. **Can J Psychiatry** 1981 Dec;26(8):569-73

The psychodynamics of drug therapy. Thompson EM, et al. **Curr Psychiatr Ther** 1981;20:239-51

Hydergine in senile mental impairment. Loew DM, et al. **Gerontology** 1982 Jan-Feb;28(1):54-74 (76 ref.)

Basic principles of psychotropic drug prescription for the elderly. Salzman C. **Hosp Community Psychiatry** 1982 Feb;33(2):133-6

Models of rationality and mental health rights. Milner N. **Int J Law Psychiatry** 1981;4(1-2):35-52

A cross-national comparison of patterns of utilization and psychiatric care. Erinosho OA, et al. **Int J Soc Psychiatry** 1981 Winter;27(4):289-96

Medication compliance among discharged psychiatric patients. Witt R. **Issues Ment Health Nurs** 1981 Oct-Dec;3(4):305-17

Fourth psychoactive drug usage guide. Appleton WS. **J Clin Psychiatry** 1982 Jan;43(1):12-27

Diagnostic profile of a family practice clinic: patients with psychosocial diagnoses. Stumbo D, et al. **J Fam Pract** 1982 Feb;14(2):281-5

How capable of driving are hospitalized psychiatric patients under psycho-active drug therapy? Hobi V, et al. **J Int Med Res** 1981; 9(6):434-47

Endorphin-mental illness link far from proved [news] Check WA. **JAMA** 1982 Feb 5;247(5):570-1, 575-7

The role of endorphins in neuropsychiatry. **Mod Probl Pharmacopsychiatry** 1981;17:1-290

WHO-coordinated collaborative studies in the effects of psychopharmacological drugs in different populations. Sartorius N. **Mod Probl Pharmacopsychiatry** 1981;16:83-93

Guidelines for the evaluation of drugs in the elderly neuropsychiatric patient (demented and non-demented). **Pharmacopsychiatria** 1981 Nov; 14(6):217-22

Gradients of monoamine metabolites and cortisol in cerebrospinal fluid of psychiatric patients and healthy controls. Bertilsson L, et al. **Psychiatry Res** 1982 Feb;6(1):77-83

Platelet monoamine oxidase activity and behavioral response to pharmacotherapy in psychiatric patients. Rosen AJ, et al. **Psychiatry Res** 1982 Feb;6(1):49-59

Comparison of biochemical properties of platelet monoamine oxidase in mentally disordered and healthy individuals. Yu PH, et al. **Psychiatry Res** 1982 Feb;6(1):107-21

Long-term psychotropic drug-taking and the process of withdrawal. Murray J. **Psychol Med** 1981 Nov;11(4):853-8

[The ego functions. A psychoanalytical objective in psychopharmacological research? (author's transl)] D'Haenen H. **Acta Psychiatr Belg** 1981 Sep-Oct;81(5):452-9 (Eng. Abstr.) (Fre)

[Psychoanalysis or pharmacologic blockage in cultivation of mentally handicapped] Baruk H. **Ann Med Psychol (Paris)** 1981;139(3):335-8 (Fre)

[Open study of minaprine in a child psychiatry population (author's transl)] de Villard R, et al. **Neuropsychiatr Enfance Adolesc** 1981 Apr-May; 29(4-5):255-8 (Eng. Abstr.) (Fre)

[Concerning the interpretation of the contingent negative variation in psychiatry (author's transl)] Timsit-Berthier M. **Rev Electroencephalogr Neurophysiol Clin** 1981 Nov;11(2):236-44 (Eng. Abstr.) (Fre)

[Semiology and clinical findings in psychiatric emergencies] Poncelet PF. **Rev Med Liege** 1981 Dec 1;36(23):850-5 (Fre)

[Misunderstanding between neuroscientists and clinicians (author's transl)] Bleuler M. **Nervenarzt** 1982 Jan;53(1):14-7 (Ger)

[Psychotherapy in psychiatric practice (author's transl)] Nedelmann C. **Nervenarzt** 1982 Jan;53(1):33-8 (Ger)

[Treatment of acute psychiatric emergencies in outpatient emergency services] Schichtl H. **Ther Ggw** 1982 Jan;121(1):46-50 (Ger)

[Peptides as carriers of information in psychiatric diseases] Reichelt KL. **Nord Med** 1980 Nov;95(11):283-6 (Nor)

[Follow-up study of patients treated with depot phenothiazines in Valparaiso, Chile] Michel G, et al. **Bol Of Sanit Panam** 1981 Nov; 91(5):418-27 (Eng. Abstr.) (Spa)

[The boundary between psychiatry and biological therapeutics] Carrillo Broatch A. **Rev Neuropsiquiatr** 1980 Jun;43(2):87-96 (Eng. Abstr.) (Spa)

MENTAL HEALTH

[Some relations of mental hygiene and psychopharmacology (author's transl)] Molčan J, et al. **Cesk Psychiatr** 1981 Jun;77(3):173-5 (Eng. Abstr.) (Slo)

MENTAL PROCESSES

Vasopressins and other neuropeptides as CNS mental modulators. A review. Edelstein EL. **Isr J Psychiatr Relat Sci** 1981;18(3):229-36

METHOTRIMEPRAZINE

Neuroleptics in neurotic anxiety. Boleloucky Z. **Agressologie** 1981 Nov; 22(D):15-7

Simultaneous determination of chlorpromazine and levomepromazine in human plasma and urine by high-performance liquid chromatography using electrochemical detection. Murakami K, et al. **J Chromatogr** 1982 Jan 8;227(1):103-12

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskiĭ Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) (Rus)

METHYLPHENIDATE

Postoperative effects of methylphenidate [letter] Fassoulaki A. **Br J Anaesth** 1981 Dec;53(12):1365-6

The use of psychopharmacology to study reciprocal influences in parent-child interaction. Barkley RA. **J Abnorm Child Psychol** 1981 Sep;9(3):303-10

A four-year follow-up study of the effects of methylphenidate on the behavior and academic achievement of hyperactive children. Charles L, et al. **J Abnorm Child Psychol** 1981 Dec;9(4):495-505

Synthesis and pharmacology of hydroxylated metabolites of methylphenidate. Patrick KS, et al. **J Med Chem** 1981 Oct; 24(10):1237-40

Methylphenidate compared with behavioral self-control in attention deficit disorder: preliminary report. Anderson EE, et al. **JDBP** 1981 Dec;2(4):137-41

The methylphenidate-induced stereotypy in the awake rat: local cerebral metabolism. Bell RD, et al. **Neurology (NY)** 1982 Apr;32(4):377-81

Growth hormone and prolactin secretion in adults and hyperactive children: relation to methylphenidate serum levels. Gualtieri CT, et al. **Psychoneuroendocrinology** 1981 Dec;6(4):331-9

METHYSERGIDE

Antagonism by methysergide of the effects of L-5-hydroxytryptophan and quipazine on schedule-controlled responding. Leander JD. **Neuropharmacology** 1981 Dec;20(12A):1141-3

MOTIVATION

Age-related decline in brain stimulation reward: rejuvenation by amphetamine. Lewis MJ. **Exp Aging Res** 1981 Fall;7(3):225-34

Differential drug effects as a function of the controlling consequences. Barrett JE. **Natl Inst Drug Abuse Res Monogr Ser** 1981 Jul; (37):159-81 (40 ref.)

MOTOR ACTIVITY

Exploitation of the antagonistic properties of some drugs against poisoning with psychochemicals. Koupilová M, et al. **Act Nerv Super (Praha)** 1981; 23(4):292-3

The effects of imipramine on socio-emotional and alimentary motivated behavior in dogs. Zagrodzka J, et al. **Acta Neurobiol Exp (Warsz)** 1981; 41(4):363–72

Functional importance of nucleus accumbens noradrenaline in the rat. Svensson L, et al. **Acta Pharmacol Toxicol (Copenh)** 1982 Jan; 50(1):22–4

Central neurotropic activity of homovanillic acid. Kleinrok Z, et al. **Acta Physiol Pol** 1981 Sep–Oct;32(5):477–85

Role of GABA neurons in the expression of striatal motor functions. Di Chiara G, et al. **Adv Biochem Psychopharmacol** 1981;30:129–63 (77 ref.)

Evidence for the involvement of nigrothalamic GABA neurons in circling behaviour in the rat. Kilpatrick IC, et al. **Adv Biochem Psychopharmacol** 1981;30:205–24

Critical role of midbrain reticular formation in the expression of dopamine–mediated circling behaviour. Reavill C, et al. **Adv Biochem Psychopharmacol** 1981;30:187–204

The GABAergic systems and the role of basal ganglia in motor control. Yoshida M. **Adv Biochem Psychopharmacol** 1981;30:37–52

Behavioral and neurochemical changes in rats simultaneously exposed to manganese and lead. Chandra AV, et al. **Arch Toxicol** 1981 NOV; 49(1):49–56

The involvement of the catecholaminergic system in physostigmine–induced hyperactivity in rats. Egbe PC. **Arzneimittelforsch** 1982;32(1):27–9

Neurochemical and behavioural correlates of the interaction between amphetamine and delta 9–tetrahydrocannabinol in the rat. LewdEO, et al. **Drug Alcohol Depend** 1981 Sep;8(2):93–101

Behavioural evidence for supersensitivity of postsynaptic dopamine receptors in the mesolimbic system after chronic administration of desipramine. Spyraki C, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2–3):195–206

p-Chloroamphetamine: effects on tonic immobility, activity, and temperature in chickens. Boren JL, et al. **J Comp Physiol Psychol** 1981 Dec;95(6):991–1002

Enhanced responsiveness of alpha–noradrenergic receptors following discrete electrolytic lesions of the nucleus locus coeruleus: a behavioral demonstration. De Carvalho LP, et al. **J Neural Transm** 1982; 53(1):23–37

Enhancement of motor–accelerating effect induced by repeated administration of methamphetamine in mice: involvement of environmental factors. Alam MR. **Jpn J Pharmacol** 1981 Dec; 31(6):897–904

Effect of low–dose nitrazepam on performance in the elderly [letter] Morgan K. **Lancet** 1982 Feb 27;1(8270):516

Motor effects following application of putative excitatory amino acid antagonists to the region of the mesencephalic dopamine cell bodies in the rat. Dawbarn D, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(2):100–4

Behavioural and neurochemical studies on apomorphine–induced hypomotility in mice. Sumners C, et al. **Neuropharmacology** 1981 Dec; 20(12A):1203–8

Persistent alteration of rat brain monoamine levels by carbon monoxide exposure: sex differences and behavioral correlation. Shellenberger MK. **Neurotoxicology (Park Forest Il)** 1981 Nov;2(3):431–41

Possible mechanism of 5–methoxy–N,N–dimethyltryptamine–induced turning behaviour in DRN lesioned rats. Blackburn TP, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):7–11

Infant rat hyperactivity elicited by home cage bedding is unaffected by neonatal telencephalic dopamine or norepinephrine depletion. Pappas BA, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):151–4

The effects of quipazine, fenfluramine and apomorphine on the morphine potentiation of tonic immobility. Wallnau LB. **Pharmacol Biochem Behav** 1981 Dec;15(6):895–901

Period lengthening and disruption of socially facilitated circadian activity rhythms of goldfish by lithium. Kavaliers M. **Physiol Behav** 1981 Oct; 27(4):625–8

Effects of cholinomimetics, cholinolytics and atypical antidepressants in the behavioral despair test in the rat. Herman ZS, et al. **Pol J Pharmacol Pharm** 1981;33(5):485–9

Differential effects of l–amphetamine on ontogeny of active avoidance, intertrial responses, and locomotor activity. Bauer R, et al. **Psychopharmacology (Berlin)** 1981;75(3):299–304

Collicular picrotoxin alleviates akinesia but not sensory neglect in rats with bilateral 6–hydroxydopamine lesions of ventral midbrain. Redgrave P, et al. **Psychopharmacology (Berlin)** 1981;75(2):204–9

[Effects of the destruction of the suprachiasmatic nuclei on the circadian rhythms of ACTH corticosterone and the general activity of female rats exposed to a aperiodic environment] Szafarczyk A, et al. **C R Soc Biol (Paris)** 1981;175(6):801–10 (Eng. Abstr.) **(Fre)**

[Effect of GABA on motor activity in the rat during the early postnatal period] Malakhovskaia DB, et al. **Zh Vyssh Nerv Deiat** 1982 Jan–Feb; 32(1):115–21 (Eng. Abstr.) **(Rus)**

[Automatic quantitative evaluation of spontaneous motor activity. Validation of the method] Tintoré I. **Arch Farmacol Toxicol** 1981 Apr; 7(1):79–82 **(Spa)**

MOTOR SKILLS

Hypnotic activity and effects on performance of lormetazepam and camazepam––analogues of temazepam. Nicholson AN, et al. **Br J Clin Pharmacol** 1982 Mar;13(3):433–9

Fine motor performance before and after treatment in schizophrenic and schizoaffective patients. Goode DJ, et al. **Psychiatry Res** 1981 Dec; 5(3):247–55

MSH

Immunoreactive gamma–melanotropin in rat pituitary and plasma: a partial characterization. Pedersen RC, et al. **Endocrinology** 1982 Mar; 110(3):825–34

Biosynthesis of pairs of peptides related to melanotropin, corticotropin and endorphin in the pars intermedia of the amphibian pituitary gland. Martens GJ, et al. **Eur J Biochem** 1982 Feb;122(1):1–10

In vitro study of frog (Rana ridibunda Pallas) neurointermediate lobe secretion by use of a simplified perifusion system. I. Effect of TRH analogs upon alpha–MSH release. Leroux P, et al. **Gen Comp Endocrinol** 1982 Jan;46(1):13–23

Presence of immunoreactive gamma–melanocyte–stimulating hormone, adrenocorticotropin, and beta–endorphin in human gastric antral mucosa. Tanaka I, et al. **J Clin Endocrinol Metab** 1982 Feb; 54(2):392–6

Beta–adrenergic stimulation induces an increase of the plasma levels of immunoreactive alpha–MSH, beta–endorphin, ACTH and of corticosterone. Berkenbosch F, et al. **Life Sci** 1981 Nov 30; 29(22):2249–56

Direct in vitro stimulation of pituitary LH release by alpha melanocyte stimulating hormone. Miyake A, et al. **Life Sci** 1981 Dec 21; 29(25):2637–40

NEUROREGULATORS

Biochemical consequences of kainic acid injection into the lateral brain ventricle in rat. Kleinrok Z, et al. **Acta Biochim Pol** 1981; 28(2):111–22

Neurotransmitter metabolizing enzymes and plasma butyrylcholinesterase in mice exposed to trichloroethylene. Kanje M, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):205–9

Transmitterlike action of serotonin in phase shifting a rhythm from the Aplysia eye. Corrent G, et al. **Am J Physiol** 1982 Mar; 242(3):R333–8

Release of transmitter at the neuromuscular junction. Standaert FG. **Br J Anaesth** 1982 Feb;54(2):131–45 (82 ref.)

Vacuolation of an identified peptidergic (proctolin-containing) neuron. Adams ME, et al. **Brain Res** 1981 Dec 28;230(1–2):439–44

Lateral asymmetry of neurotransmitters in human brain. Glick SD, et al. **Brain Res** 1982 Feb 18;234(1):53–63

Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Glickman RD, et al. **Brain Res** 1982 Feb 18;234(1):81–99

Kainic acid neurotoxicity; effect of systemic injection on neurotransmitter markers in different brain regions. Heggli DE, et al. **Brain Res** 1981 Dec 28;230(1–2):253–62

Effects of neurotransmitters and cyclic AMP on somatostatin release from cultured cerebral cortical cells. Robbins RJ, et al. **Brain Res** 1982 Feb 25;234(2):377–86

Transmitter sensitivities among various types of cultured brain stem neurons. Saji M, et al. **Brain Res** 1982 Feb 4;233(1):83–96

Regulation of thyrotropin–releasing hormone secretion from frog skin. Bolaffi JL, et al. **Endocrinology** 1982 Mar;110(3):842–6

Sex hormones and neurotransmitters as mediators for sexual differentiation of the brain. Dörner G. **Endokrinologie** 1981 Dec;78(2–3):129–38 (31 ref.)

Schistosoma mansoni: neurotransmitters, longitudinal musculature and effects of electrical stimulation. Pax RA, et al. **Exp Parasitol** 1981 Dec; 52(3):346–55

Vasopressins and other neuropeptides as CNS mental modulators. A review. Edelstein EL. **Isr J Psychiatr Relat Sci** 1981;18(3):229–36

Neurotransmitter effects on release of prolactin and growth hormone in vitro from pituitary glands of the pigeon, Columba livia. Hall TR. **J Endocrinol** 1982 Feb;92(2):303–8

Relation between subsynaptic receptor blockade and response to quantal transmitter at the mouse neuromuscular junction. Pennefather P, et al. **J Gen Physiol** 1981 Sep;78(3):313–44

Amine modulation of the neurogenic Limulus heart. Augustine GJ, et al. **J Neurobiol** 1982 Jan;13(1):61–74

Histamine: correlative studies in nucleus accumbens. Chronister RB, et al. **J Neurobiol** 1982 Jan;13(1):23–37

Physiology and in situ identification of putative aminergic neurotransmitters in the nervous system of Gyrocotyle fimbriata, a parasitic flatworm. Keenan L, et al. **J Neurobiol** 1982 Jan;13(1):9–21

Transmitter release in crayfish neuromuscular junction: comments on the article by Staggs et al. (1980). Parnas I, et al. **J Neurobiol** 1982 Jan; 13(1):75–7

Effect of motor and premotor cortex ablation on concentrations of amino acids, monoamines, and acetylcholine and on the ultrastructure in rat striatum. A confirmation of glutamate as the specific cortico-striatal transmitter. Hassler R, et al. **J Neurochem** 1982 Apr;38(4):1087-98

Identification of synapse specific components: synaptic glycoproteins, proteins, and transmitter binding sites. Mena EE, et al. **J Neurochem** 1981 Dec;37(6):1557-66

Functional activity of substantia nigra grafts reinnervating the striatum: neurotransmitter metabolism and [14C]2-deoxy-D-glucose autoradiography. Schmidt RH, et al. **J Neurochem** 1982 Mar; 38(3):737-48

The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. 2. Model experiments. Björklund A, et al. **J Neurosci Methods** 1980 Jun; 2(3):301-18

The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. I. A detailed account of the methodology for central nervous tissue using paraffin, cryostat or Vibratome sections. Lorén I, et al. **J Neurosci Methods** 1980 Jun;2(3):277-300

Induced neurotransmitter release from primary cultures of rat brain neurons. Zurgil N, et al. **Life Sci** 1981 Nov 30;29(22):2265-71

Membrane potential and conductance changes evoked by hormones and neurotransmitters in mammalian exocrine gland cells. Petersen OH, et al. **Methods Cell Biol** 1981;23:513-30 (56 ref.)

FMRFamide neuropeptides simultaneously increase and decrease K+ current in an identified neurone. Cottrell GA. **Nature** 1982 Mar; 296(5852):87-9

Inhibition of spontaneous transmitter release by the membrane ligand cationized ferritin. Publicover SJ. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):246-8

Role of cholinergic and monoaminergic brain systems in dissociated learning. Arkhipov VI, et al. **Neurosci Behav Physiol** 1981 May-Jun; 11(3):226-9

Neurotransmitter modulation of steroid action in target cells that mediate reproduction and reproductive behavior. Nock B, et al. **Neurosci Biobehav Rev** 1981 Winter;5(4):437-47

Stability of CNS bindings sites under various conditions. Uphouse L, et al. **Neurotoxicology (Park Forest Il)** 1981 Nov;2(3):533-40

Electrophysiologic evidence for involvement of acetylcholine as a neurotransmitter in the lateral vestibular nucleus. Ito J, et al. **Otolaryngol Head Neck Surg** 1981 Nov-Dec;89(6):1025-9

Nontraditional neurotransmitters and prolactin release. Donoso AO, et al. **Prog Clin Biol Res** 1981;74:219-28 (35 ref.)

The psychobiology of depressive disorders: from pathophysiology to predisposition. Depue RA, et al. **Prog Exp Pers Res** 1981;10:1-114 (436 ref.)

Aspartate: possible neurotransmitter in cerebellar climbing fibers. Wiklund L, et al. **Science** 1982 Apr 2;216(4541):78-80

Release of some neurotransmitters from the retina. Bauer B, et al. **Vision Res** 1981;21(11):1665-72

Evidence for a serotonin neurotransmitter system in bovine retina. Redburn DA, et al. **Vision Res** 1981;21(11):1673-6

[Transfer of adenohypophysis-regulating hypothalamic hormones into the anterior pituitary gland] Domański E. **Acta Physiol Pol** 1981; 32(5 Suppl 23):59-78 (68 ref.) **(Pol)**

[Characteristics of hormonal correlations in the puerperium] Sokolova ZP. **Akush Ginekol (Mosk)** 1981;(11):3-6 (43 ref.) **(Rus)**

[Effect of tetanus toxin on mechanisms by which calcium ions regulate transmitter secretion at the neuromuscular junction] Kryzhanovskiĭ GN, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):648-51 (Eng. Abstr.) **(Rus)**

[Changes in the ratio of quantum-vesicular parameters in the presence of disrupted synaptic transmitter secretion in the neuromuscular junctions of mammals] Pozdniakov OM, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):738-40 (Eng. Abstr.) **(Rus)**

[Analysis of frequency facilitation in neuromuscular synapses of the sartorius muscle in frogs] Zefirov AL. **Biull Eksp Biol Med** 1981 Oct; 91(10):389-92 (Eng. Abstr.) **(Rus)**

[Transmitter function in sympathetic ganglion cells. A review] Elfvin LG, et al. **Lakartidningen** 1981 Oct 28;78(44):3909-12 (15 ref.) (Eng. Abstr.) **(Swe)**

NEUROTENSIN

Neurotensin effects on brain dopaminergic systems. Haubrich DR, et al. **Brain Res** 1982 Jan 7;231(1):216-21

Effect of dorsal rhizotomy on the autoradiographic distribution of opiate and neurotensin receptors and neurotensin-like immunoreactivity within the rat spinal cord. Ninkovic M, et al. **Brain Res** 1981 Dec 28; 230(1-2):111-9

Distribution of neuropeptides in the dorsal pontine tegmental area of the rat. Matsuzaki T, et al. **Cell Mol Biol** 1981;27(5):499-508

Immunoreactive calcitonin in maternal milk and serum in relation to prolactin and neurotensin. Werner S, et al. **Early Hum Dev** 1982 Jan; 6(1):77-82

Amphibian neurotensin (NT) is not xenopsin (XP): dual presence of NT-like and XP-like peptides in various amphibia. Carraway R, et al. **Endocrinology** 1982 Apr;110(4):1094-101

Histamine release induced by neurotensin from rat peritoneal mast cells. Kurose M, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):129-36

Abnormalities of the colonic regulatory peptides in Hirschsprung's disease. Bishop AE, et al. **Histopathology** 1981 Nov;5(6):679-88

The regional distribution and chromatographic characterisation of neurotensin-like immunoreactivity in the rat central nervous system. Emson PC, et al. **J Neurochem** 1982 Apr;38(4):992-9

Neurohumoral control of ileal electrolyte transport. II. Neurotensin and substance P. Kachur JF, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):456-63

Pancreatic endocrine responses to physiological changes in plasma neurotensin concentration in the calf. Blackburn AM, et al. **J Physiol (Lond)** 1981 Sep;318:407-12

Effect of neurotensin on pancreatic function in man. Fletcher DR, et al. **Life Sci** 1981 Nov 23;29(21):2157-61

Neurotensin-induced release of endogenous noradrenaline from rat hypothalamic slices. Okuma Y, et al. **Life Sci** 1982 Jan 4; 30(1):77-84

An hypothesis of the molecular structure of the dopamine receptor. Smythies JR. **Med Hypotheses** 1981 Dec;7(12):1449-56

A survey of substance P, somatostatin, and neurotensin levels in aging in the rat and human central nervous system. Buck SH, et al. **Neurobiol Aging** 1981 Winter;2(4):257-64

Peptidergic innervation of the mammalian sinus nodes: vasoactive intestinal polypeptide, neurotensin, substance P. Weihe E, et al. **Neurosci Lett** 1981 Nov 4;26(3):283-8

Neurotensin inhibits LH release. Motta M, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):62-4

[Neuropeptides in the rabbit eye. I. RIA for beta-endorphin, substance P and neurotensin in the aqueous humor, iris-ciliary body and retina (author's transl)] Baba S, et al. **Nippon Ganka Gakkai Zasshi** 1981 Sep 10;85(9):1267-72 (Eng. Abstr.) **(Jpn)**

NEUROTIC DISORDERS

Anxiety and placebo reaction in neurotic patients. Plevova J, et al. **Agressologie** 1981 Oct;22(C):47-9

Anxiety and placebo reaction in neurotic patients. Plevova J, et al. **Agressologie** 1981 Nov;22(E):31-2

Clinical investigations of some anxiolytics drugs. Welbel SL. **Agressologie** 1981 Oct;22(C):39-40

Assessment of pharmacodynamics of a new 'controlled release' form of diazepam (Valium CR Roche) by quantitative EEG and psychometric analysis in neurotic subjects. Saletu B, et al. **J Int Med Res** 1981; 9(6):408-33

[Psychopharmacology and Research into Borderline states (author's transl)] Boleloucký Z, et al. **Cesk Psychiatr** 1981 Jun;77(3):148-52 (Eng. Abstr.) **(Cze)**

[Personality, antidepressant and neuroses] Boleloucký Z, et al. **Agressologie** 1981 Nov;22(E):3-5 **(Fre)**

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskiĭ Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) **(Rus)**

[Clinicobiochemical parallels in borderline neuropsychic disorders] Ushakov GK, et al. **Zh Nevropatol Psikhiatr** 1981;81(11):1663-6 (Eng. Abstr.) **(Rus)**

[Effects of piracetam in healthy dogs and dogs with experimental neuroses] Aĭrapetiants MG, et al. **Zh Vyssh Nerv Deiat** 1981 Nov-Dec; 31(6):1164-70 (Eng. Abstr.) **(Rus)**

NITRAZEPAM

Consumption of diazepam, nitrazepam and barbiturates in 5 large hospitals in Prague by defined daily doses per bed/day. Ivančová J, et al. **Act Nerv Super (Praha)** 1981;23(4):267-9

Influence of sex, menstrual cycle and oral contraception on the disposition of nitrazepam. Jochemsen R, et al. **Br J Clin Pharmacol** 1982 Mar; 13(3):319-24

Effect of low-dose nitrazepam on performance in the elderly [letter] Morgan K. **Lancet** 1982 Feb 27;1(8270):516

Differential inhibition by diazepam and nitrazepam of UDP-glucuronyltransferase activities in rats. del Villar E, et al. **Res Commun Chem Pathol Pharmacol** 1981 Sep;33(3):433-47

NOREPINEPHRINE

LCEC analysis of 5-hydroxytryptamine and norepinephrine in the human gastrointestinal tract. Smeds S, et al. **Acta Chir Scand** 1981; 147(5):361-2

Effect of 2-substituted oestrogens in vivo on the metabolism of noradrenaline in rat brain. Kö[illegible]er G, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):1-8

Investigations on possible presynaptic effect of adenosine and noradrenaline on cholinergic neurotransmission in guinea pig trachea. Grundström N, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Aug;

49(2):158–60

Functional importance of nucleus accumbens noradrenaline in the rat. Svensson L, et al. **Acta Pharmacol Toxicol (Copenh)** 1982 Jan; 50(1):22–4

Role of some biogenic amines in the pathomechanism of glomerulonephritis. II. Adrenaline, noradrenaline and serotonin in acute serum sickness in rabbits. Gębala A, et al. **Acta Physiol Pol** 1981; 32(4):363–73

Role of some biogenic amines in the pathomechanism of glomerulonephritis. Zajączkowska M, et al. **Acta Physiol Pol** 1981; 32(4):375–82

Sodium intake alters the effects of norepinephrine on the renin system and the kidney. Rankin LI, et al. **Am J Kidney Dis** 1981 Nov; 1(3):177–84

Renal handling of dopa, dopamine, norepinephrine, and epinephrine in the dog. Ball SG, et al. **Am J Physiol** 1982 Jan;242(1):F56–62

Free fatty acid mobilization in rats following intracerebroventricular norepinephrine. Barbosa MC, et al. **Am J Physiol** 1982 Apr; 242(4):E248–52

Adaptive changes of pyruvate oxidation in perfused heart during adrenergic stimulation. Bünger R, et al. **Am J Physiol** 1982 Jan; 242(1):H30–6

Rapid fluctuations in plasma catecholamines in monkeys under undisturbed conditions. Hansen BC, et al. **Am J Physiol** 1982 Jan; 242(1):E40–6

Reduced norepinephrine turnover in brown adipose tissue of ob/ob mice. Knehans AW, et al. **Am J Physiol** 1982 Apr;242(4):E253–61

Electrophysiologic correlates of steroid modulation of luteinizing hormone release. Leung PC, et al. **Am J Physiol** 1982 Mar; 242(3):E164–70

Catecholamine sensitivity in brown fat cells from cold-acclimated hamsters and rats. Nedergaard J. **Am J Physiol** 1982 Mar; 242(3):C250–7

Catecholamine release and blood pressure changes induced by exercise in dogfish. Opdyke DF, et al. **Am J Physiol** 1982 Mar; 242(3):R306–10

Regulation of norepinephrine levels in synaptic clefts of dog vascular tissue. Rorie DK, et al. **Am J Physiol** 1982 Feb;242(2):H233–9

Neural and extraneural catecholamine production by rat kidneys. Stephenson RK, et al. **Am J Physiol** 1982 Mar;242(3):F261–6

The role of calcium in the stimulation of gluconeogenesis by catecholamines. Yip BP, et al. **Arch Biochem Biophys** 1981 Dec; 212(2):370–7

Adrenergic receptor sensitivity in depression. Effects of clonidine in depressed patients and healthy subjects. Charney DS, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):290–4

The peripheral kinetics of norepinephrine in depressive illness. Esler M, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):295–300

Impaired presynaptic regulation of norepinephrine in schizophrenia. Effects of clonidine in schizophrenic patients and normal controls. Sternberg DE, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):285–9

Effect of chronic propranolol treatment and withdrawal on norepinephrine and tyrosine hydroxylase in sympathetic tissues. Atkins F, et al. **Arch Int Pharmacodyn Ther** 1981 Dec;254(2):271–81

Formation of 3H–dopamine and 3H–noradrenaline from 3H–tyrosine in the canine saphenous vein. Boels PJ, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):315–16

On the mechanism of noradrenaline–induced prostaglandin E2–Synthesis in primary cell cultures from rabbit splenic pulpa. Brückner–Schmidt R, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):266–77

Effects of renal nerve stimulation, norepinephrine and angiotensin II on renal blood flow in relation to release of PG–like substances in anesthetized dogs. Satoh S, et al. **Arch Int Pharmacodyn Ther** 1981 Dec; 254(2):304–16

Urinary excretion of catecholamines in the night monkey (Aotus trivirgatus) (Primates, Cebidae). Peyrin L, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):345–56

Cyclic AMP response to norepinephrine in the limbic forebrain of male and female rats: effect of desipramine. Mishra R, et al. **Biochem Pharmacol** 1981 Nov 15;30(22):3126–8

Catecholamine binding to the alpha–adrenergic receptors of hamster adipocytes. Evidence that guanine nucleotides regulate this binding to the alpha 2–receptor subtype. Pecquery R, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):14–25

Regional differences in the density of perivascular nerves and varicosities, noradrenaline content and responses to nerve stimulation in the rabbit ear artery. Griffith SG, et al. **Blood Vessels** 1982 Jan–Feb; 19(1):41–52

Factors influencing the release of purines and norepinephrine in the rabbit portal vein. Levitt B, et al. **Blood Vessels** 1982 Jan–Feb;19(1):30–40

The effect of age on the responses of human isolated arteries to noradrenaline. Scott PJ, et al. **Br J Clin Pharmacol** 1982 Feb; 13(2):237–9

Insulin–induced enhancement of uptake of noradrenaline in atrial strips. Bhagat B, et al. **Br J Pharmacol** 1981 Oct;74(2):325–32

Altered neuronal responsiveness to biogenic amines in rat cerebral cortex after serotonin denervation or depletion. Ferron A, et al. **Brain Res** 1982 Jan 7;231(1):93–108

Behavior during hippocampal microinfusions. I. Norepinephrine and diversive exploration. Flicker C, et al. **Brain Res** 1982 Mar; 257(1):79–103

Amygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst–motivated behavior. Lénárd L, et al. **Brain Res** 1982 Feb 4;233(1):115–32

The structure of cerebral cortex in the rat following prenatal administration of 6–hydroxydopamine. Lidov HG, et al. **Brain Res** 1982 Jan;255(1):81–108

The noradrenergic system in cultured aggregates of fetal rat brain cells: morphology of the aggregates and pharmacological indices of noradrenergic neurons. Majocha RE, et al. **Brain Res** 1981 Dec 28; 230(1–2):235–52

Involvement of GABA in the feedback action of estradiol on gonadotropin and prolactin release: hypothalamic GABA and catecholamine turnover rates. Mansky T, et al. **Brain Res** 1982 Jan 14;231(2):353–64

Inhibitory action of the ventral noradrenergic bundle on the lateral hypothalamic neurons through alpha–noradrenergic mechanisms in the rat. Miyahara S, et al. **Brain Res** 1982 Feb 25;234(2):459–63

Release of GABA from the guinea–pig neocortex induced by electrical stimulation of the 'locus coeruleus' or by norepinephrine. Moroni F, et al. **Brain Res** 1982 Jan 28;232(1):216–21

The role of the noradrenergic system on the formation of synapses in the visual cortex of the rat. Parnavelas JG, et al. **Brain Res** 1982 Jan; 255(1):140–4

Effect of des–Tyr1–gamma–endorphin and des–Tyr1–alpha–endorphin on alpha–MPT–induced catecholamine disappearance in rat brain nuclei: a dose––response study. Versteeg DH, et al. **Brain Res** 1982 Jan 14; 231(2):343–51

Purkinje cell loss and the noradrenergic system in the cerebellum of pcd mutant mice. Ghetti B, et al. **Brain Res Bull** 1981 Dec;7(6):711–4

Dual influence of hydralazine on constrictor response to noradrenaline in isolated arterial smooth muscle. Krishnamurty VS. **Can J Physiol Pharmacol** 1981 Nov;59(11):1159–69

2,4–Dinitrophenol––mechanism of action. El–Guindy MM, et al. **Cell Mol Biol** 1981;27(5):399–402

Alterations in noradrenergic function during clorgyline treatment. Pickar D, et al. **Commun Psychopharmacol** 1980;4(5):379–86

Modification of the drug talking behavior in rats by interference in the metabolism of 5–hydroxytryptamine and catecholamines. Fuchs V, et al. **Drug Alcohol Depend** 1981 Nov;8(3):235–44

Norepinephrine in Graafian follicles is depleted by follicle–stimulating hormone. Ben–Jonathan N, et al. **Endocrinology** 1982 Feb; 110(2):457–61

Involvement of alpha 1–adrenergic receptors in the inhibitory effect of catecholamines on the thyrotropin–induced release of thyroxine by the mouse thyroid. Muraki T, et al. **Endocrinology** 1982 Jan;110(1):51–4

Evidence for involvement of alpha–adrenergic receptors in norepinephrine–induced prostaglandin E2 and luteinizing hormone–releasing hormone release from the median eminence. Ojeda SR, et al. **Endocrinology** 1982 Feb;110(2):409–12

Norepinephrine mobilization of free fatty acids in endurance trained rats. Thibault MC, et al. **Eur J Applied Physiol** 1981;47(4):313–22

Rat prolactin and hypothalamic catecholamine nerve terminal systems. Evidence for rapid and discrete increases in dopamine and noradrenaline turnover in the hypophysectomized male rat. Andersson K, et al. **Eur J Pharmacol** 1981 Dec 3;76(2–3):261–5

Acute thyroid hormone increases noradrenergic responsiveness of rat atria in vitro. Eiden LE, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):91–3

ACTH1–24 increases stimulation–evoked noradrenaline release from sympathetic nerves by acting on presynaptic ACTH receptors. Göthert M. **Eur J Pharmacol** 1981 Dec 3;76(2–3):295–6

D–Amphetamine at low doses suppresses noradrenergic functions. Huang YH, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):187–95

Noradrenaline–octopamine interactions on cortical neurones in the rat. Jones RS. **Eur J Pharmacol** 1982 Jan;77(2–3):159–62

Calcium ions, morphine tolerance and noradrenergic transmission in the mouse vas deferens. Marshall I, et al. **Eur J Pharmacol** 1981 Nov 5; 75(4):205–13

Effect of norepinephrine uptake blocker on beta–adrenergic receptors of the rat cerebral cortex. Sethy VH, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):53–6

An improved pharmacological procedure for depletion of noradrenaline: pharmacology and assessment of noradrenaline–associated behaviors. Zolovick AJ, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):265–71

Aging effect on the noradrenaline content of rat brain microvessels. Embree LJ, et al. **Exp Aging Res** 1981 Fall;7(3):215–24

Complete cold substitution of noradrenaline–induced thermogenesis in the Djungarian hamster, Phodopus sungorus. Böckler H, et al. **Experientia** 1982 Feb 15;38(2):261–2

Chronic exercise does not alter the chronotropic response of isolated rat atria to catecholamines. Smith DC, et al. **Experientia** 1982 Feb 15; 38(2):260–1

Effect of diethylpyrocarbonate on pH–driven monoamine uptake by chromaffin granule ghosts. Isambert MF, et al. **FEBS Lett** 1981 Dec 21;136(1):13-8

A regional difference in the in vitro response of the rabbit vena cava to norepinephrine. Hellegouarch A, et al. **Gen Pharmacol** 1982; 13(1):41-3

Age differences in blood pressure and norepinephrine concentration in normotensive rats after higher doses of estrogen. Lew GM. **Gen Pharmacol** 1982;13(1):75-8

Sites of noradrenergic innervation of the jejunal villus. Thomas EM, et al. **Gen Pharmacol** 1982;13(1):67-9

Quantitative evidence for cochlear, non-neuronal norepinephrine. Rarey KE, et al. **Hear Res** 1981 Sep;5(1):101-8

Distribution and significance of norepinephrine in the lateral cochlear wall of pigmented and albino rats. Rarey KE, et al. **Hear Res** 1982 Jan;6(1):15-23

Associations between rates of urinary catecholamine excretion and aspects of lifestyle among adult women in some Oxfordshire villages. Harrison GA, et al. **Hum Biol** 1981 Dec;53(4):617-33

Release and vasoactive actions of catecholamines during inhibition of prostaglandin synthesis in normal man. Vierhapper H, et al. **Hypertension** 1982 Jan-Feb;4(1):112-7

Plasma catecholamines in trained and untrained volunteers during graduated exercise. Lehmann M, et al. **Int J Sports Med** 1981 Aug; 2(3):143-7

Blood flow and O2 uptake in dog hindlimb with anemia, norepinephrine, and propranolol. Chapler CK, et al. **J Appl Physiol** 1981 Sep; 51(3):565-70

Pharmacology of arterioles: some aspects of variability in response to norepinephrine, histamine, and 5-hydroxytryptamine. Burrows ME, et al. **J Cardiovasc Pharmacol** 1981 Nov-Dec;3(6):1370-80

Influence of disopyramide, compared with procainamide and quinidine, on isolated dog arteries in response to transmural stimulation and norepinephrine. Toda N, et al. **J Cardiovasc Pharmacol** 1981 Nov-Dec; 3(6):1332-41

Cat pial venoconstriction by topical microapplication of norepinephrine. Ulrich K, et al. **J Cereb Blood Flow Metab** 1982;2(1):109-11

Gas chromatographic method for the simultaneous determination of dopamine and norepinephrine metabolites. Chauhan MS, et al. **J Chromatogr** 1982 Feb 12;227(2):323-30

The effects of age on the plasma catecholamine response to mental stress in man. Barnes RF, et al. **J Clin Endocrinol Metab** 1982 Jan; 54(1):64-9

Identification of and interactions between noradrenergic and serotonergic neurites in the myenteric plexus. Gershon MD, et al. **J Comp Neurol** 1982 Feb 1;204(4):407-21

Effects of estradiol on norepinephrine and prostaglandin efflux in medial basal hypothalamus of ovariectomized rats. Cardinali DP, et al. **J Neural Transm** 1982;53(1):39-47

Influence of innervation on the levels of noradrenaline and serotonin in the circumvallate papilla of the rat. Cano J, et al. **J Neurobiol** 1982 Jan;13(1):1-7

The effects of chronic manganese chloride treatment expressed as age-dependent, transient changes in rat brain synaptosomal uptake of amines. Lai JC, et al. **J Neurochem** 1982 Mar;38(3):844-7

Unstimulated and amphetamine-stimulated release of endogenous noradrenaline and dopamine from rat brain in vivo. Philips SR, et al. **J Neurochem** 1982 Apr;38(4):1106-10

Brain (Na+, K+)-ATPase and noradrenergic activity: effects of hyperinnervation and denervation on high-affinity ouabain binding. Swann AC, et al. **J Neurochem** 1982 Mar;38(3):836-9

Control of noradrenaline release from hippocampal synaptosomes. West DP, et al. **J Neurochem** 1981 Oct;37(4):1052-3

Neonatal hormone treatment and maturation of the pineal noradrenergic system: hydrocortisone and thyroxine. Yuwiler A, et al. **J Neurochem** 1981 Oct;37(4):985-92

Evidence for a neurotropic role of noradrenaline neurons in the postnatal development of rat cerebral cortex. Felten DL, et al. **J Neurocytol** 1982 Feb;11(1):119-35

Disparate effects of infused nutrients on delayed glucoprivic feeding and hypothalamic norepinephrine turnover. Bellin SI, et al. **J Neurosci** 1981 Dec;1(12):1347-53

Neuronal cell surfaces: distinctive glycoproteins of cultured adrenergic and cholinergic sympathetic neurons. Braun SJ, et al. **J Neurosci** 1981 Dec;1(12):1397-406

Specific uptake of norepinephrine and dopamine by homogenates of rat cerebral cortex after locus ceruleus lesion. Logan WJ, et al. **J Neurosci** 1982 Mar;2(3):394-8

The role of gustatory and postingestive signals in the termination of delayed glucoprivic feeding and hypothalamic norepinephrine turnover. Ritter S, et al. **J Neurosci** 1981 Dec;1(12):1354-60

Development and aging of noradrenergic cell bodies and axon terminals in the chicken. Yurkewicz L, et al. **J Neurosci Res** 1981;6(5):621-41

Influence of dietary zinc on rat brain catecholamines. Wallwork JC, et al. **J Nutr** 1982 Mar;112(3):514-9

Modulation of central noradrenaline release by postsynaptic receptors. Wyllie MG, et al. **J Pharm Pharmacol** 1982 Jan;34(1):53-5

Effect of delta9-tetrahydrocannabinol on the synthesis of dopamine and norepinephrine in mouse brain synaptosomes. Bloom AS. **J Pharmacol Exp Ther** 1982 Apr;221(1):97-103

Evidence for the existence of two distinct pools of intracellular calcium in the rat aorta accessible to mobilization by norepinephrine. Heaslip RJ, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):7-13

gamma-Aminobutyric acid (GABA) receptor stimulation. III. Effect of progabide (SL 76002) on norepinephrine, dopamine and 5-hydroxytryptamine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):678-88

Developmental changes in the accumulation of norepinephrine and the chronotropic effects of catecholamines in isolated rat atria as influenced by dietary lipid. Wince LC, et al. **J Pharmacol Exp Ther** 1982 Feb; 220(2):340-6

Changes in plasma noradrenaline and adrenaline associated with central and peripheral thermal stimuli in the pig. Barrand MA, et al. **J Physiol (Lond)** 1981 Jul;316:139-52

Motor activity of the human Fallopian tube in vitro in relation to plasma concentration of oestradiol and progesterone, and the influence of noradrenaline. Helm G, et al. **J Reprod Fertil** 1982 Jan;64(1):233-42

Dobutamine-induced facilitation of norepinephrine efflux from spiral strips of guinea pig pulmonary arteries. Goshima Y, et al. **Jpn J Pharmacol** 1981 Dec;31(6):1091-4

Enhancement of calorigenic response to cold and to norepinephrine in physically trained rats. Hirata K, et al. **Jpn J Physiol** 1981; 31(5):657-65

Developmental difference in noradrenaline and 3-methoxy-4-hydroxyphenylethyleneglycol sulfate (MHPG-SO4) levels in rat whole brain. Kohno Y, et al. **Kurume Med J** 1981; 28(1):95-8

Physiological effects of bed rest [letter] Natelson BH, et al. **Lancet** 1982 Jan 2;1(8262):51

Neurotensin-induced release of endogenous noradrenaline from rat hypothalamic slices. Okuma Y, et al. **Life Sci** 1982 Jan 4; 30(1):77-84

Release of 3H-norepinephrine by ammonium and its modification by changes in pH. Wakade AR, et al. **Life Sci** 1981 Dec 7; 29(23):2381-9

Forebrain catecholamine concentrations in the rat after neocortical and hippocampal lesions. Woodruff ML, et al. **Life Sci** 1981 Dec 21; 29(25):2603-7

Activity of noradrenergic neurons of preoptic-anterior hypothalamic area of female rabbits in some stages of reproduction. Chomicka LK, et al. **Mater Med Pol** 1980 Jan-Jun;12(1-2):97-101

Cimetidine alters plasma catecholamine levels and cortisol and aldosterone excretion [letter] Feely J, et al. **N Engl J Med** 1982 Apr 29; 306(17):1054

3H-noradrenaline release potentiated in a clonal nerve cell line by low-intensity pulsed magnetic fields. Dixey R, et al. **Nature** 1982 Mar 18;296(5854):253-6

A kinetic study of the release of noradrenaline by tyramine. Brandao F, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec; 318(2):83-7

The disposition of 3H-(—)noradrenaline in the perfused cat and rabbit heart. Graefe KH. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec; 318(2):71-82

Tetanus toxin and botulinum A neurotoxin inhibit and at higher concentrations enhance noradrenaline outflow from particulate brain cortex in batch. Habermann E. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(2):105-11

Analysis of the effects of dopamine and noradrenaline in relation to the proposed postsynaptic dopamine receptor in rat vas deferens. Langeloh A, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb; 318(3):202-9

3H-Noradrenaline and 3H-5-hydroxytryptamine release from rat brain slices and its presynaptic alpha-adrenergic modulation after long-term desipramine pretreatment. Schoffelmeer AN, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):173-80

Metabolism of endogenous and exogenous noradrenaline in guinea-pig atria. Starke K, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov; 317(3):193-8

Deamination of released 3H-noradrenaline in the canine saphenous vein. Verbeuren TJ, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb; 318(3):148-57

Release of noradrenaline by one pulse: modulation of such release by alpha-adrenoceptor antagonists and uptake blockers. Wakade AR, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981;317(4):302-9

Characteristics of the norepinephrine-stimulated phosphatidylinositol turnover in rat pineal cell dispersions. Hauser G, et al. **Neurochem Res** 1981 Oct;6(10):1067-79

Antiestrogen-induced alterations of hypothalamic dopamine and norepinephrine levels in the female rat. Baksi SN, et al. **Neuropharmacology** 1981 Dec;20(12A):1163-7

Correlation between the rate of avoidance conditioning and the brain catecholamine level in rats. Saul'skaya NB. **Neurosci Behav Physiol** 1981 May-Jun;11(3):221-6

On the interactive role of central noradrenaline neurons and corticosterone in two-way active avoidance acquisition in the rat. Archer T, et al. **Neurosci Lett** 1981 Dec 23;27(3):341–6

Is noradrenaline a major catecholamine in the bovine retina? Nesselhut T, et al. **Neurosci Lett** 1982 Jan 22;28(1):41–5

Ionic mechanisms of alpha-autoinhibition of [3H]noradrenaline secretion in guinea-pig vas deferens: possible role of extracellular sodium. Stjärne L. **Neuroscience** 1981;6(12):2759–71

The influence of ingested aluminum upon norepinephrine and dopamine levels in the rat brain. Wenk GL, et al. **Neurotoxicology (Park Forest II)** 1981 Oct;2(2):347–53

Neonatal adaptation: sympatho-adrenal response to umbilical cord cutting. Padbury JF, et al. **Pediatr Res** 1981 Dec;15(12):1483–7

Effects of hypothalamic knife cuts on feeding induced by paraventricular norepinephrine injections. Aravich PF, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):101–11

Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Brown OM, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):911–4

Infant rat hyperactivity elicited by home cage bedding is unaffected by neonatal telencephalic dopamine or norepinephrine depletion. Pappas BA, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):151–4

The Neuroanatomy and pharmacology of the nucleus locus coeruleus. Grant SJ, et al. **Prog Clin Biol Res** 1981;71:5–27

[Role of postsynaptic noradrenergic receptors in the mechanism of action of antidepressants] Cuenca E. **Encephale** 1981;7(4 Suppl):397 (Fre)

[Antinoradrenergic activity of raubasine on isolated thoracic aorta and vas deferens of rat (author's transl)] Roquebert J, et al. **J Pharmacol** 1981 Nov–Dec;12(4):393–403 (Eng. Abstr.) (Fre)

[Effects of adrenaline, noradrenaline and isoprenaline administration on carbohydrate and lipid metabolism parameters in swine blood plasma] Brenner KV, et al. **Arch Exp Veterinarmed** 1981;35(5):697–706 (Eng. Abstr.) (Ger)

[The aerobic and anaerobic capacity of adolescents and catecholamine excretion during prolonged submaximal exercise (author's transl)] Lehmann M, et al. **Eur J Applied Physiol** 1982;48(1):135–45 (Eng. Abstr.) (Ger)

[On the National Institute of Hygienic Sciences Standard (Japanese Pharmacopoeia Standard) 'Epinephrine Bitartrate Reference Standard (Control 781)' and 'Norepinephrine Bitartrate Reference Standard (Control 791)' (author's transl)] Kimura T, et al. **Eisei Shikenjo Hokoku** 1981;99:118–21 (Eng. Abstr.) (Jpn)

[The effects of the angiotensin converting enzyme inhibitor, captopril, on catecholamine concentrations in rat plasma, heart, brain and kidneys (author's transl)] Hirata Y, et al. **Nippon Naibunpi Gakkai Zasshi** 1981 Aug 20;57(8):1097–108 (Eng. Abstr.) (Jpn)

[Effects of adrenaline, noradrenaline and pilocarpine on the oxygen uptake in rat submandibular gland (author's transl)] Sakamoto S, et al. **Nippon Seirigaku Zasshi** 1981;43(10):469–78 (Eng. Abstr.) (Jpn)

[Effect of catecholamines on the morphological picture of the peripheral autonomic nervous system of the digestive tract of rats—light-microscopical study] Jędrzejewska A, et al. **Patol Pol** 1981;32(2):233–42 (Eng. Abstr.) (Pol)

[Urinary noradrenaline excretion in workers exposed to mechanical vibration and occupational noise] Sroczyński J, et al. **Pol Tyg Lek** 1981 Sep 7;36(36):1387–8 (Eng. Abstr.) (Pol)

[Dynamics of noradrenaline concentration in the hepatic portal vein and atria of rats during stress] Manukhina EB, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):673–4 (Eng. Abstr.) (Rus)

[Changes in the activity of the brain monoaminergic systems in adaptation to high altitude] Gromova EA, et al. **Dokl Akad Nauk SSSR** 1982;262(1):245–7 (Rus)

[Adaptation of the peripheral organs of rats to noradrenaline deficiency following chronic desympathization] Berdysheva LV, et al. **Fiziol Zh SSSR** 1981 Nov;67(11):1636–42 (Eng. Abstr.) (Rus)

[Changes in intraocular pressure following local injection of catecholamines into the hypothalamus] Danilov GE, et al. **Fiziol Zh SSSR** 1981 Oct;67(10):1487–92 (Eng. Abstr.) (Rus)

[Effect of exertion on trace effects of acclimatization to cold] Sobolev VI, et al. **Fiziol Zh SSSR** 1981 Nov;67(11):1710–6 (Rus)

[Changes in the catecholamine content in adrenaline-synthetizing structures of the medulla oblongata in rats with different reactions to long-term immobilization] Kvetnanskiĭ R, et al. **Probl Endokrinol (Mosk)** 1981;27(6):58–63 (Eng. Abstr.) (Rus)

NORMETANEPHRINE

Postmortem changes of normetanephrine determined by a mass-fragmentographic technique in different rat brain areas. Mocchetti I, et al. **J Neurochem** 1981 Dec;37(6):1607–9

NORTRIPTYLINE

Nortriptyline therapy in elderly patients: dosage prediction from plasma concentration at 24 hours after a single 50 mg dose. Dawling S, et al. **Br J Psychiatry** 1981 Nov;139:413–6

Interaction of chlorpromazine and nortriptyline in patients with schizophrenia. Loga S, et al. **Clin Pharmacokinet** 1981 Nov–Dec;6(6):454–62

Demethylation and hydroxylation of amitriptyline, nortriptyline, and 10-hydroxyamitriptyline in human liver microsomes. Mellström B, et al. **Drug Metab Dispos** 1981 Nov–Dec;9(6):565–8

Treatment of unstable detrusor (irritable bladder) using fluphenazine and nortriptyline: progress report. Martin MR, et al. **Prog Clin Biol Res** 1981;78:335–8

Binding of amitriptyline and nortriptyline in plasma determined from their equilibrium distributions between red cells and plasma, and between red cells and buffer solution. Burch JE, et al. **Psychopharmacology (Berlin)** 1981;75(3):262–72

[Comparison of the effectiveness of tranylcypromine, nortriptyline, thioridazine and amitriptyline in two syndromological types of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981;77(4):245–52 (Eng. Abstr.) (Cze)

OBSESSIVE–COMPULSIVE DISORDER

Successful treatment of obsessive–compulsive disorder with clonidine hydrochloride. Knesevich JW. **Am J Psychiatry** 1982 Mar;139(3):364–5

Clomipramine and exposure for chronic obsessive–compulsive rituals: III. Two year follow-up and further findings. Mawson D, et al. **Br J Psychiatry** 1982 Jan;140:11–8

The psychopharmacological treatment of obsessive–compulsive disorder: a review. Insel TR, et al. **J Clin Psychopharmacol** 1981 Sep;1(5):304–11 (68 ref.)

ORGANIC MENTAL DISORDERS

Pharmacological treatment of chronic cognitive deficit: a review. Dowson JH. **Compr Psychiatry** 1982 Jan–Feb;23(1):85–98

OXAZEPAM

Effect of pentobarbital on the formation of diastereomeric oxazepam glucuronides in man: analysis by high performance liquid chromatography. Seideman P, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):200–4

Lorazepam and oxazepam esters. Hydrophobicity, hydrolysis rates and brain appearance. Simon-Trompler E, et al. **Arzneimittelforsch** 1982;32(2):102–5

Inhibition of morphine glucuronidation by oxazepam in human fetal liver microsomes. Pacifici GM, et al. **Drug Metab Dispos** 1981 Nov–Dec;9(6):569–72

PARANOID DISORDERS

The genetics and biochemistry of paranoid schizophrenia and other paranoid psychoses. Kendler KS, et al. **Schizophr Bull** 1981;7(4):689–709 (86 ref.)

Paranoia—prognosis and treatment: a review. Ritzler BA. **Schizophr Bull** 1981;7(4):710–28 (89 ref.)

PARASYMPATHOMIMETICS

Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Glickman RD, et al. **Brain Res** 1982 Feb 18;234(1):81–99

Synthesis and selective activity of cholinergic agents with rigid skeletons. III. Takemura S, et al. **Chem Pharm Bull (Tokyo)** 1981 Oct;29(10):3026–32

Synthesis and selective activity of cholinergic agents with rigid skeletons. II. Takemura S, et al. **Chem Pharm Bull (Tokyo)** 1981 Oct;29(10):3019–25

Effects of cholinergic agents on rat liver plasma membrane guanylate cyclase. Lippo de Becemberg I, et al. **FEBS Lett** 1982 Jan 25;137(2):303–6

Effects of parasympathomimetic and sympathomimetic drugs on the secretion and composition of rat sublingual saliva. Abe K, et al. **J Dent Res** 1982 Jan;61(1):52–6

Physiological calcium ion concentration and a cholinergic drug on activity of particulate guanylate cyclase in guinea pig taenia caecum. Hisayama T, et al. **J Pharmacobiodyn** 1981 Sep;4(9):738–41

Relationships between chemical structure and cholinergic activities of furmethides and potentiation of these activities by physostigmine. Chaturvedi AK, et al. **Pharmacol Res Commun** 1981 Oct;13(9):829–45

Effects of cholinomimetics, cholinolytics and atypical antidepressants in the behavioral despair test in the rat. Herman ZS, et al. **Pol J Pharmacol Pharm** 1981;33(5):485–9

Psychopharmacological effects of cholinomimetic agents administered into hippocampus and various hypothalamic areas in the rat. Thesis. Plech A. **Pol J Pharmacol Pharm** 1981;33(4):415–20

An EEG analysis of convulsive activity produced by cholinergic agents. Cohen SL, et al. **Prog Neuropsychopharmacol** 1981;5(4):383–8

PARGYLINE

Possible hazards in serotonin binding assays in human and rat brain: effects of ascorbate, pargyline, and buffer concentration. Weiner N, et al. **J Neurosci Methods** 1982 Jan;5(1-2):41-5

PEMOLINE

Gas/liquid chromatographic analysis of pemoline in biological fluids using electron capture detection. Igwe OJ, et al. **J Chromatogr Sci** 1981 Dec; 19(12):617-24

PENTOBARBITAL

Effects of sodium pentobarbital, ketamine, halothane, and chloralose on brainstem auditory evoked responses. Cohen MS, et. al. **Anesth Analg (Cleve)** 1982 Apr;61(4):338-43

Difference in tolerance development of hypothermia and pentobarbital-induced sleep prolongating effect of 11-hydroxy-delta 8-tetrahydrocannabinol and 11-oxo-delta 8-tetrahydrocannabinol in mice. Watanabe K, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):53-6

Manganese prolongation of pentobarbital hypnosis in the male rat. Deimling MJ, et al. **Experientia** 1981 Dec 15;37(12):1322-3

Effects of pentobarbital on contractile responses of feline cerebral arteries. Edvinsson L, et al. **J Cereb Blood Flow Metab** 1981;1(4):437-40

Simple, rapid and sensitive reversed-phase high-performance liquid chromatographic method for thiopental and pentobarbital determination in plasma and brain tissue. Shiu GK, et al. **J Chromatogr** 1982 Jan 8; 227(1):207-12

Further studies on the determinant role of brain level of pentobarbital for the development of acute hypnotic tolerance. Kaneto H, et al. **J Pharmacobiodyn** 1981 Sep;4(9):700-5

Dispositional without functional tolerance to the hypothermic effects of pentobarbital in the rat. Commissaris RL, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):536-9

Effects of ethinyl estradiol on pharmacokinetics of meperidine and pentobarbital in the rat. Knodell RG, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):1-6

Personality factors in human drug self-administration. Pickens RW, et al. **Natl Inst Drug Abuse Res Monogr Ser** 1981 Jul;(37):45-62

Orally delivered pentobarbital as a reinforcer for rhesus monkeys with concurrent access to water: effects of concentration, fixed-ratio size, and liquid positions. DeNoble VJ, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):113-7

Phencyclidine in combination with pentobarbital: supra-additive effects on complex operant behavior in patas monkeys. Thompson DM, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):159-65

Acute and chronic effects of pentobarbital on 5-hydroxytryptamine in mouse brain. Nabeshima T, et al. **Prog Neuropsychopharmacol** 1981; 5(4):373-81

Selective blockade of the discriminative stimulus effects of pentobarbital in pigeons. Herling S, et al. **Psychopharmacology (Berlin)** 1981; 75(3):321-3

Effects of pentobarbital on punished behavior: persistent increases with chronic administration. Witkin JM, et al. **Psychopharmacology (Berlin)** 1981;75(3):324-5

[The blocking potencies and the mode of blockade by pentobarbital and phenobarbital, examined on various types of ACh-receptor activities (author's transl)] Somei K. **Nippon Seirigaku Zasshi** 1981; 43(11):529-31 (Eng. Abstr.) **(Jpn)**

PEPTIDES

Chemical modification of peptides by hydrazine. Honegger A, et al. **Biochem J** 1981 Oct 1;199(1):53-9

Interaction of alpha-dansylated peptide inhibitors with porcine pepsin: detection of complex formation by fluorescence energy transfer and chromatography and evidence for a two-step binding scheme. Dunn BM, et al. **Biochemistry** 1981 Dec 8;20(25):7206-11

Chemical cleavage of tryptophanyl and tyrosyl peptide bonds via oxidative halogenation mediated by o-iodosobenzoic acid. Fontana A, et al. **Biochemistry** 1981 Nov 24;20(24):6997-7004

Effects of somatostatin and urotensin II on tilapia pituitary prolactin release and interactions between somatostatin, osmotic pressure Ca++, and adenosine 3',5'-monophosphate in prolactin release in vitro. Grau EG, et al. **Endocrinology** 1982 Mar;110(3):910-5

Bombesin stimulates prolactin and growth hormone release by pituitary cells in culture. Westendorf JM, et al. **Endocrinology** 1982 Feb; 110(2):352-8

Biosynthesis of pairs of peptides related to melanotropin, corticotropin and endorphin in the pars intermedia of the amphibian pituitary gland. Martens GJ, et al. **Eur J Biochem** 1982 Feb;122(1):1-10

Rat isolated mesenteric artery: a sensitive preparation for the bioassay of urotensin I. Muramatsu I, et al. **Gen Comp Endocrinol** 1981 Dec; 45(4):446-52

Abnormalities of the colonic regulatory peptides in Hirschsprung's disease. Bishop AE, et al. **Histopathology** 1981 Nov;5(6):679-88

Comparative study on biological activities of various anaphylatoxins (C4a, C3a, C5a). Investigations on their ability to induce platelet secretion. Meuer S, et al. **Inflammation** 1981 Dec;5(4):263-73

C3a-induced lysosomal enzyme secretion from human neutrophils: lack of inhibition by f met-leu-phe antagonists and inhibition by arachidonic acid antagonists. Showell HJ, et al. **Int Arch Allergy Appl Immunol** 1982 Mar;67(3):227-32

Low zone desensitization: a stimulus-specific control mechanism of cell response. Investigations on anaphylatoxin-induced platelet secretion. Meuer S, et al. **J Exp Med** 1982 Mar 1;155(3):698-710

Role of brain peptides in the control of pituitary hormone release. McCann SM, et al. **Mater Med Pol** 1980 Jan-Jun;12(1-2):47-52

Stimulation of tyrosine-specific phosphorylation by platelet-derived growth factor. Ek B, et al. **Nature** 1982 Feb 4;295(5848):419-20

Peptides and the new endocrinology. Schwyzer R. **Naturwissenschaften** 1982 Jan;69(1):15-20

Developmental changes in bombesin, substance P, somatostatin and vasoactive intestinal polypeptide in the rat brain. McGregor GP, et al. **Neurosci Lett** 1982 Jan 22;28(1):21-7

Inverse relationship between onset and duration of EEG effects of six peripherally administered peptides. Miller LH, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):845-8

A proposed role for prostaglandins in the modulation of the relaxation response to urotensin I in isolated rat arteries. Gerritsen ME, et al. **Prostaglandins** 1981 Dec;22(6):873-92

CNS mediated inhibition of gastric secretion by bombesin: independence from interaction with brain catecholaminergic, and serotoninergic pathways and pituitary hormones. Taché Y, et al. **Regul Pept** 1982 Jan; 3(1):51-9

Presence of ranatensin-like and bombesin-like peptides in amphibian brains. Walsh JH, et al. **Regul Pept** 1982 Jan;3(1):1-13

[Peptide bond synthesis catalyzed by various proteases (author's transl)] Morihara K. **Tanpakushitsu Kakusan Koso** 1981 Oct;26(13):1979-98 (78 ref.) **(Jpn)**

[Peptides as carriers of information in psychiatric diseases] Reichelt KL. **Nord Med** 1980 Nov;95(11):283-6 **(Nor)**

[Neuropeptides: the history of their study and the prospects for their use in medicine] Bakalkin GIa, et al. **Bol Serv Odontol Saint (Porto Alegre)** 1981;4(2):100-5 (Eng. Abstr.) **(Rus)**

PERPHENAZINE

Estrogen in high doses inhibits perphenazine-induced prolactin release. Sinha YN, et al. **Endocrinology** 1982 Jan;110(1):126-30

PHENCYCLIDINE

Novel thin-layer chromatographic visualization reagent for phencyclidine [letter] King DL, et al. **Clin Chem** 1982 Jan;28(1):247

Phencyclidine (PCP)-structure versus reactivity. Budd RD. **Clin Toxicol** 1981;18(9):1033-41

Stability of phencyclidine in stored blood. Clardy DO, et al. **Clin Toxicol** 1981 Aug;18(8):929-34

Occupational intoxication and long-term persistence of phencyclidine (PCP) in law enforcement personnel. Pitts FN Jr, et al. **Clin Toxicol** 1981;18(9):1015-20

Effects of acute and chronic administration of phencyclidine on dopaminergic receptors in rat striatum. Leelavathi DE, et al. **Commun Psychopharmacol** 1980;4(5):417-24

Detection and quantitation of phencyclidine in rat parotid saliva and plasma. Digregorio GJ, et al. **Drug Alcohol Depend** 1981 Sep; 8(2):169-73

Effects of phencyclidine on excitatory amino acid activation of spinal interneurones in the cat. Lodge D, et al. **Eur J Pharmacol** 1982 Jan; 77(2-3):203-4

Stereospecific displacement of [3H]phencyclidine (PCP) receptor binding by an enantiomeric pair of PCP analogs. Quirion R, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):107-8

Phenylclindine-induced alteration in rat muscarinic cholinergic receptor regulation. Ward D, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2-3):189-93

Unlimited access intravenous drug self-administration in rhesus monkeys. Balster RL, et al. **Fed Proc** 1982 Feb;41(2):211-5

Phencyclidine discrimination in the pigeon using color tracking under second-order schedule. McMillan DE, et al. **J Exp Anal Behav** 1982 Jan;37(1):143-7

Nitrogen-phosphorous detection of phencyclidine in blood serum. Stavchansky S, et al. **J Pharm Sci** 1982 Feb;71(2):194-6

Phencyclidine in combination with pentobarbital: supra-additive effects on complex operant behavior in patas monkeys. Thompson DM, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):159-65

The behavioral effects of phencyclidines may be due to their blockade of potassium channels. Albuquerque EX, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7792-6

PHENCYCLIDINE ABUSE

Physostigmine and haloperidol treatment of acute phencyclidine intoxication. Castellani S, et al. **Am J Psychiatry** 1982 Apr; 139(4):508–10

Physostigmine treatment of acute phencyclidine intoxication. Castellani S, et al. **J Clin Psychiatry** 1982 Jan;43(1):10–1

PHENELZINE

Phenelzine treatment without switch to mania [letter] Keitner GI. **Am J Psychiatry** 1982 Mar;139(3):386

Combined use of trimipramine and phenelzine in depression. Zetin M. **J Nerv Ment Dis** 1982 Apr;170(4):246–7

PHENETHYLAMINES

The effect of PEA on serotonin and catecholamines. Widelitz MM, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):1107–11

Deuterium isotope effects on the enzymatic oxidative deamination of trace amines. Yu PH, et al. **Biochem Pharmacol** 1981 Nov 15; 30(22):3089–94

Dopamine beta-hydroxylase: activity and inhibition in the presence of beta-substituted phenethylamines. Klinman JP, et al. **Biochemistry** 1982 Jan 5;21(1):67–75

Quantitative investigation on the urinary excretion and metabolism of 3,4-dimethoxyphenylethylamine in schizophrenics and normal individuals. Hempel K, et al. **Biol Psychiatry** 1982 Jan;17(1):49–59

Cation sensitivity of [125I]heat binding to alpha 1-adrenoceptors in rat cerebral cortex membranes. Glossmann H, et al. **Eur J Pharmacol** 1981 Oct 22;75(2–3):149–53

Behavioural effects of acute and chronic beta-phenylethylamine administration in the rat: evidence for the involvement of 5-hydroxytryptamine. Dourish CT. **Neuropharmacology** 1981 Nov; 20(11):1067–72

The effects of acute and chronic administration of beta-phenylethylamine on food intake and body weight in rats. Dourish CT, et al. **Prog Neuropsychopharmacol** 1981;5(4):411–4

Cross-cultural study of a biochemical abnormality in paranoid schizophrenia. Jeste DV, et al. **Psychiatry Res** 1981 Dec;5(3):341–52

Excretion of beta-phenethylamine is elevated in humans after profound stress. Paulos MA, et al. **Science** 1982 Feb 26;215(4536):1127–9

[Effect of solubilization by methylethylketone of rat liver mitochondrial monoamine oxidase on inhibition by clorgyline and deprenyl of the enzyme activity] Severina IS, et al. **Biokhimiia** 1981 Nov; 46(11):2043–55 (Eng. Abstr.) **(Rus)**

PHENOBARBITAL

On the inducibility of cytosolic and microsomal carboxylesterase by phenobarbital in rat tissues. Nousiainen U, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Jul;49(1):77–80

Effect of pentobarbital on the formation of diastereomeric oxazepam glucuronides in man: analysis by high performance liquid chromatography. Seideman P, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):200–4

Effect of phenobarbitol pretreatment on regeneration of plasma cholinesterase activity inhibited by parathion or dichlorovos. Purshottam T, et al. **Arch Environ Health** 1982 Jan–Feb;37(1):53–8

Role of haem in the induction of cytochrome P-450 by phenobarbitone. Studies in chick embryos in ovo and in cultured chick embryo hepatocytes. Giger U, et al. **Biochem J** 1981 Aug 15;198(2):321–9

Phenobarbital selectively modulates the glucagon-stimulated activity of adenylate cyclase by depressing the lipid phase separation occurring in the outer half of the bilayer of liver plasma membranes. Houslay MD, et al. **Biochem J** 1981 Sep 1;197(3):675–81

Mixed-function amine oxidase of the rat hepatocyte nuclear envelope. Demonstration and effects of phenobarbital and 3-methylcholanthrene. Sum CY, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):69–73

The fate of phenobarbitone in children in hypothermia and at normal body temperature. Kadar D, et al. **Can Anaesth Soc J** 1982 Jan; 29(1):16–23

Influence of vitamin D3 status, phenobarbital, and diphenylhydantoin treatment on the plasma 25-hydroxyvitamin D3 concentrations in the rat. Gascon-Barré M, et al. **Can J Physiol Pharmacol** 1981 Oct; 59(10):1073–81

Effect of phenobarbital on sleep and nighttime plasma growth hormone and cortisol levels. Prinz PN, et al. **Can J Physiol Pharmacol** 1981 Nov; 59(11):1139–45

Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin and phenobarbital on the occurrence and distribution of four cytochrome P-450 isozymes in rabbit kidney, lung, and liver. Dees JH, et al. **Cancer Res** 1982 Apr; 42(4):1423–32

Induction of rat hepatic ornithine decarboxylase by the tumor promotors 12-O-tetradecanoylphorbol-13-acetate and phenobarbital in vivo; effect of retinyl-acetate. Bisschop A, et al. **Carcinogenesis** 1981; 2(12):1283–7

Determination of phenobarbital and phenytoin by gas-liquid chromatography with on-column methylation. Solow EB. **Clin Chem** 1982 Jan;28(1):216–8

Improved isocratic liquid-chromatographic simultaneous measurement of phenytoin, phenobarbital, primidone, carbamazepine, ethosuximide, and N-desmethylmethsuximide in serum. Szabo GK, et al. **Clin Chem** 1982 Jan;28(1):100–4

2-Propanol treatment induces selectively the metabolism of carbon tetrachloride to phosgene. Implications for carbon tetrachloride hepatotoxicity. Harris RN, et al. **Drug Metab Dispos** 1981 Nov–Dec; 9(6):551–6

Intraventricular injection of follicle-stimulating hormone (FSH) during proestrus stimulates the rise in serum FSH on estrus in phenobarbital-treated hamsters through a central nervous system-dependent mechanism. Coutifaris C, et al. **Endocrinology** 1982 Jan;110(1):105–13

The effect of antipyrine, phenobarbitol and rifampicin on thyroid hormone metabolism in man. Ohnhaus EE, et al. **Eur J Clin Invest** 1981 Oct; 11(5):381–7

Distribution of nuclear size and DNA content in serial liver biopsies of rats treated with N-nitrosomorpholine, phenobarbital and butylated hydroxytoluene. Romagna F, et al. **Exp Cell Biol** 1981;49(6):294–305

Enhancing effect of barbital on N-2-fluorenylacetamide-induced rat liver lesions. Mori H, et al. **Gan** 1981 Oct;72(5):798–801

Comparative effects of phenobarbital and picrotoxin on the choline acetyltransferase activity of specific rat brain areas. Owasoyo JO. **Gen Pharmacol** 1982;13(1):71–3

Effects of 3-methylcholanthrene, beta-naphthoflavone, and phenobarbital on the 3-methylcholanthrene-inducible isozyme of cytochrome P-450 within centrilobular, midzonal, and periportal hepatocytes. Baron J, et al. **J Biol Chem** 1982 Jan 25;257(2):953–7

Phenobarbital induction of a soluble cytochrome P-450-dependent fatty acid monooxygenase in Bacillus megaterium. Narhi LO, et al. **J Biol Chem** 1982 Mar 10;257(5):2147–50

Renal cortical accumulation of phenobarbital in rats and rabbits: lack of correlation with induction of renal microsomal monooxygenases. Kuo CH, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):547–51

Effects of sex hormones and glucocorticoids on the induction of a drug metabolizing enzyme by phenobarbital in chick embryo. Nishigori H, et al. **Life Sci** 1982 Feb 1;30(5):433–9

Reproductive dysfunction in female offspring after prenatal exposure to phenobarbital: critical period of action. Gupta C, et al. **Pediatr Res** 1981 Dec;15(12):1488–91

Changes in phospholipid methyltransferases and membrane microviscosity during induction of rat liver microsomal cytochrome P-450 by phenobarbital and 3-methylcholanthrene. Sastry BV, et al. **Pharmacology** 1981;23(4):211–22

Protection against paracetamol-induced glutathione depletion following a paracetamol-acetylsalicylic acid mixture or benorilate in phenobarbital-treated rats. De Vries J, et al. **Toxicol Lett** 1981 Dec; 9(4):345–7

Selective detoxification: hemoperfusion on antiphenobarbital antibody immobilized on solid phase. Callegaro L, et al. **Trans Am Soc Artif Intern Organs** 1981;27:566–9

[The blocking potencies and the mode of blockade by pentobarbital and phenobarbital, examined on various types of ACh-receptor activities (author's transl)] Somei K. **Nippon Seirigaku Zasshi** 1981; 43(11):529–31 (Eng. Abstr.) **(Jpn)**

[The effects of phenobarbitone on the inhibitory action of GABA (author's transl)] Kaneko S, et al. **No To Shinkei** 1982 Jan;34(1):77–84 (Eng. Abstr.) **(Jpn)**

[Liberation of active substances from suppository bases. II. In vivo studies of phenobarbital suppositories] Grzesiczak A, et al. **Acta Pol Pharm** 1981;38(4):493–7 (Eng. Abstr.) **(Pol)**

[Degradation of phenobarbital by human placenta in experiments on perfused placentas in vitroj Henneberg M, et al. **Ginekol Pol** 1981; 52(10):863–7 (Eng. Abstr.) **(Pol)**

[Effect of phenobarbital on the luminescence system of luminous bacteria] Vysotskii ES, et al. **Mikrobiologiia** 1981 Nov–Dec;50(6):985–91 (Eng. Abstr.) **(Rus)**

PHENOTHIAZINE TRANQUILIZERS

Calmodulin-dependent stimulation of the NADPH oxidase of human neutrophils. Jones HP, et al. **Biochim Biophys Acta** 1982 Jan 12; 714(1):152–6

Phenothiazines inhibit prolactin secretion in vitro. A possible role for calmodulin in stimulus–-secretion coupling in the pituitary. Merritt JE, et al. **FEBS Lett** 1981 Nov 30;135(1):107–10

PHENOTHIAZINES

Identification and characterization of a phospholipase C activity in resident mouse peritoneal macrophages. Inhibition of the enzyme by phenothiazines. Wightman PD, et al. **Biochem J** 1981 Aug 1; 197(2):523–6

Phenothiazines inhibit adenosine uptake by rat brain synaptosomes. Phillis

pages tightly bound

JW, et al. **Can J Physiol Pharmacol** 1981 Oct;59(10):1108–10

Magnetic susceptibility studies of native and thionine–oxidized molybdenum–iron protein from Azotobacter vinelandii nitrogenase. Smith JP, et al. **J Biol Chem** 1982 Mar 10;257(5):2310–3

Liquid chromatography of demoxepam and phenothiazines using a post–column photochemical reactor and fluorescence detection. Brinkman UA, et al. **J Chromatogr** 1981 Nov 6;217:463–71

Reduction of vanadate, a possible explanation of the effect of phenothiazines in manic–depressive psychosis [letter] Naylor GG, et al. **Lancet** 1982 Feb 13;1(8268):395–6

The affinity of various phenothiazine drugs for membranes of intact human erythrocytes and their membrane–transforming activity. Kanaho Y, et al. **Mol Pharmacol** 1981 Nov;20(3):704–8

[Spectrofluorimetry of some phenothiazine derivatives. II. Derivatives having no substitution in position 2 and an alkylheterocyclic one in position 10 (author's transl)] Gayte–Sorbier A, et al. **Ann Pharm Fr** 1981;39(5):435–43 (Eng. Abstr.) **(Fre)**

[In vitro biopharmaceutical control of drug preparations. 2. Comparison of various extraction–testing apparatuses with coated tablets containing Aparkazin (diethazine chloride)] Keserü P, et al. **Acta Pharm Hung** 1981 Nov;51(6):264–9 (Eng. Abstr.) **(Hun)**

PHENOXYBENZAMINE

Irreversible blockade of [3H]spiperone– but not [3H]dopamine–labeled dopamine receptors with phenoxybenzamine. Titeler M. **Biochem Pharmacol** 1981 Nov 15;30(22):3031–7

Prostatodynia––physiological characteristics and rational management with muscle relaxants. Osborn DE, et al. **Br J Urol** 1981 Dec; 53(6):621–3

Phenoxybenzamine blocks dopamine autoreceptors irreversible: implications for multiple dopamine receptor hypotheses. Lehmann J, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):247–54

The effects of phenoxybenzamine on the aortic pressure–diameter relationship in dogs. Stone DN, et al. **Experientia** 1982 Feb 15; 38(2):257–8

Bladder outflow obstruction treated with phenoxybenzamine. Abrams PH, et al. **Prog Clin Biol Res** 1981;78:269–75

PHENYLALANINE

Assay for plasma free phenylalanine and tyrosine by high–pressure liquid chromatography and field desorption mass spectrometry and its application to an in vivo study of the phenylalanine hydroxylating system in man. Lehmann WD, et al. **Biomed Mass Spectrom** 1981 Dec; 8(12):598–605

Comparative utilization of the isomers of phenylalanine and phenyllactic acid by chicks and rats. Boebel KP, et al. **J Nutr** 1982 Feb; 112(2):367–76

PHENYLBUTYRATES

Lipoprotein lipase–catalyzed hydrolysis of p–nitrophenyl butyrate. Interfacial activation by phospholipid vesicles. Shirai K, et al. **J Biol Chem** 1982 Feb 10;257(3):1253–8

PHENYLPROPANOLAMINE

Secretory otitis media, oral decongestant and antihistamine. Haugeto OK, et al. **J Otolaryngol** 1981 Oct;10(5):359–62

Stability of phenylpropanolamine hydrochloride in liquid formulations containing sugars. Barry RH, et al. **J Pharm Sci** 1982 Jan; 71(1):116–8

Phenylpropanolamine [letter] Silverman HI, et al. **JAMA** 1982 Jan 22–29; 247(4):460–1

Fluorometric determination of the D–norpseudoephedrine in the plasma. Plasma levels during the resorption from the free and extended–release form. Meyer J, et al. **Pharm Acta Helv** 1982;57(1):12–5

PHENYTOIN

The bone inductive capacity of decalcified bone matrix modified by diphenylhydantoin. Oikarinen J. **Acta Orthop Scand** 1981 Oct; 52(5):505–11

Phenytoin pharmacokinetics: inappropriate data analysis. Grasela TH, et al. **Am J Hosp Pharm** 1982 Jan;39(1):41–3

Graphic methods of predicting phenytoin dosage and plasma concentrations [letter] Wallace SM. **Am J Hosp Pharm** 1981 Dec; 38(12):1879, 1882

Bioavailability of four brands of phenytoin. Cid E, et al. **Biopharm Drug Dispos** 1981 Oct–Dec;2(4):391–4

Pharmacokinetics of phenytoin in children. Blain PG, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):659–61

A comparison of the bioavailability of two brands of phenytoin. Gibberd FB, et al. **Br J Clin Pharmacol** 1982 Mar;13(3):455–6

Plasma protein binding of phenytoin in the aged: in vivo studies. Patterson M, et al. **Br J Clin Pharmacol** 1982 Mar;13(3):423–5

Influence of vitamin D3 status, phenobarbital, and diphenylhydantoin treatment on the plasma 25–hydroxyvitamin D3 concentrations in the rat. Gascon–Barré M, et al. **Can J Physiol Pharmacol** 1981 Oct; 59(10):1073–81

Determination of phenobarbital and phenytoin by gas–liquid chromatography with on–column methylation. Solow EB. **Clin Chem** 1982 Jan;28(1):216–8

Improved isocratic liquid–chromatographic simultaneous measurement of phenytoin, phenobarbital, primidone, carbamazepine, ethosuximide, and N–desmethylmethsuximide in serum. Szabo GK, et al. **Clin Chem** 1982 Jan;28(1):100–4

Disposition of antipyrine and phenytoin correlated with age and liver volume in man. Bach B, et al. **Clin Pharmacokinet** 1981 Sep–Oct; 6(5):389–96

Fatal hydantoin syndrome: congenital malformation of the urinary tract–a case report. Michalodimitrakis M, et al. **Clin Toxicol** 1981; 18(9):1095–7

The effect of diphenylhydantoin (Dilantin) on thallium–201 chloride uptake. Schachner ER, et al. **Eur J Nucl Med** 1981 Dec;6(12):585–6

Effect of phenytoin on mitotic activity of gingival tissue and cultured fibroblasts. Al–Ubaidy SS, et al. **J Periodontol** 1981 Dec; 52(12):747–9

Phenytoin antagonism of electrically induced maximal seizures in frogs and mice and effects on central nervous system levels of adenosine 3',5'–monophosphate and guanosine 3',5'–monophosphate. Johnson SW, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):139–45

Application of spin labeling to drug assays. II. Determination of the binding of [14C]–phenytoin and spin–labeled phenytoins to albumin and human serum. Chou D, et al. **Mol Pharmacol** 1981 Nov; 20(3):674–80

Effects of sodium valproate on the serum protein binding of phenytoin, and on liver enzyme activity. Richens A, et al. **Monogr Neural Sci** 1981; 5:221–8

Preliminary pharmacological investigations of N–amino–diphenyl–hydantoin, a new hydantoin derivative with prolonged action. Rump S, et al. **Monogr Neural Sci** 1981;5:163–7

Transient antibody deficiency and abnormal t–suppressor cells induced by phenytoin. Dosch HM, et al. **N Engl J Med** 1982 Feb 18; 306(7):406–9

Binding of (3H)–5,5 diphenylhydantoin to rat brain membranes. Shah DS, et al. **Neuropharmacology** 1981 Nov;20(11):1115–9

Phenytoin intoxication and sulphonamides [letter] Paxton JW. **NZ Med J** 1981 Nov 25;94(696):396–7

Pharmacological properties of N–aminodiphenylhydantoin, a new hydantoin derivative with anticonvulsant activity. Rump S, et al. **Pharmazie** 1981 Nov;36(11):780–1

Anticonvulsant intoxication precipitated by azapropazone. Roberts CJ, et al. **Postgrad Med J** 1981 Mar;57(665):191–2

Single point estimation of phenytoin dosing: a reappraisal. Koup JR, et al. **Res Commun Chem Pathol Pharmacol** 1981 Nov;34(2):231–9

Phenytoin toxicity induced by antituberculosis drugs [letter] Sandyk R. **S Afr Med J** 1982 Mar 13;61(11):382

Effect of prenatal phenytoin administration on postnatal development of the rat: a behavioral teratology study. Elmazar MM, et al. **Teratology** 1981 Oct;24(2):115–24

Digoxin and Phenytoin analyses as part of consultations in clinical pharmacology: a study on the use of drugs. Bergman U, et al. **Ther Drug Monit** 1981;3(3):259–69

Effect of antacids on phenytoin bioavailability. Carter BL, et al. **Ther Drug Monit** 1981;3(4):333–40

Differences in single dose phenytoin kinetics between Greenland Eskimos and Danes. Kromann N, et al. **Ther Drug Monit** 1981;3(3):239–45

[Bioavailability of two commercial phenytoin preparations (author's transl)] Yahaba Y, et al. **Seishin Shinkeigaku Zasshi** 1981; 83(9):582–96 (Eng. Abstr.) **(Jpn)**

[Biopharmaceutical studies of drugs. V. Dissolution properties and bioavailability of ground mixtures of poorly water soluble drugs and soluble proteins (author's transl)] Kigasawa K, et al. **Yakugaku Zasshi** 1981 Aug;101(8):733–9 (Eng. Abstr.) **(Jpn)**

PHOBIC DISORDERS

Level of ego development and psychotherapy outcome in phobic patients. Rock MH, et al. **Br J Med Psychol** 1981 Dec;54(Pt 4):319–28

PHYSOSTIGMINE

Physostigmine's use questioned for amoxapine overdose [letter] **Am J Hosp Pharm** 1981 Dec;38(12):1882, 1889

Physostigmine and haloperidol treatment of acute phencyclidine intoxication. Castellani S, et al. **Am J Psychiatry** 1982 Apr; 139(4):508–10

Central cardiovascular effects of physostigmine in the cat; possible cholinergic aspects of blood pressure regulation. de Wildt DJ, et al. **Arch Int Pharmacodyn Ther** 1981 Sep;253(1):22–39

The influence of physostigmine on sympathetic outflow and haemodynamics by an action upon the pontomedullary region of the cat. de Wildt DJ, et al. **Arch Int Pharmacodyn Ther** 1981 Sep;

29(1):40-51

Effects of physostigmine on benzodiazepine toxicity. Ongini E, et al. **Arch Int Pharmacodyn Ther** 1981 Sep;253(1):164-76

The involvement of the catecholaminergic system in physostigmine-induced hyperactivity in rats. Egbe PC. **Arzneimittelforsch** 1982;32(1):27-9

Antagonism of ketamine by 4-aminopyridine and physostigmine [letter] Martinez-Aguirre E. **Br J Anaesth** 1982 Jan;54(1):110

Dose-dependent feeding in the rat following substantia nigra acetylcholinesterase blockade. Winn P, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):421-5

Physostigmine treatment of acute phencyclidine intoxication. Castellani S, et al. **J Clin Psychiatry** 1982 Jan;43(1):10-1

Cardiovascular response to microinjection of physostigmine and choline into the dorsal medullary site of the rat. Kubo T, et al. **Neuropharmacology** 1981 Nov;20(11):1091-5

Treatment of tricyclic poisoning [letter] Fujita P. **Pediatrics** 1981 Dec; 68(6):912

Relationships between chemical structure and cholinergic activities of [illegible] and potentiation of these activities by physostigmine. Chaturvedi AK, et al. **Pharmacol Res Commun** 1981 Oct; 13(9):829-45

[The antagonistic effect of physostigmine on sedation by lormetazepam (author's transl) Grote B, et al. **Anaesthesist** 1981 Dec;30(12):627-32 (Eng. Abstr.) (Ger)

PILOCARPINE

Regulation of intestinal goblet cell secretion. I. Role of parasympathetic stimulation. Specian RD, et al. **Am J Physiol** 1982 Apr; 242(4):G370-9

Ultrastructural stereologic analysis of fetal rabbit type II alveolar epithelial cells following maternal pilocarpine treatment or fasting. Smith DM, et al. **Anat Rec** 1982 Jan;202(1):23-31

Amylase released from the parotid gland by pilocarpine elevates the enzyme activity in the submandibular and sublingual glands of rats. Ikeno T, et al. **Experientia** 1982 Feb 15;38(2):251-2

The proportion of ribosomes engaged in rat pancreatic polysomal structures as influenced by pilocarpine injection. Poort C, et al. **J Cell Sci** 1981 Aug;50:165-9

[Study of isotonization by means of osmometry] Kovacs P, et al. **Acta Pharm Hung** 1982 Jan;52(1):22-32 (Eng. Abstr.) (Hun)

[Effects of adrenaline, noradrenaline and pilocarpine on the oxygen uptake in rat submandibular gland (author's transl)] Sakamoto S, et al. **Nippon Seirigaku Zasshi** 1981;43(10):469-78 (Eng. Abstr.) (Jpn)

PITUITARY HORMONE RELEASING HORMONES

Gonadotrophin releasing hormone causes a biphasic secretion of luteinizing hormone and follicle stimulating hormone by cultures of rat anterior pituitary cells. Eddie LW, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):44-9

The effect of gonadotropin-releasing hormone on ovarian estradiol secretion. Kletzky OA, et al. **Am J Obstet Gynecol** 1982 Feb 15; 142(4):427-31

Reduction of pituitary nucleic acids, proteins, LH and FSH by melatonin-free pineal extract in rats stimulated with gonadotropin releasing hormone. Damian E, et al. **Endocrinologie** 1981 Oct-Dec; 19(4):227-30

Interaction of gonadotropin-releasing hormone agonist and antagonist with progesterone, prolactin, or human chorionic gonadotropin during pregnancy in the rat. Rivier C, et al. **Endocrinology** 1982 Feb; 110(2):347-51

Effect of unilateral castration and unilateral cryptorchidism on gonadotropin and testosterone response to gonadotropin releasing hormone in the bull. Barnes MA, et al. **J Anim Sci** 1981 Nov; 53(5):1341-50

Diminution of the in vitro response to luteinizing hormone by corpora lutea induced by gonadotropin releasing hormone treatment of postpartum suckled beef cows. Kesler DJ, et al. **J Anim Sci** 1981 Sep; 53(3):749-54

Pituitary sensitivity to gonadotrophin releasing hormone after hyperprolactinaemia induced with neuroleptics and domperidone in the rat. Carter DA, et al. **J Endocrinol** 1981 Dec;91(3):439-46

Plasma LH and testosterone responses to synthetic gonadotrophin-releasing hormone (GnRH) or dexamethasone-GnRH combined treatment and their relationship to semen output in bulls. Abdel Malak G, et al. **J Reprod Fertil** 1982 Jan;64(1):107-13

Induction of cyclic ovarian activity in seasonally anoestrous ewes with exogenous GnRH. McNatty KP, et al. **J Reprod Fertil** 1982 Jan; 64(1):93-6

Biosynthesis, in vivo, of gonadotropin-releasing hormone in the hypothalamus of normal and ovariectomized female rats. Kochman K, et al. **Mol Cell Endocrinol** 1982 Feb;25(2):193-202

Female sexual behaviour in the GnRH deficient, hypogonadal (hpg) mouse. Ward BJ, et al. **Physiol Behav** 1981 Dec;27(6):1107-9

The hypophysiotrophic hormones. Buckingham JC. **Prog Med Chem** 1978; 15:165-210 (380 ref.)

PITUITARY HORMONES

Role of brain peptides in the control of pituitary hormone release. McCann SM, et al. **Mater Med Pol** 1980 Jan-Jun;12(1-2):47-52

In vivo thyroxine release in day-old cockerels in response to acute stimulation by mammalian and avian pituitary hormones. MacKenzie DS. **Poult Sci** 1981 Sep;60(9):2136-43

PITUITARY HORMONES, ANTERIOR

The effects of propranolol and acebutolol on the overnight plasma levels of anterior pituitary and related hormones. Lewis MJ, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):737-42

Evidence for intragranular processing of pro-opiocortin in the mouse pituitary intermediate lobe. Loh YP, et al. **Eur J Cell Biol** 1981 Dec; 26(1):177-83

PROCHLORPERAZINE

Phenothiazine biphasic effect on dopamine concentrations in the basal ganglia of subhuman primates. Bird ED, et al. **Psychiatry Res** 1982 Feb;6(1):1-6

PROGESTERONE

Effects of ovarian steroids on serotonin metabolism within grossly dissected and microdissected brain regions of the ovariectomized rat. Cone RI, et al. **Brain Res Bull** 1981 Dec;7(6):639-44

Calmodulin is involved in the first step of oocyte maturation: effects of the antipsychotic drug fluphenazine and of anticalmodulin antibodies on the progesterone-induced maturation of xenopus laevis oocyte. Cartaud A, et al. **Cell Differ** 1981 Dec;10(6):357-63

Stimulation of progesterone and prostaglandin E accumulation by luteinizing hormone-releasing hormone (LHRH) and LHRH analogs in rat granulosa cells. Clark MR. **Endocrinology** 1982 Jan; 110(1):146-52

Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Padmanabhan V, et al. **Endocrinology** 1982 Mar;110(3):717-21

Interaction of gonadotropin-releasing hormone agonist and antagonist with progesterone, prolactin, or human chorionic gonadotropin during pregnancy in the rat. Rivier C, et al. **Endocrinology** 1982 Feb; 110(2):347-51

Sensitivity of pituitary and corpus luteum responses to single intranasal administration of (D-ser[TBU]6-des-gly-NH2(10)) luteinizing hormone-releasing hormone ethylamide (Buserelin) in normal women. Lemay A, et al. **Fertil Steril** 1982 Feb;37(2):193-200

Inhibin-like activity and steroid content in human follicular fluid during the periovulatory period., Lefevre B, et al. **Int J Fertil** 1981; 26(4):295-6

Inhibition of human granulosa cell progesterone secretion by a gonadotropin-releasing hormone agonist. Tureck RW, et al. **J Clin Endocrinol Metab** 1982 May;54(5):1078-80

Effects of an intermittent lighting schedule on the time of egg-laying and the levels of luteinizing hormone, progesterone and corticosterone in the plasma of the domestic hen. Duplaix M, et al. **J Endocrinol** 1981 Dec;91(3):375-83

Motor activity of the human Fallopian tube in vitro in relation to plasma concentration of oestradiol and progesterone, and the influence of noradrenaline. Helm G, et al. **J Reprod Fertil** 1982 Jan;64(1):233-42

In vivo antiglucocorticoids: Comparison between in vivo activity and in vitro competition of progestins for the glucocorticoid receptor. Naylor PH, et al. **J Steroid Biochem** 1981 Dec;14(12):1303-9

Comparison of steroid and LH-RH effects on the responsiveness of hemipituitary glands and dispersed pituitary cells. Speight A, et al. **Mol Cell Endocrinol** 1981 Dec;24(3):267-81

Cyclic AMP-mediated control of meiosis: effects of progesterone, cholera toxin, and membrane-active drugs in Xenopus laevis oocytes. Schorderet-Slatkine S, et al. **Proc Natl Acud Sci USA** 1982 Feb; 79(3):850-4

[Ureteral response, through adrenergic stimulation, to the action of progesterone and estradiol] García Sacristán A, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):129-32 (Spa)

PROLACTIN

Pattern of prolactin secretion and pituitary responsiveness to LRH in pseudopregnant rats maintained in constant light. Koiter TR, et al. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):31-8

Physiological role of endorphins in neuroendocrinology. Dupont A, et al. **Acta Physiol Pol** 1981;32(5 Suppl 23):37-57 (45 ref.)

Autoregulation of rat pituitary prolactin secretion demonstrated by a new perfusion method. Zacur HA, et al. **Am J Physiol** 1982 Apr; 242(4):E226-33

The amino acid composition of secreted mouse prolactin, growth hormone, and hamster prolactin: the presence of one tryptophan in mouse prolactin. Colosi P, et al. **Arch Biochem Biophys** 1981 Dec; 212(2):759-61

Suppression of mammotropic development and prolactin release by sympathomimetic drugs in rats. Shani J, et al. **Arch Farmacol Toxicol** 1981 Aug;7(2):201-8

Effect of domperidone on prolactin (PRL)and thyrotrophin (TSH) secretion. Kaufman JM, et al. **Arch Int Pharmacodyn Ther** 1981 Dec; 254(2):293-303

The extracerebral dopamine antagonist domperidone block the suppressive effect of bromocriptine on prolactin and TSH secretion in man. Svet-Moldavsky I, et al. **Biomedicine** 1981 Oct;35(5):142-4

Changes in prolactin binding sites in the rabbit hypothalamus induced by physiological and pharmacological variations of prolactin serum levels. Di Carlo R, et al. **Brain Res** 1981 Dec 28;230(1-2):445-50

Comparative effects of estrogens and prolactin on nigral and striatal GAD activity. Nicoletti F, et al. **Brain Res** 1982 Jan 28;232(1):238-41

Somatostatin inhibits prolactin secretion in the estradiol primed male rat. Cooper GR, et al. **Can J Physiol Pharmacol** 1981 Oct;59(10):1082-8

Immunoreactive calcitonin in maternal milk and serum in relation to prolactin and neurotensin. Werner S, et al. **Early Hum Dev** 1982 Jan; 6(1):77-82

Induction of testicular gonadotropin-releasing hormone (GnRH) receptors by GnRH: effects of pituitary hormones and relationship to inhibition of testosterone production. Bourne GA, et al. **Endocrinology** 1982 Mar;110(3):727-33

Evidence for the involvement of central epinephrine systems in the regulation of luteinizing hormone, prolactin, and growth hormone release in female rats. Crowley WR, et al. **Endocrinology** 1982 Apr; 110(4):1102-7

Inhibition of lordosis behavior in the female rat by intraventricular infusion of prolactin and by chronic hyperprolactinemia. Dudley CA, et al. **Endocrinology** 1982 Feb;110(2):677-9

Effects of somatostatin and urotensin II on tilapia pituitary prolactin release and interactions between somatostatin, osmotic pressure Ca++, and adenosine 3',5'-monophosphate in prolactin release in vitro. Grau EG, et al. **Endocrinology** 1982 Mar;110(3):910-5

Interaction of gonadotropin-releasing hormone agonist and antagonist with progesterone, prolactin, or human chorionic gonadotropin during pregnancy in the rat. Rivier C, et al. **Endocrinology** 1982 Feb; 110(2):347-51

Catecholestrogens and release of anterior pituitary gland hormones. II. Prolactin. Rodriguez-Sierra JF, et al. **Endocrinology** 1982 Feb; 110(2):325-9

Estrogen in high doses inhibits perphenazine-induced prolactin release. Sinha YN, et al. **Endocrinology** 1982 Jan;110(1):126-30

Bombesin stimulates prolactin and growth hormone release by pituitary cells in culture. Westendorf JM, et al. **Endocrinology** 1982 Feb; 110(2):352-8

Lactation-inhibiting and prolactin-lowering effect of lisuride and bromocriptine: a comparative study. Van Dam LJ, et al. **Eur J Obstet Gynecol Reprod Biol** 1981 Nov;12(5):323-30

Rat prolactin and hypothalamic catecholamine nerve terminal systems. Evidence for rapid and discrete increases in dopamine and noradrenaline turnover in the hypophysectomized male rat. Andersson K, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):261-5

ACTH1-24 counteracts the prolactin-releasing effect of an opioid. Ferri S, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):143-5

Sulpiride effects on nigral and striatal glutamic acid decarboxylase activity: a possible involvement of prolactin. Nicoletti F, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):131-5

Phenothiazines inhibit prolactin secretion in vitro. A possible role for calmodulin in stimulus—secretion coupling in the pituitary. Merritt JE, et al. **FEBS Lett** 1981 Nov 30;135(1):107-10

Pituitary hormonal response to the orthopramides clebopride, bromopride, metoclopramide, and sulpiride. Pérez-López FR, et al. **Fertil Steril** 1982 Mar;37(3):445-8

Differential effects of bromocriptine treatment on LH release and copulatory behavior in hyperprolactinemic male rats. Doherty PC, et al. **Horm Behav** 1981 Dec;15(4):436-50

Prolactin responsiveness to repeated decremental doses of sulpiride. Tormey WP, et al. **Horm Metab Res** 1981 Aug;13(8):454-5

Prolactin suppression and spermatogenic developments in maturing rats. A quantitative study. Nag S, et al. **Horm Res** 1981;15(2):72-7

Prolactin resistance to bromocryptine treatment: a case report. Borenstein R, et al. **Int J Fertil** 1981;26(4):287-9

Combined bromocryptine and hMG treatment in hyperprolactinemic infertility. Katz Z, et al. **Int J Fertil** 1981;26(4):290-2

Failure of stress and supplemental lighting to affect release of prolactin in swine. Hoagland TA, et al. **J Anim Sci** 1981 Aug;53(2):467-72

Pituitary sensitivity to gonadotrophin releasing hormone after hyperprolactinaemia induced with neuroleptics and domperidone in the rat. Carter DA, et al. **J Endocrinol** 1981 Dec;91(3):439-46

Neurotransmitter effects on release of prolactin and growth hormone in vitro from pituitary glands of the pigeon, Columba livia. Hall TR. **J Endocrinol** 1982 Feb;92(2):303-8

Drug-induced hyperprolactinaemia and discharges of luteinizing hormone evoked by oestrogen in ovariectomized rhesus monkeys. Martensz ND, et al. **J Endocrinol** 1982 Jan;92(1):111-22

Circadian rhythmicity of prolactin secretion in elderly subjects: changes during bromocriptine treatment. Polleri A, et al. **J Endocrinol Invest** 1981 Jul-Sep;4(3):317-21

In-vivo and in-vitro effects of domperidone on the release of prolactin and LH in male and female rats. Carter DA, et al. **J Reprod Fertil** 1982 Jan;64(1):191-7

Influence of adrenocorticotropin and adrenalectomy on gonadotropin secretion in immature rats. Mann DR, et al. **Neuroendocrinology** 1982 Jan;34(1):20-6

Temporal and other effects of catechol estrogens on prolactin secretion in the rat. Shin SH, et al. **Neuroendocrinology** 1981 Dec;33(6):352-7

The effect of monoamine oxidase A and B inhibitors on rat serum prolactin. Keane PE, et al. **Neuropharmacology** 1981 Dec; 20(12A):1157-62

Rapid glucocorticoid inhibition of vasoactive intestinal peptide-induced cyclic AMP accumulation and prolactin release in rat pituitary cells in culture. Rotsztejn WH, et al. **Proc Natl Acad Sci USA** 1981 Dec; 78(12):7584-8

Differential effects of warm- and cold-ambient temperature on blood levels of beta-endorphin and prolactin in the rat. Deeter WT 3d, et al. **Proc Soc Exp Biol Med** 1981 Dec;168(3):369-72

Hyperprolactinemia and hyperadrenocorticism accompanied by normal blood pressure in Sprague-Dawley rats. McMurtry JP, et al. **Proc Soc Exp Biol Med** 1981 Oct;168(1):114-8

Nontraditional neurotransmitters and prolactin release. Donoso AO, et al. **Prog Clin Biol Res** 1981;74:219-28 (35 ref.)

Inhibitors of prolactin secretion: a mini-review. Slaunwhite WR Jr. **Prog Clin Biol Res** 1981;75B:19-29 (42 ref.)

Tolerance to the prolactin-elevating effect of neuroleptics. Brown WA, et al. **Psychiatry Res** 1981 Dec;5(3):317-22

(Des-tyrosine1)-gamma-endorphin in schizophrenia: clinical, biochemical, and hormonal aspects. Verhoeven WM, et al. **Psychiatry Res** 1981 Dec;5(3):293-309

Growth hormone and prolactin secretion in adults and hyperactive children: relation to methylphenidate serum levels. Gualtieri CT, et al. **Psychoneuroendocrinology** 1981 Dec;6(4):331-9

[Validity of radioimmunoassay for blood and pituitary prolactin in the male rat. Effect of bromocriptine and thyrotropin-releasing hormone] André M, et al. **C R Soc Biol (Paris)** 1981;175(6):792-800 (Eng. Abstr.) (Fre)

[Clinical aspects of the sensitivity of the prolactin system to daily fluctuation] Rindt W, et al. **Methods Find Exp Clin Pharmacol** 1981; 3 Suppl 1:115S-118S (Ger)

[The effect of bromocriptine induced estradiol-17 beta in amenorrhea patients with normoprolactinemia and hyperprolactinemia (author's transl)] Kato K, et al. **Horumon To Rinsho** 1981 Aug;29(8):931-5 (Jpn)

PROMETHAZINE

Effect of promethazine hydrochloride on bone resorption in tissue culture. Goldhaber P, et al. **Proc Soc Exp Biol Med** 1982 Jan;169(1):105-9

[Metabolic interactions of promethazine (author's transl)] Pfeifer S, et al. **Pharmazie** 1981 Dec;36(12):815-8 (Eng. Abstr.) (Ger)

PROPANEDIOLS

The effect of pH, temperature and certain media constituents on the stability and activity of the preservative, bronopol. Moore KE, et al. **J Appl Bacteriol** 1981 Dec;51(3):483-94

Intracoronary propylene glycol [letter] Pepine CJ, et al. **N Engl J Med** 1982 Apr 8;306(14):868-9

Comparative short-term inhalation toxicity of ethylene glycol monomethyl ether and propylene glycol monomethyl ether in rats and mouse. Miller RR, et al. **Toxicol Appl Pharmacol** 1981 Dec; 61(3):368-77

PROPRANOLOL

Effect of chronic propranolol treatment and withdrawal on norepinephrine and tyrosine hydroxylase in sympathetic tissues. Atkins F, et al. **Arch Int Pharmacodyn Ther** 1981 Dec;254(2):271-81

Effect of L-propranolol on the binding, Internalization and degradation of 125I-low density lipoproteins by human skin fibroblasts. Ghiselli G, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):1060-8

The influence of propranolol on the concentration of heme and on the activity of delta aminolevulinate synthase in monolayers of chick embryo liver cells. Epstein O, et al. **Biochem Pharmacol** 1982 Feb 15; 31(4):485-9

Regulation of adrenergic stimulation of hepatic adenylate cyclase by divalent cations. Jackowski MM, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):74-83

The effects of propranolol and acebutolol on the overnight plasma levels of anterior pituitary and related hormones. Lewis MJ, et al. **Br J Clin Pharmacol** 1981 Nov;12(5):737–42

The use of buccal partitioning as a model to examine the effects of aluminium hydroxide gel on the absorption of propranolol. McElnay JC, et al. **Br J Clin Pharmacol** 1982 Mar;13(3):399–403

Effect of propranolol on the airway response to prostaglandin E2 in normal man. Seth RV, et al. **Br J Clin Pharmacol** 1981 Nov; 12(5):731–5

Comparative studies of (−)-, (+/−)-propranolol, atenolol, guanethidine, bretylium and tetracaine on adrenergic transmission. Kaiho M, et al. **Br J Pharmacol** 1981 Oct;74(2):365–70

Diazepam, propranolol and their combination in the management of chronic anxiety. Hallstrom C, et al. **Br J Psychiatry** 1981 Nov; 139:417–21

Propranolol in experimentally induced stress. Taylor EA, et al. **Br J Psychiatry** 1981 Dec;139:545–9

Attenuation of exercise conditioning by beta-adrenergic blockade. Sable DL, et al. **Circulation** 1982 Apr;65(4):679–84

Selective chemical hepatic sympathectomy in the dog. Allman FD, et al. **Crit Care Med** 1982 Feb;10(2):100–3

In vivo study of propranolol and metabolite(s) disposition in rat liver. Ong H, et al. **Drug Metab Dispos** 1981 Nov–Dec;9(6):529–34

Pharmacokinetics of bendroflumethiazide alone and in combination with propranolol and hydralazine. Schäfer-Korting M, et al. **Eur J Clin Pharmacol** 1982;21(4):315–23

Plasma triiodothyronine response to thyrotropin releasing hormone, thyrotropin and propranolol in old age. Szabolcs I, et al. **Exp Gerontol** 1981;16(4):309–16

Effects of isoproterenol on vectorcardiographic pattern of 'early repolarization syndrome'. Fantini F, et al. **G Ital Cardiol** 1981; 11(6):797–802

Glucagon in anaphylaxis [letter] Lee ML. **J Allergy Clin Immunol** 1982 Mar;69(3):331–2

Blood flow and O2 uptake in dog hindlimb with anemia, norepinephrine, and propranolol. Chapler CK, et al. **J Appl Physiol** 1981 Sep; 51(3):565–70

Effect of propranolol on local cerebral blood flow under normocapnic and hypercapnic conditions. Dahlgren N, et al. **J Cereb Blood Flow Metab** 1981;1(4):429–36

Comparative bioavailability of propranolol: twice-daily versus four times-daily administration. Dvornik D, et al. **J Clin Pharmacol** 1981 Nov–Dec;21(11–12 Pt 1):472–6

Is propranolol antischizophrenic? Peet M. **Neuropharmacology** 1981 Dec; 20(12B):1303–7 (36 ref.)

Electrocardiographic and metabolic investigations concerning the exhaustive exercise under conditions of adrenergic blocking in rats. Schneider F, et al. **Physiologie** 1982 Jan–Mar;19(1):31–3

Alpha- and beta-adrenergic control of pancreatic polypeptide and insulin secretion in adult chickens. Smith MK, et al. **Proc Soc Exp Biol Med** 1981 Dec;168(3):319–24

Chemical trapping of labile aldehyde intermediates in the metabolism of propranolol and oxprenolol. Goldszer F, et al. **Res Commun Chem Pathol Pharmacol** 1981 Nov;34(2):193–205

The effect of adrenoceptor blockade on the release of gastric inhibitory polypeptide after intraduodenal glucose in humans. Flaten O. **Scand J Gastroenterol** 1981;16(5):641–5

The effect of propranolol on insulin-stimulated gastric secretion in dogs. Grabner P, et al. **Scand J Gastroenterol** 1981;16(8):1067–72

[Pharmacokinetics of propranolol in healthy humans] Steinhoff J, et al. **Pharmazie** 1981 Nov;36(11):785–6 (Ger)

[Pharmacoprophylaxis of an experimental neurogenic pancreatic injury] Nilova TN. **Farmakol Toksikol** 1982 Jan–Feb;45(1):62–5 (Eng. Abstr.) (Rus)

[Action of propranolol, nifenalol, and pindolol on the lipolytic effect of adrenaline in the rat epididymis] Sánchez-Cuadrado MC, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):181–2 (Spa)

PROSTAGLANDINS

Effect of bisenoic prostaglandins and arachidonic acid on the uterine vasculature of pregnant sheep. Clark KE, et al. **Am J Obstet Gynecol** 1982 Feb 1;142(3):261–8

Effects of renal nerve stimulation, norepinephrine and angiotensin II on renal blood flow in relation to release of PG-like substances in anesthetized dogs. Satoh S, et al. **Arch Int Pharmacodyn Ther** 1981 Dec; 254(2):304–16

Evidence against the involvement of prostaglandins in the vasoconstrictor action of calcium ion in rat mesenteric blood vessels. Coupar IM. **Br J Pharmacol** 1981 Oct;74(2):477–84

Glucocorticoids as inhibitors of prostaglandin synthesis. Russo-Marie F, et al. **Bull Eur Physiopathol Respir** 1981;17(4):587–94 (38 ref.)

Enhancement by prostacyclin of the contractility of the guinea-pig airways smooth muscle. Vargaftig BB, et al. **Eur J Pharmacol** 1981 Sep 11;74(2–3):141–8

Stimulation of prostaglandin synthesis in rat cerebral cortex via a beta-adrenoceptor. Hillier K, et al. **Gen Pharmacol** 1982;13(1):21–5

Evidence for a direct stimulatory effect of prostacyclin on renin release in man. Patrono C, et al. **J Clin Invest** 1982 Jan;69(1):231–9

Central cardiovascular effects of prostacyclin. Feuerstein G, et al. **Neuropharmacology** 1981 Nov;20(11):1085–90

Studies on the behavioral and hypotensive effects of intraventricular prostacyclin (PGI2) in rats. Brus K, et al. **Pol J Pharmacol Pharm** 1981; 33(4):467–74

Effect of corticosterone, hydrocortisone and prostaglandin fatty acid precursors on the spontaneous motility of the uterus isolated from ovariectomized rats. Bonacossa A, et al. **Prostaglandins** 1982 Jan; 23(1):113–28

A proposed role for prostaglandins in the modulation of the relaxation response to urotensin I in isolated rat arteries. Gerritsen ME, et al. **Prostaglandins** 1981 Dec;22(6):873–92

PSYCHIATRY

A program for late twentieth-century psychiatry. Unger RM. **Am J Psychiatry** 1982 Feb;139(2):155–64

[Misunderstanding between neuroscientists and clinicians (author's transl)] Bleuler M. **Nervenarzt** 1982 Jan;53(1):14–7 (Ger)

[The boundary between psychiatry and biological therapeutics] Carrillo Broatch A. **Rev Neuropsiquiatr** 1980 Jun;43(2):87–96 (Eng. Abstr.) (Spa)

[Psychiatry in China. Doubts about Freud, various forms of herbal medicine and Western psychotropic drugs] Calltorp J. **Lakartidningen** 1981 Oct 21;78(43):3788–91 (Eng. Abstr.) (Swe)

PSYCHOLOGY, CLINICAL

[Medical psychology – a tradition-laden area or the expression of a new development in medicine?] Szewczyk H. **Psychiatr Neurol Med Psychol (Leipz)** 1981 Oct;33(10):589–96 (Eng. Abstr.) (Ger)

PSYCHOMOTOR AGITATION

A trial of dextroamphetamine in patients with involutional agitated depression. Ward NG, et al. **J Clin Psychiatry** 1982 Jan;43(1):35–6

PSYCHOPHARMACOLOGY

[Psychoanalysis or pharmacologic blockage in cultivation of mentally handicapped] Baruk H. **Ann Med Psychol (Paris)** 1981;139(3):335–8 (Fre)

[The boundary between psychiatry and biological therapeutics] Carrillo Broatch A. **Rev Neuropsiquiatr** 1980 Jun;43(2):87–96 (Eng. Abstr.) (Spa)

PSYCHOPHYSIOLOGIC DISORDERS

A new model of integrating Occidental and Oriental approaches. Nagakawa T, et al. **J Psychosom Res** 1982;26(1):57–62

Minor tranquilizers: prescribing practices of primary physicians. Rittelmeyer LF Jr. **Psychosomatics** 1982 Jan;23(1):23–6

[Psychotropic drugs in non-psychiatric practice (author's transl)] Reimer F. **HNO** 1981 Dec;29(12):415–7 (Eng. Abstr.) (Ger)

PSYCHOSES, SUBSTANCE-INDUCED

Steroid psychosis and tricyclic antidepressants [letter] Dietch JT. **Arch Gen Psychiatry** 1982 Feb;39(2):236

Lithium withdrawal triggers psychotic states [letter] Klein HE, et al. **Br J Psychiatry** 1981 Sep;139:255–6

Amphetamine psychosis and schizophrenia: a dual model. Kokkinidis L, et al. **Neurosci Biobehav Rev** 1981 Winter;5(4):449–61 (173 ref.)

PSYCHOTHERAPY

Level of ego development and psychotherapy outcome in phobic patients. Rock MH, et al. **Br J Med Psychol** 1981 Dec;54(Pt 4):319–28

The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy, each alone and in combination. Blackburn IM, et al. **Br J Psychiatry** 1981 Sep;139:181–9

Cognitive therapy for depression [editorial] Goldberg D. **Br Med J [Clin Res]** 1982 Jan 16;284(6310):143–4

Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Phillips RH. **Psychosomatics** 1982 Jan;23(1):81–7

[Depression. Treatment] Hougardy G. **Rev Med Liege** 1982 Jan 1; 37(1):14–6 (Fre)

[Psychotherapy in psychiatric practice (author's transl)] Nedelmann C. **Nervenarzt** 1982 Jan;53(1):33–8 (Ger)

PSYCHOTHERAPY, GROUP

What's a medication group? Larkin AR. **J Psychosoc Nur Ment Health Serv** 1982 Feb;20(2):35–7

[Group psychotherapy of chronic schizophrenics in an external milieu]. Filotto JF. **Can J Psychiatry** 1981 Dec;26(8):558–61 (Eng. Abstr.) (Fre)

PSYCHOTIC DISORDERS

Influence of different psychotropic drugs on psychotic anxiety. Nahunek K, et al. **Agressologie** 1981 Nov;22(D):11-3

Periodic psychosis of puberty: a case report. Berlin FS, et al. **Am J Psychiatry** 1982 Jan;139(1):119-20

Sustaining treatment with the hospitalized patient who refuses treatment. Geller JL. **Am J Psychiatry** 1982 Jan;139(1):112-3

Distribution of lithium elimination rates in a selected population of psychiatric patients. Thornhill DP, et al. **Eur J Clin Pharmacol** 1982; 21(4):351-4

What's a medication group? Larkin AR. **J Psychosoc Nur Ment Health Serv** 1982 Feb;20(2):35-7

Stress, endorphins and psychosis. A hypothesis. Amir S, et al. **Mod Probl Pharmacopsychiatry** 1981;17:192-201

Measurement of endorphins in CSF. Relationship to psychiatric diagnosis. Pickar D, et al. **Mod Probl Pharmacopsychiatry** 1981;17:246-62

Neuroleptic-like and antipsychotic effects of gamma-type endorphins. Van Ree JM, et al. **Mod Probl Pharmacopsychiatry** 1981;17:266-78

Fine motor performance before and after treatment in schizophrenic and schizoaffective patients Goode DJ, et al. **Psychiatry Res** 1981 Dec; 5(3):247-55

Red blood cell/plasma haloperidol ratios and antipsychotic efficacy [letter] Neborsky RJ, et al. **Psychiatry Res** 1982 Feb;6(1):123-4

[Treatment of schizophrenic psychoses by sustained-action neuroleptics in psychiatric outpatients' treatment (author's transl)] Poláček J. **Cesk Psychiatr** 1982 Feb;78(1):49-55 (Eng. Abstr.) **(Cze)**

[Depot Neuroleptic preparations in psychiatric practice (author's transl)] Svestka J, et al. **Cesk Psychiatr** 1981 Jun;77(3):187-97 (Eng. Abstr.) **(Cze)**

[Conditions for prolonged prescription of neuroleptics with reference to several clinical cases] Tholose A. **Ann Med Psychol (Paris)** 1981; 139(8):894-9 **(Fre)**

[Night sleep study in chronic psychotics under long term flupenthixol treatment (author's transl)] Serbanescou T, et al. **Encephale** 1981; 7(5):623-9 (Eng. Abstr.) **(Fre)**

[Comparison between the effectiveness of fluphenazine decanoate and oxyprothepin decanoate in schizophrenia (double-blind crossover study)] Balon R, et al. **Zh Nevropatol Psikhiatr** 1982;82(1):116-8 (Eng. Abstr.) **(Rus)**

QUINIDINE

Hemoperfusion in quinidine intoxication. Haapanen EJ, et al. **Acta Med Scand** 1981;210(6):515-6

Digoxin--quinidine interaction [letter] Das G. **Am J Cardiol** 1982 Feb 1;49(2):495

Pharmacokinetic analysis of intravenously and orally administered quinidine in cows. McGuirk SM, et al. **Am J Vet Res** 1981 Sep; 42(9):1482-7

Shortening of the action potential and reduction of pacemaker activity by lidocaine, quinidine, and procainamide in sheep cardiac purkinje fibers. An effect on Na or K currents? Carmeliet E, et al. **Circ Res** 1982 Feb;50(2):257-72

Mechanisms of action of lidocaine and quinidine on action potential duration in rabbit cardiac Purkinje fibers. An effect on steady state sodium currents? Colatsky TJ. **Circ Res** 1982 Jan;50(1):17-27

Mechanisms of quinidine-induced depression of maximum upstroke velocity in ovine cardiac Purkinje fibers. Weld FM, et al. **Circ Res** 1982 Mar;50(3):369-76

Age-related differences in the protein binding of quinidine. Pickoff AS, et al. **Dev Pharmacol Ther** 1981;3(2):108-15

Absorption of quinidine and dihydroquinidine in humans. Hailey DM, et al. **Eur J Clin Pharmacol** 1981;21(3):195-9

Digoxin - quinidine interaction [letter] Cheng TO. **J Am Geriatr Soc** 1982 Jan;30(1):79-80

Influence of disopyramide, compared with procainamide and quinidine, on isolated dog arteries in response to transmural stimulation and norepinephrine. Toda N, et al. **J Cardiovasc Pharmacol** 1981 Nov-Dec; 3(6):1332-41

Investigation of digoxin, quinidine, and disopyramide interactions in rats utilizing parotid saliva, blood, and other tissues. DiGregorio GJ, et al. **J Pharm Sci** 1982 Feb;71(2):211-3

Enzyme immunoassay and two fluorometric methods compared for the determination of quinidine in serum. Pape BE. **Ther Drug Monit** 1981; 3(4):357-63

REACTION TIME

Acute behavioral effects of styrene exposure: a further analysis. Cherry N, et al. **Br J Ind Med** 1981 Nov;38(4):346-50

RECEPTORS, ADRENERGIC

Receptor supersensitivity in mental disease. Westermann KH, et al. **Agressologie** 1981 Nov;22(E):33-5

Studies on the mechanism of action of somatostatin on renal gluconeogenesis: evidence for the involvement of alpha 1-adrenergic stimuli. Dileepan KN, et al. **Arch Biochem Biophys** 1982 Jan; 213(1):169-76

Adrenergic receptor sensitivity in depression. Effects of clonidine in depressed patients and healthy subjects. Charney DS, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):290-4

Catecholamine binding to the alpha-adrenergic receptors of hamster adipocytes. Evidence that guanine nucleotides regulate this binding to the alpha 2-receptor subtype. Pecquery R, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):14-25

Inhibitory action of the ventral noradrenergic bundle on the lateral hypothalamic neurons through alpha-noradrenergic mechanisms in the rat. Miyahara S, et al. **Brain Res** 1982 Feb 25;234(2):459-63

The regulation of striatal DOPA synthesis by alpha 2-adrenoreceptors. Rabey JM, et al. **Brain Res** 1981 Dec 28;230(1-2):422-6

Guanine nucleotide and magnesium ion regulation of the interaction of gonadotropic and beta-adrenergic receptors with their hormones: a comparative study using a single membrane system. Abramowitz J, et al. **Endocrinology** 1982 Feb;110(2):336-46

Differential effects of pharmacological manipulations of central alpha 1- and alpha 2-adrenergic receptors on the secretion of thyrotropin and growth hormone in male rats. Krulich L, et al. **Endocrinology** 1982 Mar;110(3):796-804

Involvement of alpha 1-adrenergic receptors in the inhibitory effect of catecholamines on the thyrotropin-induced release of thyroxine by the mouse thyroid. Muraki T, et al. **Endocrinology** 1982 Jan;110(1):51-4

Evidence for involvement of alpha-adrenergic receptors in norepinephrine-induced prostaglandin E2 and luteinizing hormone-releasing hormone release from the median eminence. Ojeda SR, et al. **Endocrinology** 1982 Feb;110(2):409-12

Adrenergic mechanisms involved in the control of pituitary-adrenal activity in the rat: a beta-adrenergic stimulatory mechanism. Tilders FJ, et al. **Endocrinology** 1982 Jan;110(1):114-20

Cation sensitivity of [125I]heat binding to alpha 1-adrenoceptors in rat cerebral cortex membranes. Glossmann H, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):149-53

Discrepancy in the regulatory effects of sodium and guanine nucleotides on adrenaline and clonidine binding to alpha 2-adrenoceptors in human fat cell membranes. Gonzalez JL, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):289-93

The increase of cardiac beta 1-subtype of beta-adrenergic receptors in adult rats following neonatal 6-hydroxydopa treatment. Kajiyama H, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):75-7

alpha 1-Adrenoceptor-mediated responses in the lateral geniculate nucleus are enhanced by chronic antidepressant treatment. Menkes DB, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):27-35

Influence of age on the effects of chronic fluphenazine on receptor binding in rat brain. Misra CH, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):317-24

Adrenal steroid-induced changes in beta-adrenergic receptor binding in rat hippocampus. Roberts DC, et al. **Eur J Pharmacol** 1981 Aug 27; 74(1):37-41

Haemophilus influenzae induced loss of lung beta-adrenoceptor binding sites and modulation by changes in peripheral catecholaminergic input. Schreurs AJ, et al. **Eur J Pharmacol** 1982 Jan;77(2-3):95-102

Effect of norepinephrine uptake blocker on beta-adrenergic receptors of the rat cerebral cortex. Sethy VH, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):53-6

Reserpine-induced supersensitivity and the proliferation of cardiac beta-adrenoceptors. Tenner TE Jr, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):61-5

Agonistic actions of DPI (2-(3,4-dihydroxyphenylimino)-imidazolidine) on alpha-adrenoceptors and dopamine receptors. Woodman OL, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):11-9

Desensitization of the beta-adrenergic receptor-adenylate cyclase complex in rabbit iris-ciliary body induced by topical epinephrine. Mittag T, et al. **Exp Eye Res** 1981 Nov;33(5):497-503

Stimulation of prostaglandin synthesis in rat cerebral cortex via a beta-adrenoceptor. Hillier K, et al. **Gen Pharmacol** 1982;13(1):21-5

Synthesis and adrenoceptor affinity of some highly polar beta-substituted catecholamines. Henkel JG, et al. **J Med Chem** 1981 Oct; 24(10):1258-60

(alpha S)-erythro-alpha-methylepinephrine: preparation and stereoselective binding to adrenergic receptors in rat forebrain. Taylor CA Jr, et al. **J Med Chem** 1981 Oct;24(10):1261-3

Enhanced responsiveness of alpha-noradrenergic receptors following discrete electrolytic lesions of the nucleus locus coeruleus: a behavioral demonstration. De Carvalho LP, et al. **J Neural Transm** 1982; 53(1):23-37

Electroconvulsive shock and reserpine: effects on beta-adrenergic receptors in rat brain. Kellar KJ, et al. **J Neurochem** 1981 Oct; 37(4):830-6

Modulation of central noradrenaline release by postsynaptic receptors. Wyllie MG, et al. **J Pharm Pharmacol** 1982 Jan;34(1):53-5

Calcium and the alpha-action of catecholamines on guinea-pig taenia caeci. Den Hertog A. **J Physiol (Lond)** 1981 Jul;316:109-25

Alpha 2 adrenergic receptors in depression [editorial] **Lancet** 1982 Apr 3;1(8275):781

Development of stimulus-secretion coupling in salivary glands. Cutler LS, et al. **Methods Cell Biol** 1981;23:531–45

Antagonistic properties of quipazine at presynaptic serotonin receptors and alpha-adrenoceptors in rat brain cortex slices. Schlicker E, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):204–8

3H-Noradrenaline and 3H-5-hydroxytryptamine release from rat brain slices and its presynaptic alpha-adrenergic modulation after long-term desipramine pretreatment. Schoffelmeer AN, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):173–80

Beta-adrenergic receptors in rat cerebellum after neonatal X-irradiation: effect of prolonged imipramine and lithium treatment. Türck M, et al. **Neurosci Lett** 1981 Dec 23;27(3):357–62

Characterization of catecholamine binding sites in the rat brain. Agrawal AK, et al. **Neurotoxicology (Park Forest II)** 1981 Oct;2(2):365–71

Brain reinforcement mechanisms: alpha-adrenergic and dopaminergic agonists and antagonists. Wauquier A, et al. **Prog Clin Biol Res** 1981; 71:177–96

Subsensitivity of human beta-adrenergic adenylate cyclase after salbutamol treatment of depression. Lerer B, et al. **Psychopharmacology (Berlin)** 1981;75(2):169–72

[Role of postsynaptic noradrenergic receptors in the mechanism of action of antidepressants] Cuenca E. **Encephale** 1981;7(4 Suppl):397 (Fre)

RECEPTORS, CHOLINERGIC

Increase of acetylcholine-receptor sensitivity by adenosine triphosphate: a novel action of ATP on ACh-sensitivity. Akasu T, et al. **Br J Pharmacol** 1981 Oct;74(2):505–7

Muscarinic acetylcholine receptors of the small intestine and pancreas of the rat: distribution and the effect of vagotomy. Isaacs PE, et al. **Clin Sci** 1982 Feb;62(2):203–7

Autoregulation of acetylcholine release in isolated hippocampal nerve endings. Marchi M, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):75–9

Influence of age on the effects of chronic fluphenazine on receptor binding in rat brain. Misra CH, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):317–24

Phenylclindine-induced alteration in rat muscarinic cholinergic receptor regulation. Ward D, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2–3):189–93

Relation between subsynaptic receptor blockade and response to quantal transmitter at the mouse neuromuscular junction. Pennefather P, et al. **J Gen Physiol** 1981 Sep;78(3):313–44

Adenylate cyclase of Torpedo synaptosomes is inhibited by calcium and not affected by muscarinic ligands. Pinchasi I, et al. **J Neurochem** 1982 May;38(5):1223–9

The kinetics of acetylcholine turnover in a resting cholinergic nerve terminal and the magnitude of the cytoplasmic compartment. Weiler M, et al. **J Neurochem** 1982 May;38(5):1187–91

Loss of muscarinic receptors and of stimulated phospholipid labeling in ibotenate-treated hippocampus. Fisher SK, et al. **J Neurosci** 1981 Dec; 1(12):1407–13

A study of desensitization of acetylcholine receptors using nerve-released transmitter in the frog. Magleby KL, et al. **J Physiol (Lond)** 1981 Jul; 316:225–50

Interaction of tricyclic antidepressants with the ionic channel of the acetylcholine receptor of Torpedo electric organ. Shaker N, et al. **Mol Pharmacol** 1981 Nov;20(3):511–8

Sympathetic Nerve Stimulation on the perfused rat heart. Affinities of N-methylatropine and pirenzepine at pre- and postsynaptic muscarine receptors. Fuder H, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):210–9

Decreased 3H-L-quinuclidinyl benzilate binding and muscarine receptor subsensitivity after chronic gamma-butyrolactone treatment. Giorgi O, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Dec;318(1):14–8

Cholinergic actions of false neurotransmitters: acetyldiethylcholine. Aronstam RS, et al **Neurosci Lett** 1982 Jan 22;28(1):51–6

Changes in rat hippocampal benzodiazepine receptors and lack of changes in muscarinic receptors after fimbria-fornix lesions. Sábato UC, et al. **Neurosci Lett** 1981 Dec 11;27(2):193–7

Changes in neuromuscular junction endplate current time constants produced by sulfhydryl reagents. Steinacker A, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7806–9

3-Chlorodibenzazepine binding to cholinergic receptors and ion channels. Aronstam RS, et al. **Res Commun Chem Pathol Pharmacol** 1981 Dec; 34(3):551–4

[The blocking potencies and the mode of blockade by pentobarbital and phenobarbital, examined on various types of ACh-receptor activities (author's transl)] Somei K. **Nippon Seirigaku Zasshi** 1981; 43(11):529–31 (Eng. Abstr.) (Jpn)

[Psychological component of human stress (author's transl)] Vargas Fernández L. **Rev Med Chil** 1981 May;109(5):441–51 (Eng. Abstr.) (Spa)

RECEPTORS, DOPAMINE

Intestinal pharmacomanometry and glucose tolerance: two kinds of dopaminergic mechanisms in the human. Lechin F, et al. **Acta Gastroenterol Latinoam** 1981;11(2):247–59 (116 ref.)

An attempt to use central dopaminergic stimulation as a reinforcement for T-maze learning in rats. Jurkowlaniec E, et al. **Acta Neurobiol Exp (Warsz)** 1981;41(4):357–62

Receptor supersensitivity in mental disease. Westermann KH, et al. **Agressologie** 1981 Nov;22(E):33–5

Prejunctional inhibitory dopamine receptors in the rat isolated vas deferens. Tayo FM. **Arch Int Pharmacodyn Ther** 1981 Nov; 254(1):28–37

Subsensitivity of the presynaptic dopamine receptors in cat heart after the termination of chronic haloperidol treatment. Verimer T, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):233–40

Irreversible blockade of [3H]spiperone- but not [3H]dopamine-labeled dopamine receptors with phenoxybenzamine. Titeler M. **Biochem Pharmacol** 1981 Nov 15;30(22):3031–7

N-n-propyl-norapomorphine: an extremely potent stimulant of dopamine autoreceptors. Argiolas A, et al. **Brain Res** 1982 Jan 7;231(1):109–16

Evidence for dopamine autoreceptors controlling dopamine synthesis in the substantia nigra. Argiolas A, et al. **Brain Res** 1982 Feb 18; 234(1):177–81

ACTH 1–24 and lysine vasopressin selectively activate dopamine synthesis in frontal cortex. Delanoy RL, et al. **Brain Res** 1982 Jan 7; 231(1):117–29

Characterization of high affinity dopamine uptake into the dopamine neurons of the hypothalamus. George SR, et al. **Brain Res** 1982 Feb 25;234(2):339–55

Neurotensin effects on brain dopaminergic systems. Haubrich DR, et al. **Brain Res** 1982 Jan 7;231(1):216–21

Effects of acute and chronic administration of phencyclidine on dopaminergic receptors in rat striatum. Leelavathi DE, et al. **Commun Psychopharmacol** 1980;4(5):417–24

The role of dopaminergic and serotonergic mechanisms in the development of swimming ability of young rats. Tamásy V, et al. **Dev Neurosci** 1981;4(5):389–400

Guanine nucleotides regulate both dopaminergic agonist and antagonist binding in porcine anterior pituitary. De Lean A, et al. **Endocrinology** 1982 Mar;110(3):1064–6

Dopaminergic inhibition of pituitary beta-endorphin-like immunoreactivity secretion in the rat. Farah JM Jr, et al. **Endocrinology** 1982 Feb;110(2):657–9

An orally effective, long-acting dopaminergic prodrug: (-)-10,11-methylenedioxy-N-propylnoraporphine. Baldessarini RJ, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):87–8

Hypophysectomy does not prevent development of striatal dopamine receptor supersensitivity induced by repeated neuroleptic treatment. Jenner P, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):31–6

Phenoxybenzamine blocks dopamine autoreceptors irreversible: implications for multiple dopamine receptor hypotheses. Lehmann J, et al. **Eur J Pharmacol** 1981 Nov 5;75(4):247–54

Pharmacological profiles of the putative dopamine autoreceptor agonists 3-PPP and TL-99. Martin GE, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):15–23

Irreversible blockade of striatal dopamine receptors in vivo by a derivative of alpha-flupenthixol. Schuster DI, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):313–6

Behavioural evidence for supersensitivity of postsynaptic dopamine receptors in the mesolimbic system after chronic administration of desipramine. Spyraki C, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2–3):195–206

Stereospecific long-term effects of amphetamine on striatal dopamine neurons in rats. Steranka LR. **Eur J Pharmacol** 1981 Dec 17; 76(4):443–6

Agonistic actions of DPI (2-(3,4-dihydroxyphenylimino)-imidazolidine) on alpha-adrenoceptors and dopamine receptors. Woodman OL, et al. **Eur J Pharmacol** 1981 Oct 15;75(1):11–9

Effect of metoclopramide in guinea-pig ileum longitudinal muscle: evidence against dopamine-mediation. Zar MA, et al. **Gut** 1982 Jan; 23(1):66–70

Future directions in dopaminergic nervous system and dopaminergic agonists. Cannon JG, et al. **J Med Chem** 1981 Oct;24(10):1113–8 (66 ref.)

Stereospecific blockade of alpha 2-adrenoceptors by (+)-butaclamol: implications for the characterization of dopamine receptors. Spedding M, et al. **J Pharm Pharmacol** 1982 Jan;34(1):56–8

The vascular dopamine receptor : a review. Schmidt M, et al. **J Pharmacol** 1981 Nov-Dec;12(4):355–82 (183 ref.)

Acute changes in the state of dopamine receptors; in vitro monitoring with 3H-dopamine. Bacopoulos NG. **Life Sci** 1981 Dec 7; 29(23):2407–14

Evidence for a coupling between dopaminergic receptors and phospholipid methylation in mouse B lymphocytes. Le Fur G, et al. **Life Sci** 1981 Dec 28;29(26):2737–49

Solubilization and characterization of 3H-spiroperidol binding sites of calf caudate. Lerner MH, et al. **Life Sci** 1981 Dec 7;29(23):2367-74

An hypothesis of the molecular structure of the dopamine receptor. Smythies JR. **Med Hypotheses** 1981 Dec;7(12):1449-56

Unique response to antipsychotic drugs is due to absence of terminal autoreceptors in mesocortical dopamine neurones. Bannon MJ, et al. **Nature** 1982 Apr 1;296(5856):444-6

Analysis of the effects of dopamine and noradrenaline in relation to the proposed postsynaptic dopamine receptor in rat vas deferens. Langeloh A, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb; 318(3):202-9

Neuroleptic malignant syndrome caused by dopamine depleting drugs [letter] Login IS, et al. **Neurology (NY)** 1982 Feb;32(2):218-9

Differential involvement of dopamine-containing tracts in 5-hydroxytryptamine-dependent behaviours caused by amphetamine in large doses. Andrews CD, et al. **Neuropharmacology** 1982 Jan; 21(1):63-8

Site-specific blockade of dopamine receptors by neuroleptic agents in human brain. Borison RL, et al. **Neuropharmacology** 1981 Dec; 20(12B):1321-2

Are striatal [3H]spiperone radioreceptor assays indicative of multiple dopamine receptor interactions? Clements-Jewery S, et al. **Neuropharmacology** 1981 Dec;20(12B):1295-8

Chronic electroconvulsive shock and chronic haloperidol administration are not additive in effects on dopamine receptors. Globus M, et al. **Neuropharmacology** 1981 Nov;20(11):1125-8

Studies on the action of (+/-)sulpiride on dopamine receptors in the rat brain in vivo. Hasan F, et al. **Neuropharmacology** 1981 Dec; 20(12B):1327-30

Cocaine-induced supersensitivity of striatal dopamine receptors: role of endogenous calmodulin. Memo M, et al. **Neuropharmacology** 1981 Dec; 20(12A):1145-50

Possible mixed agonist—antagonist activity of D-sulpiride at dopamine receptor level in man. Benfenati F, et al. **Neurosci Lett** 1981 Nov 4; 26(3):289-95

Failure to obtain functional equivalence between dopamine receptor blockade and extinction: evidence supporting a sensory-motor conditioning hypothesis. Tombaugh TN, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):67-72

Isolated horizontal cells from carp retina demonstrate dopamine-dependent accumulation of cyclic AMP. Van Buskirk R, et al. **Proc Natl Acad Sci USA** 1981 Dec;78(12):7825-9

Brain reinforcement mechanisms: alpha-adrenergic and dopaminergic agonists and antagonists. Wauquier A, et al. **Prog Clin Biol Res** 1981; 71:177-96

Phenothiazine biphasic effect on dopamine concentrations in the basal ganglia of subhuman primates. Bird ED, et al. **Psychiatry Res** 1982 Feb;6(1):1-6

The role of dopaminergic mechanisms in the rat hippocampus for the consolidation in a brightness discrimination. Grecksch G, et al. **Psychopharmacology (Berlin)** 1981;75(2):165-8

Flupentixol and dopamine receptor selectivity [letter] Hyttel J. **Psychopharmacology (Berlin)** 1981;75(2):217

Assessing pharmacologically induced dopamine receptor sensitivity changes with the Ungerstedt turning model. Siever L, et al. **Psychopharmacology (Berlin)** 1981;75(2):212-3

Binding of antiparkinsonian ergot derivatives to the dopamine receptor. Weir RL, et al. **Psychopharmacology (Berlin)** 1981;75(2):119-23

Differential inhibitory effects of ascorbic acid on the binding of dopamine agonists and antagonists to neostriatal membrane preparations: correlations with behavioral effects. Heikkila RE, et al. **Res Commun Chem Pathol Pharmacol** 1981 Dec;34(3):409-21

[Effect of chronic administration of lithium chloride on the development of dopamine receptor sensitivity during morphine withdrawal in rats] Allikmets LKh, et al. **Biull Eksp Biol Med** 1981 Nov;92(11):571-2 (Eng. Abstr.) **(Rus)**

[Ligand-dopaminergic receptor bond in the guinea pig bladder] Idoipe Tomás C, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):123-4 **(Spa)**

RECEPTORS, DRUG

Localization of the site of the anticonflict action of benzodiazepines in the amygdaloid nucleus of rats. Shibata K, et al. **Brain Res** 1982 Feb 25;234(2):442-6

Ontogeny of 3H-diazepam binding sites in different rat brain area. Effect of GABA. Aldinio C, et al. **Dev Neurosci** 1981;4(6):461-6

The effect of GTP on benzodiazepine receptors. Fong JC, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):57-9

In situ molecular weight determination of brain and peripheral benzodiazepine binding sites. Paul SM, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):465-6

Stereospecific displacement of [3H]phencyclidine (PCP) receptor binding by an enantiomeric pair of PCP analogs. Quirion R, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):107-8

Interactions of beta-carbolines with the benzodiazepine receptor: structure-activity relationships. Robertson HA, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):281-4

3H-Diazepam binding sites in Roman high- and low-avoidance rats. Gentsch C, et al. **Experientia** 1981 Dec 15;37(12):1315-6

gamma-Aminobutyric acid- and benzodiazepine-binding sites in human anterior pituitary tissue. Grandison L, et al. **J Clin Endocrinol Metab** 1982 Mar;54(3):597-601

Identification of synapse specific components: synaptic glycoproteins, proteins, and transmitter binding sites. Mena EE, et al. **J Neurochem** 1981 Dec;37(6):1557-66

Molecular interactions of etazolate with benzodiazepine and picrotoxinin binding sites. Ticku MK, et al. **J Neurochem** 1982 Apr;38(4):1180-2

Effects of putative endogenous benzodiazepine receptor ligands on the potentiation of adenosine by benzodiazepines in isolated smooth muscle. Slater P, et al. **J Pharm Pharmacol** 1982 Jan;34(1):42-4

Comparison of the effects of GABA and chloride ion on the affinities of ligands for the benzodiazepine receptor. Fujimoto M, et al. **Life Sci** 1982 Jan 4;30(1):51-7

Halide- and gamma-aminobutyric acid-induced enhancement of diazepam receptors in rat brain. Reversal by disulfonic stilbene blockers of anion channels. Costa T, et al. **Mol Pharmacol** 1981 Nov;20(3):470-6

gamma-Aminobutyric acid enhancement of CL 218,872 affinity and evidence of benzodiazepine receptor heterogeneity. Regan JW, et al. **Mol Pharmacol** 1981 Nov;20(3):477-83

Benzodizepines: biochemistry of function. Tallman JF. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(33):4-11

Molecular size of benzodiazepine receptor in rat brain in situ: evidence for a functional dimer? Doble A, et al. **Nature** 1982 Feb 11; 295(5849):522-3

Agonist and antagonist benzodiazepine receptor interaction in vitro. Möhler H, et al. **Nature** 1981 Dec 24;294(5843):763-5

Functional interaction between benzodiazepine and GABA recognition sites in aged rats. Calderini G, et al. **Neurobiol Aging** 1981 Winter; 2(4):309-13

Chronic clonazepam administration induces benzodiazepine receptor subsensitivity. Crawley JN, et al. **Neuropharmacology** 1982 Jan; 21(1):85-9

[3H]Sulpiride, a ligand for neuroleptic receptors. Freedman SB, et al. **Neuropharmacology** 1981 Dec;20(12B):1323-6

6 -Hydroxydopamine decreases benzodiazepine but not GABA receptor binding in rat cerebellum. Doble A, et al. **Neurosci Lett** 1981 Dec 11; 27(2):199-204

Desensitization-like changes in GABA receptor binding of rat fascia dentata after entorhinal lesion. Nadler JV. **Neurosci Lett** 1981 Nov 4; 26(3):275-81

Changes in rat hippocampal benzodiazepine receptors and lack of changes in muscarinic receptors after fimbria-fornix lesions. Sábato UC, et al. **Neurosci Lett** 1981 Dec 11;27(2):193-7

The effects of acute administration of diazepam on the binding of [3H]-diazepam and [3H]-gaba to rat cortical membranes. Coupet J, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):965-8

Human platelet imipramine recognition sites: biochemical and pharmacological characterization. Wennogle LP, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):975-82

[Value of the binding site for tritiated imipramine in the pharmacology of antidepressants] Zarifian E. **Encephale** 1981;7(4 Suppl):405-7 **(Fre)**

[Molecular mechanisms of the pharmacologic action of benzodiazepines] Korneev AIa, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):20-8 (Eng. Abstr.) **(Rus)**

[Physicochemical heterogeneity of the GABA receptors and the detection of the differences in their structural relation with benzodiazepine receptors] Korneev AIa, et al. **Zh Nevropatol Psikhiatr** 1981; 81(11):1661-2 (Eng. Abstr.) **(Rus)**

RECEPTORS, ENDORPHIN

Endorphins and behavior. Bolles RC, et al. **Annu Rev Psychol** 1982; 33:87-101

Neostriatal enkephalin-immunoreactive neurones project to the globus pallidus. Del Fiacco M, et al. **Brain Res** 1982 Jan 7;231(1):1-17

Effect of dorsal rhizotomy on the autoradiographic distribution of opiate and neurotensin receptors and neurotensin-like immunoreactivity within the rat spinal cord. Ninkovic M, et al. **Brain Res** 1981 Dec 28; 230(1-2):111-9

Interaction of p-nitrophenylalanine enkephalins with mu-, delta- and kappa-subtypes of the opiate receptor. Fauchère JL, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):339-42

Opiate receptor-binding activity of [D-Thr2,Thz5]-and [D-Met2,Thz5]-enkephalinamides. Ferrara P, et al. **Eur J Pharmacol** 1981 Jul 17;73(1):69-73

Excitability ot beta-endorphin, morphine and catecholamines of the vas deferens of the rat at different stages of development. Huidobro-Toro JP, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):115-8

Mixed type inhibition of [D-Ala2, D-Leu5]enkephalin binding to mu-opiate binding sites by mu-, but not by kappa-opiate ligands. Pfeiffer A, et al. **Eur J Pharmacol** 1982 Feb 5;77(4):359-61

Dynorphins: similar relative potencies on mu, delta- and kappa-opiate receptors. Quirion R, et al. **Eur J Pharmacol** 1981 Dec 17; 76(4):467-8

Psychotomimetic opioid binding: specific binding of [3H]SKF-10047 to etorphine-inaccessible sites in guinea-pig brain. Su TP. **Eur J Pharmacol** 1981 Oct 15;75(1):81-2

Comparative immunocytochemical localization of putative opioid ligands in the central nervous system. Stengaard-Pedersen K, et al. **Histochemistry** 1981;73(1):89-114 (50 ref.)

beta-Endorphin and deletion peptides. A correlation of opiate receptor affinity with helix potential. Hammonds RG Jr, et al. **J Biol Chem** 1982 Mar 25;257(6):2990-5

Stress and endogenous opioid peptides: a review. Millan MJ. **Med Probl Pharmacopsychiatry** 1981;17:49-67

Localization and modulation of enkephalins, endorphins and opiate receptors in the CNS and the pituitary gland. Simantov R. **Med Probl Pharmacopsychiatry** 1981;17:38-48

Endorphins, opiate receptors and their evolving biology. Smith JR, et al. **Pathobiol Annu** 1981;11:87-126 (212 ref.)

The correlation between swim-stress induced antinociception and [3H] leu-enkephalin binding to brain homogenates in mice. Christie MJ, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):853-7

Method of sacrifice influences leucine enkephalin binding to mouse brain. Christie MJ, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):849-51

RECEPTORS, HORMONE

Studies on the mechanism of the GABAergic inhibition of TSH secretion in male rats. Mattila J. **Acta Pharmacol Toxicol (Copenh)** 1981 Apr; 48(4):320-5

Interaction of tryptophan-modified analogues of cholecystokinin-octapeptide with cholecystokinin receptors on pancreatic acini. Adachi H, et al. **Biochim Biophys Acta** 1981 Dec 18; 678(3):358-63

Changes in prolactin binding sites in the rabbit hypothalamus induced by physiological and pharmacological variations of prolactin serum levels. Di Carlo R, et al. **Brain Res** 1981 Dec 28;230(1-2):445-50

Evidence for GABA receptors on serotonergic afferent terminals in the substantia nigra and on nigral efferent projections to the caudal mesencephalon. Gale K. **Brain Res** 1982 Jan 7;231(1):209-15

Effect of dorsal rhizotomy on the autoradiographic distribution of opiate and neurotensin receptors and neurotensin-like immunoreactivity within the rat spinal cord. Ninkovic M, et al. **Brain Res** 1981 Dec 28; 230(1-2):111-9

Guanine nucleotide and magnesium ion regulation of the interaction of gonadotropic and beta-adrenergic receptors with their hormones: a comparative study using a single membrane system. Abramowitz J, et al. **Endocrinology** 1982 Feb;110(2):336-46

The postnatal development of the pituitary thyrotropin-releasing hormone receptor in male and female rats. Banerji A, et al. **Endocrinology** 1982 Feb;110(2):663-4

Induction of testicular gonadotropin-releasing hormone (GnRH) receptors by GnRH: effects of pituitary hormones and relationship to inhibition of testosterone production. Bourne GA, et al. **Endocrinology** 1982 Mar;110(3):727-33

Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of hypothalamic lesions and a gonadotropin-releasing hormone antagonist. Clayton RN, et al. **Endocrinology** 1982 Apr; 110(4):1108-15

Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of gonadotropin-releasing hormone immunoneutralization. Clayton RN, et al. **Endocrinology** 1982 Apr; 110(4):1116-22

Pituitary receptor sites for gonadotropin-releasing hormone: effect of castration and substitutive therapy with sex steroids in the male rat. Conne BS, et al. **Endocrinology** 1982 Jan;110(1):70-9

Dependence of pituitary gonadotropin-releasing hormone (GnRH) receptors on GnRH secretion from the hypothalamus. Pieper DR, et al. **Endocrinology** 1982 Mar;110(3):749-53

Affinity of thiocolchicoside and thiocolchicoside analogues for the postsynaptic GABA receptor site. Biziere K, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):167-8

Endogenous GABA determines the characteristics of [3H]GABA-binding. Gardner CR, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):83-92

ACTH1-24 increases stimulation-evoked noradrenaline release from sympathetic nerves by acting on presynaptic ACTH receptors. Göthert M. **Eur J Pharmacol** 1981 Dec 3;76(2-3):295-6

Effect of Nin-formylation of the tryptophan residue on gastrin (HG-13) binding and on gastric acid secretion. Magous R, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):11-6

Pituitary somatostatin receptors. Characterization by binding with a nondegradable peptide analogue. Aguilera G, et al. **J Biol Chem** 1982 Feb 10;257(3):1134-7

gamma-Aminobutyric acid- and benzodiazepine-binding sites in human anterior pituitary tissue. Grandison L, et al. **J Clin Endocrinol Metab** 1982 Mar;54(3):597-601

Inhibition of [3H]GABA binding to postsynaptic receptors in human cerebellar synaptic membranes by carboxyl and amino derivatives of GABA. Breckenridge RJ, et al. **J Neurochem** 1981 Oct;37(4):837-44

The binding of the GABA agonist [3H]THIP to rat brain synaptic membranes. Falch E, et al. **J Neurochem** 1982 Apr;38(4):1123-9

Effect of homo-beta-proline and other heterocyclic GABA analogues on GABA uptake in neurons and astroglial cells and on GABA receptor binding. Larsson OM, et al. **J Neurochem** 1981 Dec;37(6):1509-16

gamma-Aminobutyric acid (GABA) receptor stimulation. II. Specificity of progabide (SL 76002) and SL 75102 for the GABA receptor. Lloyd KG, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):672-7

Functional interaction between benzodiazepine and GABA recognition sites in aged rats. Calderini G, et al. **Neurobiol Aging** 1981 Winter; 2(4):309-13

6 -Hydroxydopamine decreases benzodiazepine but not GABA receptor binding in rat cerebellum. Doble A, et al. **Neurosci Lett** 1981 Dec 11; 27(2):199-204

The effects of acute administration of diazepam on the binding of [3H]-diazepam and [3H]-gaba to rat cortical membranes. Coupet J, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):965-8

Regulation of gonadotropin secretion in the anterior pituitary. Hopkins CR, et al. **Philos Trans R Soc Lond [Biol]** 1981 Dec 18; 296(1080):73-81

[Mianserin, presynaptic receptor and biochemical model of depression of Tissot (author's transl)] Dereux JF. **Encephale** 1981; 7(4 Suppl):399-400 (Eng. Abstr.) **(Fre)**

[Molecular mechanisms of the pharmacologic action of benzodiazepines] Korneev AIa, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):20-8 (Eng. Abstr.) **(Rus)**

RECEPTORS, SEROTONIN

On the interaction of histamine with the tryptaminergic smooth-muscle receptors. Todorov S, et al. **Acta Physiol Pharmacol Bulg** 1980; 6(4):47-54

Receptor supersensitivity in mental disease. Westermann KH, et al. **Agressologie** 1981 Nov;22(E):33-5

5-HT receptors and hyper- or hypothermia: elucidation by catecholamine antagonists injected into the cat hypothalamus. Ruwe WD, et al. **Brain Res Bull** 1982 Jan;8(1):79-86

The role of dopaminergic and serotonergic mechanisms in the development of swimming ability of young rats. Tamásy V, et al. **Dev Neurosci** 1981;4(5):389-400

Substance P, but not TRH, modulates the 5-HT autoreceptor in ventral lumbar spinal cord. Mitchell R, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):119-20

Enhancement of responsiveness of the central serotonergic system and serotonin-2 receptor density in rat frontal cortex by electroconvulsive treatment. Vetulani J, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):81-5

Modulation by estradiol of serotonin receptors in brain. Biegon A, et al. **J Neurosci** 1982 Feb;2(2):199-205

Possible hazards in serotonin binding assays in human and rat brain: effects of ascorbate, pargyline, and buffer concentration. Weiner N, et al. **J Neurosci Methods** 1982 Jan;5(1-2):41-5

Antagonistic properties of quipazine at presynaptic serotonin receptors and alpha-adrenoceptors in rat brain cortex slices. Schlicker E, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):204-8

Sleep suppressant action of quipazine: relation to central serotonergic stimulation. Fornal C, et al. **Pharmacol Biochem Behav** 1981 Dec; 15(6):937-44

REFLEX

Central and peripheral adrenergic modulation of carotid sinus-induced renin release. Schultz HD, et al. **Am J Physiol** 1982 Mar; 242(3):R318-25

Reflex sympathetic augmentation of left-ventricular inotropic state in the conscious dog. Yoran C, et al. **Am J Physiol** 1981 Dec; 241(6):H857-63

Feather position of the pigeon after intrahypothalamic injections of noradrenaline, 5-hydroxytryptamine and carbachol. Rintamäki H, et al. **Experientia** 1981 Nov 15;37(11):1173-5

[Effect of phentolamine on carotid reflexes induced by acetylcholine] Silva Carvalho L, et al. **C R Soc Biol (Paris)** 1981;175(6):913-5 (Eng. Abstr.) **(Fre)**

[Comparative characteristics of the reactions of small intestine vessels to neurogenic influences and catecholamine application] Polenov SA, et al. **Fiziol Zh SSSR** 1981 Dec;67(12):1845-52 (Eng. Abstr.) **(Rus)**

REINFORCEMENT (PSYCHOLOGY)

An attempt to use central dopaminergic stimulation as a reinforcement for T-maze learning in rats. Jurkowlaniec E, et al. **Acta Neurobiol Exp (Warsz)** 1981;41(4):357-62

The effect of intrahypothalamic serotonin reinforcement on directional preference in rats. Lesiecka M, et al. **Acta Neurobiol Exp (Warsz)** 1981; 41(5):439-46

Brain reinforcement mechanisms: alpha-adrenergic and dopaminergic agonists and antagonists. Wauquier A, et al. **Prog Clin Biol Res** 1981;

71:177–96

Reinstatement of cocaine-reinforced responding in the rat. de Wit H, et al. **Psychopharmacology (Berlin)** 1981;75(2):134–43

[Effects of afloqualone, a new centrally acting muscle relaxant, on DRL response and CER in rats (author's transl)] Yamamura M, et al. **Nippon Yakurigaku Zasshi** 1981 Oct;78(4):381–92 (Eng. Abstr.) **(Jpn)**

REINFORCEMENT SCHEDULE

Phencyclidine discrimination in the pigeon using color tracking under second-order schedule. McMillan DE, et al. **J Exp Anal Behav** 1982 Jan;37(1):143–7

RESERPINE

Reserpine-induced supersensitivity and the proliferation of cardiac beta-adrenoceptors. Tenner TE Jr, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):61–5

Electroconvulsive shock and reserpine: effects on beta-adrenergic receptors in rat brain. Kellar KJ, et al. **J Neurochem** 1981 Oct; 37(4):830–6

Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Brown OM, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):911–4

[Effect of alpha-methyl-para-tyrosine on 'methamphetamine-induced sterotype and hypermotility' of reserpinized rats (author's transl)] Nakajima H, et al. **Nippon Yakurigaku Zasshi** 1981 Dec;78(6):557–69 (Eng. Abstr.) **(Jpn)**

[Peripheral mechanisms implicated in the interaction of atropine, amphetamine and reserpine on body temperature in the conscious rat] Milanés MV, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):77–8 **(Spa)**

RUBIDIUM

The uptake and extrusion of salts by the halotolerant bacterium, Ba1. Shnaiderman R, et al. **Arch Biochem Biophys** 1982 Jan;213(1):177–85

Amino acid transport and rubidium-ion uptake in monolayer cultures of hepatocytes from neonatal rats. Bellemann P. **Biochem J** 1981 Sep 15; 198(3):475–83

Evaluation of inorganic adsorbents for the rubidium-82 generator: I. Hydrous SnO2. Neirinckx RD, et al. **J Nucl Med** 1982 Mar; 23(3):245–9

The half-life of 87Rb. Akatsu E. **Radioisotopes** 1981 Dec;30(12):647–8

[A factor influencing in vitro the influx of 86Rb+ into erythrocytes as an impurity of a commercial preparation of testosterone (author's transl)] Schreiber V, et al. **Sb Lek** 1981;83(11–12):305–8 (Eng. Abstr.) **(Cze)**

SCHIZOPHRENIA

Fluphenazine and flupenthixol decanoate in psychiatric outpatients practice. Coufal J, et al. **Act Nerv Super (Praha)** 1981;23(4):269–71

Further clinical experience with oxyprothepin-decanoate. Kalvach Z, et al. **Act Nerv Super (Praha)** 1981;23(4):271–2

Penfluridol in chronic schizophrenia. Doongaji DR, et al. **Acta Psychiatr Belg** 1981 Jul–Aug;81(4):407–15

Differentiated psychopharmacotherapy in anxiety states of slowly progressive schizophrenia. Smulevitch A. **Agressologie** 1981 Nov; 22(D):31–2

Diazepam in schizophrenia: a preliminary double-blind trial. Jimerson DC, et al. **Am J Psychiatry** 1982 Apr;139(4):489–91

Abrupt versus gradual withdrawal of antiparkinsonians [letter] Weiner WJ. **Am J Psychiatry** 1982 Feb;139(2):256–7

Serum level monitoring of thiothixene in schizophrenia: acute single-dose levels at fixed doses. Yesavage JA, et al. **Am J Psychiatry** 1982 Feb; 139(2):174–8

Stimulated lymphocytes in schizophrenia. Hirata-Hibi M, et al. **Arch Gen Psychiatry** 1982 Jan;39(1):82–7

Fluphenazine vs placebo in patients with remitted, acute first-episóde schizophrenia. Kane JM, et al. **Arch Gen Psychiatry** 1982 Jan; 39(1):70–3

Antipsychotic effects of ceruletide (caerulein) on chronic schizophrenia [letter] Moroji T, et al. **Arch Gen Psychiatry** 1982 Apr;39(4):485–6

Impaired presynaptic regulation of norepinephrine in schizophrenia. Effects of clonidine in schizophrenic patients and normal controls. Sternberg DE, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):285–9

CSF levels of gamma-aminobutyric acid in schizophrenia. Low values in recently ill patients. van Kammen DP, et al. **Arch Gen Psychiatry** 1982 Jan;39(1):91–7

Plasma copper and dopamine-beta-hydroxylase in schizophrenia. Baron M, et al. **Biol Psychiatry** 1982 Jan;17(1):115–20

Quantitative investigation on the urinary excretion and metabolism of 3,4-dimethoxyphenylethylamine in schizophrenics and normal individuals. Hempel K, et al. **Biol Psychiatry** 1982 Jan;17(1):49–59

The treatment of schizophrenic psychoses with gamma-type endorphins. van Praag HM, et al. **Biol Psychiatry** 1982 Jan;17(1):83–98

Positive and negative schizophrenia symptoms and the role of dopamine. Crow TJ. **Br J Psychiatry** 1981 Sep;139:251–4

Elevated serum levels of lactoferrin and eosinophil cationic protein in schizophrenic patients. Hällgren R, et al. **Br J Psychiatry** 1982 Jan; 140:55–60

Effects of neuroleptic drugs on MAO activity [letter] Reveley AM, et al. **Br J Psychiatry** 1981 Nov;139:475–6

Long term care for the chronic schizophrenic patient. Pyke J, et al. **Can Nurse** 1982 Jan;78(1):37–44

Interaction of chlorpromazine and nortriptyline in patients with schizophrenia. Loga S, et al. **Clin Pharmacokinet** 1981 Nov–Dec; 6(6):454–62

The comprehensive treatment of schizophrenics. Fleck S, et al. **Curr Psychiatr Ther** 1981;20:313–27

The treatment of refractory schizophrenia: pharmacotherapy and clinical implications of blood level measurement of neuroleptics. Pi EH, et al. **Int Pharmacopsychiatry** 1981;16(3):154–61

Pimozide versus chlorpromazine in chronic schizophrenia: a 52 week double-blind study of maintenance therapy. Wilson LG, et al. **J Clin Psychiatry** 1982 Feb;43(2):62–5

Catastrophe theory of dopaminergic transmission: a revised dopamine hypothesis of schizophrenia. King R, et al. **J Theor Biol** 1981 Oct 21; 92(4):373–400

Drug management in chronic schizophrenia. Tune LE, et al. **Johns Hopkins Med J** 1982 Jan;150(1):45–8

Cerebral ventricular size in twins discordant for schizophrenia. Reveley AM, et al. **Lancet** 1982 Mar 6;1(8271):540–1

Action of [Des-Tyr1]-gamma-endorphin in schizophrenia. Emrich HM, et al. **Mod Probl Pharmacopsychiatry** 1981;17:279–86

beta-Endorphin studies in psychiatric patients. Gorelick DA, et al. **Mod Probl Pharmacopsychiatry** 1981;17:236–45

Detoxication treatment of schizophrenic patients: a possible role of endorphins? Nedopil N, et al. **Mod Probl Pharmacopsychiatry** 1981; 17:263–5

The use of dopamine agonists in the treatment of schizophrenia. Conini GU, et al. **Neuropharmacology** 1981 Dec;20(12B):1309–13

Is propranolol antischizophrenic? Peet M. **Neuropharmacology** 1981 Dec; 20(12B):1303–7 (36 ref.)

Endorphins in schizophrenia. van Ree JM, et al. **Neuropharmacology** 1981 Dec;20(12B):1271–7 (93 ref.)

Amphetamine psychosis and schizophrenia: a dual model. Kokkinidis L, et al. **Neurosci Biobehav Rev** 1981 Winter;5(4):449–61 (173 ref.)

Initial improvement as predictor of outcome of neuroleptic treatment. Nedopil N, et al. **Pharmacopsychiatria** 1981 Nov;14(6):205–7

Tolerance to the prolactin-elevating effect of neuroleptics. Brown WA, et al. **Psychiatry Res** 1981 Dec;5(3):317–22

Fine motor performance before and after treatment in schizophrenic and schizoaffective patients. Goode DJ, et al. **Psychiatry Res** 1981 Dec; 5(3):247–55

(Des-tyrosine1)-gamma-endorphin in schizophrenia: clinical, biochemical, and hormonal aspects. Verhoeven WM, et al. **Psychiatry Res** 1981 Dec;5(3):293–309

Does a plasma level of chlorpromazine help? Van Putten T, et al. **Psychol Med** 1981 Nov;11(4):729–34

beta-Endorphin and beta-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. Brambilla F, et al. **Psychoneuroendocrinology** 1981 Dec; 6(4):321–30

The use of fluphenazine decanoate (Modecate)depot therapy in outpatient schizophrenics-a retrospective study. Tan CT, et al. **Singapore Med J** 1981 Aug;22(4):214–8

[Clinical observation on 81 cases of schizophrenia treated with domestic penfluridol (author's transl)] Jin HM. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1981 Aug; 14(3):186–8 **(Chi)**

[Clinical observation on the effect of domestic fluphenazine decanoate in the treatment of schizophrenia——report of 431 cases (author's transl)] Zhang YF. **Chung Hua Shen Ching Ching Shen Ko Tsa Chih** 1981 Aug; 14(3):182–5 **(Chi)**

[Treatment of schizophrenic psychoses by sustained-action neuroleptics in psychiatric outpatients' treatment (author's transl)] Poláček J. **Cesk Psychiatr** 1982 Feb;78(1):49–55 (Eng. Abstr.) **(Cze)**

[Group psychotherapy of chronic schizophrenics in an external milieu]. Filotto JF. **Can J Psychiatry** 1981 Dec;26(8):558–61 (Eng. Abstr.) **(Fre)**

[Biologic therapy of schizophrenia] Lambert PA, et al. **Soins Psychiatr** 1981 Dec;(14):19–22 **(Fre)**

[Biochemical analysis of dopaminergic nerve terminals of post-mortem brain from schizophrenic patients (author's transl)] Toru M, et al. **Seishin Shinkeigaku Zasshi** 1981;83(7):430–47 (Eng. Abstr.) **(Jpn)**

[Various features of dopamine metabolism in schizophrenia] Anokhina IP, et al. **Zh Nevropatol Psikhiatr** 1981;81(9):1343–7 (Eng. Abstr.) **(Rus)**

[Comparison between the effectiveness of fluphenazine decanoate and oxyprothepin decanoate in schizophrenia (double-blind crossover study)] Balon R, et al. **Zh Nevropatol Psikhiatr** 1982;82(1):116–8 (Eng. Abstr.) **(Rus)**

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskii Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) **(Rus)**

[Predicting the effect of psychopharmacotherapy in schizophrenic patients] Dikil NT. **Zh Nevropatol Psikhiatr** 1982;82(1):110-5 (Eng. Abstr.) **(Rus)**

SCHIZOPHRENIA, PARANOID

High doses of haloperidol in schizophrenia. A clinical, biochemical, and pharmacokinetic study. Zarifian E, et al. **Arch Gen Psychiatry** 1982 Feb; 39(2):212-5

Cross-cultural study of a biochemical abnormality in paranoid schizophrenia. Jeste DV, et al. **Psychiatry Res** 1981 Dec;5(3):341-52

The genetics and biochemistry of paranoid schizophrenia and other paranoid psychoses. Kendler KS, et al. **Schizophr Bull** 1981; 7(4):689-709 (86 ref.)

SCHIZOTYPAL PERSONALITY DISORDER

[Psychopharmacologic approach to studying various problems in slowly progressive schizophrenia] Boleloutskii Z. **Zh Nevropatol Psikhiatr** 1982; 82(1):105-10 (Eng. Abstr.) **(Rus)**

SELF STIMULATION

Intracranial self-stimulation. Redgrave P, et al. **Br Med Bull** 1981 May; 37(2):141-6 (71 ref.)

Pimozide attenuates conditioned taste preferences induced by self-stimulation in rats. Ettenberg A, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):915-9

Brain reinforcement mechanisms: alpha-adrenergic and dopaminergic agonists and antagonists. Wauquier A, et al. **Prog Clin Biol Res** 1981; 71:177-96

SEROTONIN

LCEC analysis of 5-hydroxytryptamine and norepinephrine in the human gastrointestinal tract. Smeds S, et al. **Acta Chir Scand** 1981; 147(5):361-2

The effect of intrahypothalamic serotonin reinforcement on directional preference in rats. Lesiecka M, et al. **Acta Neurobiol Exp (Warsz)** 1981; 41(5):439-46

Halothane inhibits the pulmonary clearance of 5-hydroxytryptamine in isolated perfused rat lungs [letter] Hede AR, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):239-40

Role of some biogenic amines in the pathomechanism of glomerulonephritis. II. Adrenaline, noradrenaline and serotonin in acute serum sickness in rabbits. Gębala A, et al. **Acta Physiol Pol** 1981; 32(4):363-73

Role of some biogenic amines in the pathomechanism of glomerulonephritis. Zajączkowska M, et al. **Acta Physiol Pol** 1981; 32(4):375-82

Entrainment of the circadian rhythm from the eye of Aplysia: role of serotonin. Corrent G, et al. **Am J Physiol** 1982 Mar;242(3):R326-32

Transmitterlike action of serotonin in phase shifting a rhythm from the Aplysia eye. Corrent G, et al. **Am J Physiol** 1982 Mar; 242(3):R333-8

Biochemical differences in children with conduct disorder socialized and undersocialized. Rogeness GA, et al. **Am J Psychiatry** 1982 Mar; 139(3):307-11

Effects of carotid Body chemoreceptor stimulation by 5-HT on phrenic nerve activity and ventilation in the rabbit. Matsumoto S. **Arch Int Pharmacodyn Ther** 1981 Dec;254(2):282-92

Direct and indirect actions of 5-hydroxytryptamine in the rat anococcygeus muscle. Oriowo MA. **Arch Int Pharmacodyn Ther** 1981 Nov;254(1):13-9

Comparison of the cardiovascular responses to intracerebroventricular administration of tryptamine, 5-hydroxytryptamine, tryptophan and 5-hydroxytryptophan in rats. Krstić MK, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):385-91

Correlation of inbibitory activity of tryptamine derivatives on serotonin uptake in thrombocyte with van der Waals volume. Gupta SP, et al. **Arzneimittelforsch** 1981;31(12):2053-5

The effect of PEA on serotonin and catecholamines. Widelitz MM, et al. **Biochem Biophys Res Commun** 1981 Dec 15;103(3):1107-11

Immunoglobulin E decapeptide-induced 5-hydroxytryptamine release from rat peritoneal mast cells. Comparison with corticotropin-(1-24)-peptide, polyarginine, polylysine and antigen. Coleman JW, et al. **Biochem J** 1981 Sep 15;198(3):615-9

Participation of a transmembrane proton gradient in 5-hydroxytryptamine transport by platelet dense granules and dense-granule ghosts. Wilkins JA, et al. **Biochem J** 1981 Jul 15;198(1):113-23

K+-evoked [3H]-5-HT release from rat frontal cortex slices: the effect of 5-HT agonists and antagonists. Mounsey I, et al. **Biochem Pharmacol** 1982 Jan 1;31(1):49-53

Behavioral effects and physiological disposition of some beta-hydroxylated indoleamines in the rat. Gentile NT, et al. **Biol Psychiatry** 1982 Jan;17(1):109-13

Platelet serotonin uptake in depressed patients: circadian effect. Rausch JL, et al. **Biol Psychiatry** 1982 Jan;17(1):121-3

Cerebral circulatory response to hypercapnia: effects of lesions of central dopaminergic and serotoninergic neuron systems. Dahlgren N, et al. **Brain Res** 1981 Dec 28;230(1-2):221-33

Altered neuronal responsiveness to biogenic amines in rat cerebral cortex after serotonin denervation or depletion. Ferron A, et al. **Brain Res** 1982 Jan 7;231(1):93-108

Evidence for GABA receptors on serotonergic afferent terminals in the substantia nigra and on nigral efferent projections to the caudal mesencephalon. Gale K. **Brain Res** 1982 Jan 7;231(1):209-15

Sensory stimuli differentially affect in vivo nigral and striatal [3H]serotonin release in the cat. Reisine T, et al. **Brain Res** 1982 Jan 28;232(1):77-87

Fetal raphe and hippocampal transplants into adult and aged C57BL/6N mice: a preliminary immunocytochemical study. Azmitia EC, et al. **Brain Res Bull** 1981 Dec;7(6):703-10

Effects of ovarian steroids on serotonin metabolism within grossly dissected and microdissected brain regions of the ovariectomized rat. Cone RI, et al. **Brain Res Bull** 1981 Dec;7(6):639-44

Chemoreceptors for serotonin (5-HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma-aminobutyric acid (GABA) on rabbit visceral afferent neurons. Higashi H, et al. **Brain Res Bull** 1982 Jan; 8(1):23-32

5-HT receptors and hyper- or hypothermia: elucidation by catecholamine antagonists injected into the cat hypothalamus. Ruwe WD, et al. **Brain Res Bull** 1982 Jan;8(1):79-86

Effect of dl-3-pyridylalanine on serotonin concentration and tryptophan-serotonin metabolizing enzymes in rats. Shimeno H, et al. **Chem Pharm Bull (Tokyo)** 1981 Oct;29(10):2940-8

Modification of the drug talking behavior in rats by interference in the metabolism of 5-hydroxytryptamine and catecholamines. Fuchs V, et al. **Drug Alcohol Depend** 1981 Nov;8(3):235-44

Distribution of catecholamines and serotonin in 17 portions of rat ventromedial nucleus and effect of acute immobilization stress. Kiss A, et al. **Endocrinol Exp (Bratisl)** 1981 Dec;15(4):219-28

Specific in vitro upteke of serotonin by cells in the anterior pituitary of the rat. Johns MA, et al. **Endocrinology** 1982 Mar;110(3):754-60

Effect of Mount St. Helens ash on the response of rat trachea to smooth muscle agonists. Fedan JS, et al. **Environ Res** 1981 Dec; 26(2):497-502

Effect of 1-aminoadamantanes on adenine nucleotide and serotonin storage in blood platelets. Wesemann W, et al. **Eur J Cell Biol** 1981 Dec;26(1):158-67

The effect of some anti-epilepsy drugs on enhancement of the monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. Bhavsar VH, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):243-7

Adenosine contracts the isolated rat tail artery by releasing endogenous 5-hydroxytryptamine. Brown CM, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):275-7

The effects of 5-hydroxytryptamine-depleting drugs on peptides in the ventral spinal cord. Gilbert RF, et al. **Eur J Pharmacol** 1981 Dec 3; 76(2-3):203-10

Interaction between 5-hydroxytryptamine and other vasoconstrictor substances in the isolated femoral artery of the rabbit; effect of ketanserin (R 41 468). Van Nueten JM, et al. **Eur J Pharmacol** 1982 Feb 5; 77(4):281-7

5-Hydroxytryptamine in the retina of some mammals. Ehinger B, et al. **Exp Eye Res** 1981 Dec;33(6):663-72

Nuclear magnetic resonance studies of amine storage in pig platelets. Costa JL, et al. **FEBS Lett** 1981 Dec 28;136(2):325-8

Effect of diethylpyrocarbonate on pH-driven monoamine uptake by chromaffin granule ghosts. Isambert MF, et al. **FEBS Lett** 1981 Dec 21;136(1):13-8

The effects of the specific uptake inhibitor Lu 10-171 (citalopram) upon brain indoleamine stores in the maturing mouse. Baker PC, et al. **Gen Pharmacol** 1982;13(1):59-61

Autoradiography of (3H)-5-hydroxytryptamine uptake in the retina of some mammals. Ehinger B, et al. **Graefes Arch Clin Exp Ophthalmol** 1982;218(1):1-8

Glial uptake of monoamines in primary cultures of rat median raphe nucleus and cerebellum. A combined monoamine fluorescence and glial fibrillary acidic protein immunofluorescence study. Liesi P, et al. **Histochemistry** 1981;73(2):239-50

Comparative study on biological activities of various anaphylatoxins (C4a, C3a, C5a). Investigations on their ability to induce platelet secretion. Meuer S, et al. **Inflammation** 1981 Dec;5(4):263-73

Increased serotonin level via augmented tryptophan diet and its effect on escape learning. Yehuda S, et al. **Int J Neurosci** 1981; 15(4):193-6

Effects of 5-hydroxytryptamine on neuroeffector junction in human pulmonary artery. Freeman WK, et al. **J Appl Physiol** 1981 Sep; 51(3):693-8

Coupling of transmembrane proton gradients to platelet serotonin transport. Keyes SR, et al. **J Biol Chem** 1982 Feb 10;257(3):1172–6

Pharmacology of arterioles: some aspects of variability in response to norepinephrine, histamine, and 5-hydroxytryptamine. Burrows ME, et al. **J Cardiovasc Pharmacol** 1981 Nov–Dec;3(6):1370–80

Determination of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in rat and human brain and biological fluids by reversed-phase high-performance liquid chromatography with electrochemical detection. Semerdjian-Rouquier L, et al. **J Chromatogr** 1981 Nov 20;218:663–70

Bilateral serotonergic projections to the dorsal hippocampus of the rat: simultaneous localization of 3H-5HT and HRP after retrograde transport. Azmitia EC. **J Comp Neurol** 1981 Dec 20;203(4):737–43

Identification of and interactions between noradrenergic and serotonergic neurites in the myenteric plexus. Gershon MD, et al. **J Comp Neurol** 1982 Feb 1;204(4):407–21

The level of N-acetylserotonin and melatonin in the brain of male rats: diurnal variations and effects of pinealectomy. Pang SF, et al. **J Exp Zool** 1982 Feb 20;219(3):271–6

Immunocytochemical detection of serotonin with monoclonal antibodies. Consolazione A, et al. **J Histochem Cytochem** 1981 Dec; 29(12):1425–30

Uptake of 5-hydroxytryptamine by gonadotrophs of the bat's pituitary: A combined immunocytochemical radioautographic analysis. Nunez EA, et al. **J Histochem Cytochem** 1981 Nov;29(11):1336–46

Influence of innervation on the levels of noradrenaline and serotonin in the circumvallate papilla of the rat. Cano J, et al. **J Neurobiol** 1982 Jan;13(1):1–7

Effects of long-term low dietary tryptophan intake on determinants of 5-hydroxytryptamine metabolism in the brains of young rats. Ashley DV, et al. **J Neurochem** 1981 Dec;37(6):1385–93

Serotonin and gamma-aminobutyric acid turnover after injection into the median raphe of substance P and D-ala-met-enkephalin amide. Forchetti CM, et al. **J Neurochem** 1982 May;38(5):1336–41

Deamination of 5-hydroxytryptamine by both forms of monoamine oxidase in the rat brain. Fowler CJ, et al. **J Neurochem** 1982 Mar; 38(3):733–6

Presence of conjugated 5-hydroxytryptamine in in vivo superfusates of rat spinal cord. Hammond DL, et al. **J Neurochem** 1981 Oct; 37(4):1068–71

The effects of chronic manganese chloride treatment expressed as age-dependent, transient changes in rat brain synaptosomal uptake of amines. Lai JC, et al. **J Neurochem** 1982 Mar;38(3):844–7

Simultaneous determination of serotonin, 5-hydroxindoleacetic acid, 3,4-dihydroxyphenylacetic acid and homovanillic acid by high performance liquid chromatography with electrochemical detection. Sperk G. **J Neurochem** 1982 Mar;38(3):840–3

Correlative firing patterns of serotonergic neurons in rat dorsal raphe nucleus. Wang RY, et al. **J Neurosci** 1982 Jan;2(1):11–6

Possible hazards in serotonin binding assays in human and rat brain: effects of ascorbate, pargyline, and buffer concentration. Weiner N, et al. **J Neurosci Methods** 1982 Jan;5(1–2):41–5

Chronic treatment with haloperidol or fluphenazine decanoate: regional effects on dopamine and serotonin metabolism in primate brain. Bacopoulos NG, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):22–8

Depression of serotonin uptake by rat lungs exposed to paraquat. Block ER, et al. **J Pharmacol Exp Ther** 1982 Apr;221(1):254–60

Long-term infusion of L-5-hydroxytryptophan increases brain serotonin turnover and decreases blood pressure in normotensive rats. Echizen H, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):579–84

The effects of stereoisomers of 2- and 9- aminobenzonorbornenes on food intake, brain serotonin concentration and monoamine oxidase activity in the rat. Gray NM, et al. **J Pharmacol Exp Ther** 1982 Apr; 221(1):58–62

Apomorphine-induced aggression in rats chronically treated with oral clonidine: modulation by central serotonergic mechanisms. Hahn RA, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):389–93

gamma-Aminobutyric acid (GABA) receptor stimulation. III. Effect of progabide (SL 76002) on norepinephrine, dopamine and 5-hydroxytryptamine turnover in rat brain areas. Scatton B, et al. **J Pharmacol Exp Ther** 1982 Mar;220(3):678–88

Applicability of models for carrier-mediated serotonin transport to pools of serotonin in intact human platelets. Costa JL, et al. **J Physiol (Lond)** 1981 Jul;316:153–61

Action of 5-hydroxytryptamine on intestinal ion transport in the rat. Hardcastle J, et al. **J Physiol (Lond)** 1981 Nov;320:41–55

Mediators of slow synaptic potentials in the myenteric plexus of the guinea-pig ileum. Johnson SM, et al. **J Physiol (Lond)** 1981 Nov; 320:175–86

Hallucinogens as discriminative stimuli: a comparison of 4-OMe DMT and 5-OMe DMT with their methythio counterparts. Glennon RA, et al. **Life Sci** 1982 Feb 1;30(5):465–7

Defective serotonin transport mechanism in platelets from endogenously depressed patients. Malmgren R, et al. **Life Sci** 1981 Dec 21; 29(25):2649–58

Effect of 5-hydroxytryptamine (5-HT; serotonin) on in vitro glucose uptake and glycogen reserves in Hymenolepis diminuta. Mettrick DF, et al. **Mol Biochem Parasitol** 1981 Dec;4(3–4):217–23

Dopamine- and serotonin-sensitive adenylate cyclase in the fill of Aplysia californica. Weiss S, et al. **Mol Pharmacol** 1981 Nov;20(3):592–7

Serotonin-activated adenylate cyclase during early development of Schistosoma mansoni. Kasschau MR, et al. **Nature** 1982 Mar; 296(5852):66–8

Characterization of the receptor subtype involved in alpha-adrenoceptor-mediated modulation of serotonin release from rat brain cortex slices. Göthert M, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981 Nov;317(3):199–203

3H-Imipramine binding sites in the rat brain. Selective localization on serotoninergic neurones. Gross G, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1981;317(4):310–4

3H-Noradrenaline and 3H-5-hydroxytryptamine release from rat brain slices and its presynaptic alpha-adrenergic modulation after long-term desipramine pretreatment. Schoffelmeer AN, et al. **Naunyn Schmiedebergs Arch Pharmacol** 1982 Feb;318(3):173–80

Dissociation of the effects of gonadal steroids on brain serotonin metabolism and sexual behavior in the male rat. Bradshaw WG, et al. **Neuroendocrinology** 1982 Jan;34(1):38–45

Evidence that the effects of 5-hydroxytryptophan on the secretion of ACTH and growth hormone in dogs are not mediated by central release of serotonin. Zimmermann H, et al. **Neuroendocrinology** 1982 Jan; 34(1):27–31

Differential involvement of dopamine-containing tracts in 5-hydroxytryptamine-dependent behaviours caused by amphetamine in large doses. Andrews CD, et al. **Neuropharmacology** 1982 Jan; 21(1):63–8

Long-term effects of methamphetamine on the synthesis and metabolism of 5-hydroxytryptamine in various regions of the rat brain. Bakhit C, et al. **Neuropharmacology** 1981 Dec;20(12A):1135–40

Behavioural effects of acute and chronic beta-phenylethylamine administration in the rat: evidence for the involvement of 5-hydroxytryptamine. Dourish CT. **Neuropharmacology** 1981 Nov; 20(11):1067–72

In vivo voltammetry in the rat hippocampus as in index of drug effects on extraneuronal 5-HT. Joseph MH, et al. **Neuropharmacology** 1981 Dec;20(12B):1361–4

The effect of niaprazine on the turnover of 5-hydroxytryptamine in the rat brain. Keane PE, et al. **Neuropharmacology** 1982 Feb;21(2):163–9

Ketamine inhibits serotonin uptake in vivo. Martin LL, et al. **Neuropharmacology** 1982 Feb;21(2):113–8

Ketamine inhibits serotonin synthesis and metabolism in vivo. Martin LL, et al. **Neuropharmacology** 1982 Feb;21(2):119–25

Lidocaine selectively diminishes medullary serotonin metabolism in the rat. Riker DK, et al. **Neuropharmacology** 1981 Dec;20(12A):1233–6

Depolarizing responses recorded from nodose ganglion cells of the rabbit evoked by 5-hydroxytryptamine and other substances. Wallis DI, et al. **Neuropharmacology** 1982 Jan;21(1):31–40

Effect of serotonin injected into the amygdala on conditioned and unconditioned food reflexes and the EEG in cats. Gasanov GG, et al. **Neurosci Behav Physiol** 1981 May–Jun;11(3):207–12

Effect of serotonin on formation and fixation of various conditioned reflexes. Getsova VM. **Neurosci Behav Physiol** 1981 May–Jun; 11(3):280–5

5-hydroxytryptophan uptake in indoleaminergic nerve fibers within rat cerebrovascular tree. Napoleone P, et al. **Neurosci Lett** 1982 Jan 22; 28(1):57–60

The importance of 5-hydroxytryptamine turnover for the analgesic effect of morphine in the chicken. Fan SG, et al. **Neuroscience** 1981; 6(11):2223–7

Release of endogenous 5-hydroxytryptamine from resting and stimulated enteric neurons. Gershon MD, et al. **Neuroscience** 1981; 6(11):2277–86

Arginine vasotocin: effects on open field behavior, whole brain monoamines and plasma corticosterone. Golus P, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):437–40

Possible mechanism of 5-methoxy-N,N-dimethyltryptamine-induced turning behaviour in DRN lesioned rats. Blackburn TP, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):7–11

Measurement of metabolites of dopamine and 5-hydroxytryptamine in cerebroventricular perfusates of unanesthetized, freely-moving rats: selective effects of drugs. Nielsen JA, et al. **Pharmacol Biochem Behav** 1982 Jan;16(1):131–7

Adrenalectomy reverses the effects of delta-9-THC on mouse brain 5-hydroxytryptamine turnover. Johnson KM, et al. **Pharmacology** 1981; 23(4):223–9

The effect of pyrazidol on the central serotonergic system. Sypniewska M, et al. **Pol J Pharmacol Pharm** 1981;33(3):313–9

Acute and chronic effects of pentobarbital on 5-hydroxytryptamine in mouse brain. Nabeshima T, et al. **Prog Neuropsychopharmacol** 1981; 5(4):373–81

Role played by serotonin in the control of estrous receptivity. Ovarian activity and ovulation in the cyclic female rat. Satli MA, et al. **Psychoneuroendocrinology** 1981;6(2):121–9

CNS mediated inhibition of gastric secretion by bombesin: independence from interaction with brain catecholaminergic, and serotoninergic pathways and pituitary hormones. Taché Y, et al. **Regul Pept** 1982 Jan; 3(1):51–9

Structural specificity of the inhibition of serotonin accumulation in rat lung slices. Mais DE, et al. **Res Commun Chem Pathol Pharmacol** 1981 Nov;34(2):241–50

Uptake mechanisms of 5–HT in pancreatic beta–cells. Lindström P, et al. **Ups J Med Sci** 1981;86(2):143–8

Evidence for a serotonin neurotransmitter system in bovine retina. Redburn DA, et al. **Vision Res** 1981;21(11):1673–6

[Pharmacology of puerarin. V. Effects of puerarin on platelet aggregation and release of 5–HT from platelets] Yin ZZ, et al. **Chung Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao** 1981 Jun; 3 Suppl 1:44–7 (Eng. Abstr.) **(Chi)**

[Demonstration of glutamate decarboxylase and serotonin in the same neuron of the nucleus raphe dorsalis of the rat by the methods of immunocytochemical doubling labelling] Belin MF, et al. **C R Seances Acad Sci [III]** 1981 Oct 19;293(6):337–41 **(Fre)**

[Effects of cigarette smoking on pulmonary functions and on plasma levels of serotonin, histamine and serum angiotensin I converting enzyme activity (author's transl)] Ishihara Y, et al. **Nippon Kyobu Shikkan Gakkai Zasshi** 1981 Oct;19(10):721–7 (Eng. Abstr.) **(Jpn)**

[Sites responsible for stimulation of brain Na,K–ATPase by serotonin] Novitskaia NA, et al. **Biokhimiia** 1981 Nov;46(11):1981–3 (Eng. Abstr.) **(Rus)**

[Atypical antidepressants: effect on synaptosomal uptake of serotonin and GABA] Avdulov NA, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):564–6 (Eng. Abstr.) **(Rus)**

[Effect of serotonin and prostaglandins on the permeability of model lipid membranes] Badzhinian SA, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):557–9 (Eng. Abstr.) **(Rus)**

[Binding of 3H–serotonin, 3H–diazepam and lipid peroxidation in brain membranes] Libe ML, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):552–4 (Eng. Abstr.) **(Rus)**

[Changes in the activity of the brain monoaminergic systems in adaptation to high altitude] Gromova EA, et al. **Dokl Akad Nauk SSSR** 1982; 262(1):245–7 **(Rus)**

[Serotonin and histamine liberation in experimental skin wounds] Lipshits RU, et al. **Fiziol Zh** 1982 Jan–Feb;28(1):107–9 **(Rus)**

[Effect of serotonin on contractile thermogenesis] Kudriavtseva NN, et al. **Fiziol Zh SSSR** 1981 Dec;67(12):1862–5 (Eng. Abstr.) **(Rus)**

[Study of serotonin and histamine metabolism in cosmonauts] Dolgun ZS, et al. **Kosm Biol Aviakosm Med** 1982 Jan–Feb;16(1):89–91 **(Rus)**

[Fluorimetric determination of serotonin and histamine in one sample] Sominskiĭ VN, et al. **Lab Delo** 1982;(2):104–7 (Eng. Abstr.) **(Rus)**

[Comparison of the acetylation of nuclear proteins in the liver and thymus of rats exposed to radiation damage with protection by serotonin] Babeniuk IuD, et al. **Radiobiologiia** 1982 Jan–Feb;22(1):13–8 (Eng. Abstr.) **(Rus)**

[Release of serotonin in vivo by mast cells exposed to MEA] Goncharenko EN, et al. **Radiobiologiia** 1982 Jan–Feb;22(1):94–6 **(Rus)**

[Catecholaminergic and serotoninergic systems in depression] Puzhin'skiĭ S, et al. **Vestn Akad Med Nauk SSSR** 1982;(1):66–8 (Eng. Abstr.) **(Rus)**

SEX BEHAVIOR, ANIMAL

Inhibition of lordosis behavior in the female rat by intraventricular infusion of prolactin and by chronic hyperprolactinemia. Dudley CA, et al. **Endocrinology** 1982 Feb;110(2):677–9

Sex hormones and neurotransmitters as mediators for sexual differentiation of the brain. Dörner G. **Endokrinologie** 1981 Dec;78(2–3):129–38 (31 ref.)

Differential effects of bromocriptine treatment on LH release and copulatory behavior in hyperprolactinemic male rats. Doherty PC, et al. **Horm Behav** 1981 Dec;15(4):436–50

Dissociation of the effects of gonadal steroids on brain serotonin metabolism and sexual behavior in the male rat. Bradshaw WG, et al. **Neuroendocrinology** 1982 Jan;34(1):38–45

The effect of LHRH antagonist analogs and an antibody to LHRH on mating behavior in female rats. Dudley CA, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):393–6

Facilitation of sexual receptivity in the rat by an ovulation–inhibiting analog of LHRH. Zadina JE, et al. **Pharmacol Biochem Behav** 1981 Dec;15(6):961–4

Female sexual behaviour in the GnRH deficient, hypogonadal (hpg) mouse. Ward BJ, et al. **Physiol Behav** 1981 Dec;27(6):1107–9

Role played by serotonin in the control of estrous receptivity. Ovarian activity and ovulation in the cyclic female rat. Satli MA, et al. **Psychoneuroendocrinology** 1981;6(2):121–9

SLEEP

Effects of oxolinic acid on the sleep–wakefulness cycle of the rat. D'Angelo L, et al. **Br J Pharmacol** 1981 Oct;74(2):399–404

Effect of phenobarbital on sleep and nighttime plasma growth hormone and cortisol levels. Prinz PN, et al. **Can J Physiol Pharmacol** 1981 Nov; 59(11):1139–45

Difference in tolerance development of hypothermia and pentobarbital–induced sleep prolongating effect of 11–hydroxy–delta 8–tetrahydrocannabinol and 11–oxo–delta 8–tetrahydrocannabinol in mice. Watanabe K, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):53–6

Further studies on the determinant role of brain level of pentobarbital for the development of acute hypnotic tolerance. Kaneto H, et al. **J Pharmacobiodyn** 1981 Sep;4(9):700–5

[Night sleep study in chronic psychotics under long term flupenthixol treatment (author's transl)] Serbanescou T, et al. **Encephale** 1981; 7(5):623–9 (Eng. Abstr.) **(Fre)**

SLEEP DEPRIVATION

[Antidepressive effect of partial sleep deprivation during the 1st half of the night] Goetze U, et al. **Psychiatr Clin (Basel)** 1981;14(3):129–49 (Eng. Abstr.) **(Ger)**

SLEEP, REM

Duration of REM sleep latency as predictor of effect of antidepressant therapy. A preliminary report. Svendsen K, et al. **Acta Psychiatr Scand** 1981 Sep;64(3):238–43

[Decrease of paradoxical sleep in the rat under tricyclic antidepressant: the role of collateral inhibition (author's transl)] Justafre JC, et al. **Rev Electroencephalogr Neurophysiol Clin** 1981 Nov;11(2):228–35 (Eng. Abstr.) **(Fre)**

[The effects of butoctamide hydrogen succinate (BAHS) on the sleep of the aged people (author's transl)] Hayashi Y, et al. **No To Shinkei** 1981 Dec;33(12):1243–50 (Eng. Abstr.) **(Jpn)**

SLEEP STAGES

EEG spectral analysis in vital depression: ultradian cycles. Lange H. **Biol Psychiatry** 1982 Jan;17(1):3–21

Neuronal discharge patterns in the occipital cortex of developing rats during active and quiet sleep. Mirmiran M, et al. **Brain Res** 1982 Jan; 255(1):37–48

Sleep suppressant action of quipazine: relation to central serotonergic stimulation. Fornal C, et al. **Pharmacol Biochem Behav** 1981 Dec; 15(6):937–44

[Effects of afloqualone, a centrally acting muscle relaxant, on the sleep–wakefulness cycle in cats with chronically implanted electrodes (author's transl)] Kojima M, et al. **Nippon Yakurigaku Zasshi** 1981 Nov; 78(5):471–82 (Eng. Abstr.) **(Jpn)**

SOCIAL ADJUSTMENT

The effects of labeling: blind and nonblind ratings of social skills in schizophrenic and nonschizophrenic control subjects. Lindsay WR. **Am J Psychiatry** 1982 Feb;139(2):216–9

SODIUM

The concentrations of trace elements in blood from healthy newborn infants. Meurling S, et al. **Acta Chir Scand** 1981;147(6):481–5

Effects of ACTH on the zona glomerulosa of sodium–loaded timolol maleate–treated rats: stereology and plasma hormone concentrations. Nussdorfer GG, et al. **Acta Endocrinol (Copenh)** 1982 Feb; 99(2):256–62

Sodium intake alters the effects of norepinephrine on the renin system and the kidney. Rankin LI, et al. **Am J Kidney Dis** 1981 Nov; 1(3):177–84

Aldosterone and the enhanced natriuresis of hypertonic infusions in the dog. Childers JW, et al. **Am J Physiol** 1982 Jan;242(1):F30–7

Effect of tryptophan on transport properties of newborn rabbit jejunum. Cooke HJ, et al. **Am J Physiol** 1982 Apr;242(4):G308–12

The uptake and extrusion of salts by the halotolerant bacterium, Ba1. Shnaiderman R, et al. **Arch Biochem Biophys** 1982 Jan;213(1):177–85

Synthesis and migration of proteins and glycoproteins in juxtaglomerular cells of sodium–deficient rats. An ultrastructural radioautographic study. Désormeaux Y, et al. **Cell Tissue Res** 1982 Jan;222(1):53–67

Dietary sodium, erythrocyte sodium concentration, sodium–stimulated lithium efflux and blood pressure. Trevisan M, et al. **Clin Sci [Suppl]** 1981 Dec;61(7):29s–32s

Sodium– and calcium–dependent somatostatin release from dissociated cerebral cortical cells in culture. Robbins RJ, et al. **Endocrinology** 1982 Feb;110(2):496–9

Discrepancy in the regulatory effects of sodium and guanine nucleotides on adrenaline and clonidine binding to alpha 2–adrenoceptors in human fat cell membranes. Gonzalez JL, et al. **Eur J Pharmacol** 1981 Dec 3;76(2–3):289–93

Competitive inhibition of sodium–dependent high affinity choline uptake by harmala alkaloids. Smart L. **Eur J Pharmacol** 1981 Nov 5; 75(4):265–9

Effect of Na+, K+ and Li+ on pH dependence of in situ beta–galactosidase from E. coli. de Arriaga D, et al. **Int J Biochem**

1982;14(1):47-52

Furosemide-sensitive salt transport in the Madin-Darby canine kidney cell line. Evidence for the cotransport of Na+, K+, and Cl-. McRoberts JA, et al. **J Biol Chem** 1982 Mar 10;257(5):2260-6

(Na+,K+)-cotransport in the Madin-Darby canine kidney cell line. Kinetic characterization of the interaction between Na+ and K+. Rindler MJ, et al. **J Biol Chem** 1982 Mar 10;257(5):2254-9

Influence of sodium and sulphydryl groups on [3H]sulpiride binding sites in rat striatal membranes. Freedman SB, et al. **J Neurochem** 1982 May; 38(5):1459-65

Ontogenetic development of the striatal [3H]spiperone binding: regulation by sodium and guanine nucleotide in rats. Nomura Y, et al. **J Neurochem** 1982 Apr;38(4):902-8

Inhibition by somatostatin of bovine growth hormone secretion following sodium channel activation. Bicknell RJ, et al. **J Physiol (Lond)** 1981 Jul;316:85-96

The interaction of potassium ions and ATP on the sodium pump of resealed red cell ghosts. Eisner DA, et al. **J Physiol (Lond)** 1981; 319:403-18

Internal potassium stimulates the sodium-potassium pump by increasing cell ATP concentration. Sachs JR. **J Physiol (Lond)** 1981; 319:515-28

Calcium-dependent secretion of catecholamines from the perfused bovine adrenal medulla by sodium deprivation. Sorimachi M, et al. **Jpn J Physiol** 1981;31(5):753-56

On the mechanism of the inhibition of fast axonal transport caused by exposure of frog spinal ganglia to the sodium-deficient medium. Lavoie PA. **Neurosci Lett** 1981 Dec 11;27(2):131-4

Ionic mechanisms of alpha-autoinhibition of [3H]noradrenaline secretion in guinea-pig vas deferens: possible role of extracellular sodium. Stjärne L. **Neuroscience** 1981;6(12):2759-71

Catecholamines and the sodium pump in excitable cells. Phillis JW, et al. **Prog Neurobiol** 1981;17(3):141-84 (320 ref.)

[Effect of the structural integrity of Na,K-ATPase preparations on the ability of lithium to substitute for sodium in enzyme activation] Skul'skil IA, et al. **Tsitologiia** 1982 Jan;24(1):95-8 (Eng. Abstr.) **(Rus)**

SOMATOTROPIN RELEASE INHIBITING HORMONE

Tolbutamide, glucose, calcium, and somatostatin secretion. Hermansen K. **Acta Endocrinol (Copenh)** 1982 Jan;99(1):86-93

Effect of somatostatin on determinants of bile flow in unanesthetized dogs. Lewis MH, et al. **Ann Surg** 1982 Jan;195(1):97-103

Studies on the mechanism of action of somatostatin on renal gluconeogenesis: evidence for the involvement of alpha 1-adrenergic stimuli. Dileepan KN, et al. **Arch Biochem Biophys** 1982 Jan; 213(1):169-76

High-field 1H NMR studies of synthetic analogs of somatostatin. Structural features involving aromatic residues in an active eight-membered ring analog. Cutnell JD, et al. **Biochim Biophys Acta** 1982 Jan 4;700(1):59-66

The interaction of glucagon, gastric inhibitory peptide and somatostatin with cyclic AMP production systems present in rat gastric glands. Gespach C, et al. **Biochim Biophys Acta** 1982 Feb 10;720(1):7-16

The conformational properties of somatostatin. IV. The conformers contributing to the conformation equilibrium of somatostatin in aqueous solution as found by semi-empirical energy calculations and high-resolution NMR experiments. Knappenberg M, et al. **Biochim Biophys Acta** 1982 Jan 18;700(2):229-46

Topography of median eminence somatostatinergic innervation. Epelbaum J, et al. **Brain Res** 1981 Dec 28;230(1-2):412-6

The actions of neuropeptides on dorsal horn neurons in the rat spinal cord slice preparation: an intracellular study. Murase K, et al. **Brain Res** 1982 Feb 18;234(1):170-6

Effects of neurotransmitters and cyclic AMP on somatostatin release from cultured cerebral cortical cells. Robbins RJ, et al. **Brain Res** 1982 Feb 25;234(2):377-86

Distribution of somatostatin in the mouse brain: effects of neonatal MSG treatment. Romagnano MA, et al. **Brain Res** 1982 Feb 25; 234(2):387-98

Somatostatin inhibits prolactin secretion in the estradiol primed male rat. Cooper GR, et al. **Can J Physiol Pharmacol** 1981 Oct;59(10):1082-8

Distribution of neuropeptides in the dorsal pontine tegmental area of the rat. Matsuzaki T, et al. **Cell Mol Biol** 1981;27(5):499-508

Immunocytochemical localization of hormone-producing cells within the pancreatic islets of the rainbow trout (Salmo gairdneri). Wagner GF, et al. **Cell Tissue Res** 1981;221(1):181-92

Influence of somatostatin on plasma cyclic AMP and metabolic substrate responses to i.v. adrenaline and glucagon in humans. Nistrup Madsen S, et al. **Clin Endocrinol (Oxf)** 1981 Nov;15(5):431-7

Effects of K+ and arginine on insulin, glucagon, and somatostatin release from the in vitro perfused rat pancreas. Frankel BJ, et al. **Endocrinology** 1982 Feb;110(2):428-31

Effects of somatostatin and urotensin II on tilapia pituitary prolactin release and interactions between somatostatin, osmotic pressure Ca++, and adenosine 3',5'-monophosphate in prolactin release in vitro. Grau EG, et al. **Endocrinology** 1982 Mar;110(3):910-5

High somatostatin uptake by the isolated perfused dog pancreas consistent with 'insulo-acinar' axis. Kawai K, et al. **Endocrinology** 1982 Feb; 110(2):660-2

Influence of endogenous somatostatin on growth hormone and thyrotropin secretion in neonatal rats. Oliver C, et al. **Endocrinology** 1982 Mar; 110(3):1018-22

Sodium- and calcium-dependent somatostatin release from dissociated cerebral cortical cells in culture. Robbins RJ, et al. **Endocrinology** 1982 Feb;110(2):496-9

Selective processing of the 15 000 Mr prosomatostatin by mouse hypothalamic extracts releases the tetradecapeptide. Morel A, et al. **FEBS Lett** 1981 Dec 28;136(2):316-8

Effect of food deprivation on rat gastric somatostatin and gastrin release. Koop H, et al. **Gastroenterology** 1982 May;82(5 Pt 1):871-6

Abnormalities of the colonic regulatory peptides in Hirschsprung's disease. Bishop AE, et al. **Histopathology** 1981 Nov;5(6):679-88

Route of administration as a factor in the selectivity of hormone suppression of a somatostatin analog in rats. Lien EL, et al. **Horm Metab Res** 1981 Dec;13(12):675-8

Infusion of somatostatin antiserum in the rat—failure to raise stress induced low gastric acid secretion. Schwille PO, et al. **Horm Metab Res** 1981 Dec;13(12):710-1

Pituitary somatostatin receptors. Characterization by binding with a nondegradable peptide analogue. Aguilera G, et al. **J Biol Chem** 1982 Feb 10;257(3):1134-7

Localization of methionine-enkephalin, substance P, and somatostatin immunoreactivities in the main olfactory bulb of the hamster. Davis BJ, et al. **J Comp Neurol** 1982 Feb 1;204(4):377-83

Ontogeny of somatostatin-containing neuron system of the rat: immunohistochemical analysis. II. Forebrain and diencephalon. Shiosaka S, et al. **J Comp Neurol** 1982 Jan 20;204(3):211-24

Evidence for ascending and descending intraspinal as well as primary sensory somatostatin projections in the rat spinal cord. Stine SM, et al. **J Neurochem** 1982 Apr;38(4):1144-50

Depletion of somatostatin-like immunoreactivity in the rat central nervous system by cysteamine. Sagar SM, et al. **J Neurosci** 1982 Feb; 2(2):225-31

Inhibition by somatostatin of bovine growth hormone secretion following sodium channel activation. Bicknell RJ, et al. **J Physiol (Lond)** 1981 Jul;316:85-96

A role of endogenous somatostatin and glucagon in insulin release from pancreatic islets. Taniguchi H, et al. **Kobe J Med Sci** 1981 Dec; 27(6):213-24

A survey of substance P, somatostatin, and neurotensin levels in aging in the rat and human central nervous system. Buck SH, et al. **Neurobiol Aging** 1981 Winter;2(4):257-64

Somatostatin immunoreactive cell bodies in the dorsal horn and the parasympathetic intermediolateral nucleus of the rat spinal cord. Dalsgaard CJ, et al. **Neurosci Lett** 1981 Dec 23;27(3):335-9

Developmental changes in bombesin, substance P, somatostatin and vasoactive intestinal polypeptide in the rat brain. McGregor GP, et al. **Neurosci Lett** 1982 Jan 22;28(1):21-7

Discrete distributions of putative cholinergic and somatostatinergic amacrine cell dendrites in chicken retina. Morgan IG, et al. **Neurosci Lett** 1981 Nov 18;27(1):55-60

The immunocytochemical localization of somatostatin-containing neurons in the rat central nervous system. Finley JC, et al. **Neuroscience** 1981; 6(11):2173-92

Presence of somatostatin-28-(1-12) in hypothalamus and pancreas. Benoit R, et al. **Proc Natl Acad Sci USA** 1982 Feb;79(3):917-21

Effect of parathyroid hormone on gastrin and somatostatin release from the gastric antrum. Selking O, et al. **Ups J Med Sci** 1981; 86(3):259-67

[Inhibition of growth-hormone release in man: comparative study between somatostatin-14 and -28 (author's transl)] Pradayrol L, et al. **Gastroenterol Clin Biol** 1982 Feb;6(2):166-9 (Eng. Abstr.) **(Fre)**

[Behavior of secretin-pancreozymin-stimulated pancreatic secretion, gallbladder contraction and choleresis after somatostatin administration] von Kleist D, et al. **Dtsch Z Verdau Stoffwechselkr** 1981; 41(5):219-24 (Eng. Abstr.) **(Ger)**

[The effect of chronic administration of somatostatin on the hemostatic system in the dog (author's transl)] Gabryelewicz A, et al. **Przegl Lek** 1981;38(10):719-21 (Eng. Abstr.) **(Pol)**

[Effect of somatostatin on pancreatic secretion in the dog] Fokina AA, et al. **Fiziol Zh SSSR** 1981 Nov;67(11):1737-9 **(Rus)**

SOMATOTROPIN RELEASING HORMONE

Evidence that reduced growth hormone secretion observed in monosodium glutamate-treated rats is the result of a deficiency in growth hormone-releasing factor. Millard WJ, et al. **Endocrinology** 1982 Feb;110(2):540-50

Growth hormone releasing activity persists in the deafferented medial-basal hypothalamus of the rat. Antoni FA, et al. **J Endocrinol** 1981 Dec;91(3):415-25

STARTLE REACTION

Spinal modulation of acoustic startle: opposite effects of clonidine and d-amphetamine. Davis M, et al. **Psychopharmacology (Berlin)** 1981; 75(3):219–25

STEREOTYPED BEHAVIOR

Study of the neural basis of circling behavior induced by L-dopa in lesioned entopeduncular cats. Pazo JH, et al. **Brain Res** 1982 Feb 11; 233(2):337–45

Opposed stages of continuous amphetamine administration: parallel alterations in motor stereotypies and in vivo spiroperidol accumulation. Ellison G, et al. **Eur J Pharmacol** 1981 Sep 11;74(2–3):207–14

Behavioural evidence for supersensitivity of postsynaptic dopamine receptors in the mesolimbic system after chronic administration of desipramine. Spyraki C, et al. **Eur J Pharmacol** 1981 Sep 11; 74(2–3):195–206

The chronic effect of nomifensine on rat stereotyped behavior. Muto K, et al. **Kurume Med J** 1981;28(2):173–5

The methylphenidate-induced stereotypy in the awake rat: local cerebral metabolism. Bell RD, et al. **Neurology (NY)** 1982 Apr;32(4):377–81

Further evidence for a GABA-like action on kojic amine. Martin GE, et al. **Neurosci Lett** 1981 Nov 18;27(1):37–40

Gnawing and changes in reactivity produced by microinjections of picrotoxin into the superior colliculus of rats. Redgrave P, et al. **Psychopharmacology (Berlin)** 1981;75(2):198–203

[Effect of alpha-methyl-para-tyrosine on 'methamphetamine-induced sterotype and hypermotility' of reserpinized rats (author's transl)] Nakajima H, et al. **Nippon Yakurigaku Zasshi** 1981 Dec;78(6):557–69 (Eng. Abstr.) **(Jpn)**

[Effect of phenamine and haloperidol on stereotyped behavior in response to electric stimulation of the substantia nigra in cats] Arushanian EB, et al. **Biull Eksp Biol Med** 1981 Oct;91(10):444–7 (Eng. Abstr.) **(Rus)**

[Effect of amizil and galantamin on the behavioral effects of apomorphine in rats] Bandman AL, et al. **Biull Eksp Biol Med** 1981 Nov; 92(11):566–9 (Eng. Abstr.) **(Rus)**

[Comparison of clebopride, domperidone, metopimazine, and trimebutine as antiemetics and inducers of gastrointestinal peristalsis] Berga P, et al. **Arch Farmacol Toxicol** 1981 Apr;7(1):189–92 **(Spa)**

[Effect of N-(4-picolyl)-3,5 dimethylbenzamide (M-14012-4) on stereotyped behavior induced by apomorphine and amphetamine in the rat and mouse] Casais PL, et al. **Arch Farmacol Toxicol** 1981 Apr; 7(1):65–72 **(Spa)**

STRESS, PSYCHOLOGICAL

Effect of noise on blood pressure and 'stress' hormones. Andrén L, et al. **Clin Sci** 1982 Feb;62(2):137–41

Stress-modulated alteration of brain biogenic amines in the rat: effects of L-tryptophan. Quirce CM, et al. **Commun Psychopharmacol** 1980; 4(5):371–7

Effect of immobilization stress & ascorbic acid on acetylcholine & plasma cortisol in albino rats. Gode JD, et al. **Indian J Exp Biol** 1981 Dec; 19(12):1175–6

The effects of age on the plasma catecholamine response to mental stress in man. Barnes RF, et al. **J Clin Endocrinol Metab** 1982 Jan; 54(1):64–9

Interaction of apomorphine and stressors in the production of hyperthermia in the rabbit. Snow AE, et al. **J Pharmacol Exp Ther** 1982 Feb;220(2):335–9

[Dynamics of noradrenaline concentration in the hepatic portal vein and atria of rats during stress] Manukhina EB, et al. **Biull Eksp Biol Med** 1981 Dec;92(12):673–4 (Eng. Abstr.) **(Rus)**

[Changes in the catecholamine content in adrenaline-synthetizing structures of the medulla oblongata in rats with different reactions to long-term immobilization] Kvetnanskil R, et al. **Probl Endokrinol (Mosk)** 1981;27(6):58–63 (Eng. Abstr.) **(Rus)**

[Psychological component of human stress (author's transl)] Vargas Fernández L. **Rev Med Chil** 1981 May;109(5):441–51 (Eng. Abstr.) **(Spa)**

SUBSTANCE P

In vitro degradation of substance P: new rapid assay and distribution in rat brain. Akopyan TN, et al. **Acta Biol Med Ger** 1981; 40(6):779–84

Depletion of primary afferent substance P by capsaicin and dihydrocapsaicin without altered thermal sensitivity in rats. Buck SH, et al. **Brain Res** 1982 Feb 4;233(1):216–20

Immunoreactive substance P in the substantia nigra of the monkey: light and electron microscopic localization. DiFiglia M, et al. **Brain Res** 1982 Feb 11;233(2):381–8

Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Glickman RD, et al. **Brain Res** 1982 Feb 18;234(1):81–99

Synthesis, and central and peripheral axonal transport of substance P in a dorsal root ganglion-nerve preparation in vitro. Harmar A, et al. **Brain Res** 1982 Jan 14;231(2):379–85

Effect of spinal ganglionectomy on substance P-like immunoreactivity in the gastroduodenal tract of cats. Hayashi H, et al. **Brain Res** 1982 Jan 28;232(1):227–30

Regulation of substance P in adult rat sympathetic ganglia. Kessler JA, et al. **Brain Res** 1982 Feb 18;234(1):182–7

The actions of neuropeptides on dorsal horn neurons in the rat spinal cord slice preparation: an intracellular study. Murase K, et al. **Brain Res** 1982 Feb 18;234(1):170–6

Dual effects of substance P on the excitability of single cutaneous primary afferent C- and A-fibers in the cat spinal cord. Randić M, et al. **Brain Res** 1982 Feb 11;233(2):389–93

Evidence for the existence of a substance P-containing pathway from the nucleus laterodorsalis tegmenti (Castaldi) to the lateral septal area of the rat. Sakanaka M, et al. **Brain Res** 1981 Dec 28; 230(1–2):351–5

Spinal neurons mediate return of substance P following deafferentation of cat spinal cord. Tessler A, et al. **Brain Res** 1981 Dec 28; 230(1–2):263–81

Distribution of neuropeptides in the dorsal pontine tegmental area of the rat. Matsuzaki T, et al. **Cell Mol Biol** 1981;27(5):499–508

Substance P-immunoreactive nerve fibres in the anterior segment of the rabbit eye. Distribution and possible physiological significance. Tornqvist K, et al. **Cell Tissue Res** 1982;222(3):467–77

Substance P immunoreactivity in the anterior pituitary gland of the guinea pig. DePalatis LR, et al. **Endocrinology** 1982 Jan;110(1):282–4

Antagonists of substance P. Caranikas S, et al. **Eur J Pharmacol** 1982 Jan;77(2–3):205–6

The effects of 5-hydroxytryptamine-depleting drugs on peptides in the ventral spinal cord. Gilbert RF, et al. **Eur J Pharmacol** 1981 Dec 3; 76(2–3):203–10

Substance P, but not TRH, modulates the 5-HT autoreceptor in ventral lumbar spinal cord. Mitchell R, et al. **Eur J Pharmacol** 1981 Nov 19; 76(1):119–20

Synthesis and metabolic stability of a tritium-labelled substance P analogue. Sandberg BE, et al. **FEBS Lett** 1982 Jan 25;137(2):236–40

Localization of substance P-like immunoreactivity in the anterior eye segment of squirrels: an immunohistochemical analysis. Shimizu Y, et al. **Invest Ophthalmol Vis Sci** 1982 Feb;22(2):259–63

Substance P-like immunoreactivity in the intramural nerve plexuses of the guinea-pig ureter: a light and electron microscopical study. Sikri KL, et al. **J Anat** 1981 Oct;133(Pt 3):425–42

Perivascular substance P: occurrence and distribution in mammalian pial vessels. Uddman R, et al. **J Cereb Blood Flow Metab** 1981; 1(2):227–32

Localization of methionine-enkephalin, substance P, and somatostatin immunoreactivities in the main olfactory bulb of the hamster. Davis BJ, et al. **J Comp Neurol** 1982 Feb 1;204(4):377–83

Serotonin and gamma-aminobutyric acid turnover after injection into the median raphe of substance P and D-ala-met-enkephalin amide. Forchetti CM, et al. **J Neurochem** 1982 May;38(5):1336–41

Active uptake of substance P carboxy-terminal heptapeptide (5–11) into rat brain and rabbit spinal cord slices. Nakata Y, et al. **J Neurochem** 1981 Dec;37(6):1529–34

Enzyme-linked immunosorbent assay of substance P: a study in the eye. Stjernschantz J, et al. **J Neurochem** 1982 May;38(5):1323–8

Substance P-like immunoreactivity in neurons in dissociated cell cultures of mammalian spinal cord and dorsal root ganglia. Neale EA, et al. **J Neurosci** 1982 Feb;2(2):169–77

Neurohumoral control of ileal electrolyte transport. II. Neurotensin and substance P. Kachur JF, et al. **J Pharmacol Exp Ther** 1982 Mar; 220(3):456–63

Substance P: immunohistochemical localization and effect upon cat pial arteries in vitro and in situ. Edvinsson L, et al. **J Physiol (Lond)** 1981 Sep;318:251–8

Mediators of slow synaptic potentials in the myenteric plexus of the guinea-pig ileum. Johnson SM, et al. **J Physiol (Lond)** 1981 Nov; 320:175–86

Noncholinergic, nonadrenergic contraction and substance P in rabbit iris sphincter muscle. Ueda N, et al. **Jpn J Pharmacol** 1981 Dec; 31(6):1071–9

Age-related changes in central nervous system enkephalins and substance P. Dupont A, et al. **Life Sci** 1981 Nov 30;29(22):2317–22

Biological activity of substance P methyl ester. Cascieri MA, et al. **Mol Pharmacol** 1981 Nov;20(3):457–9

Co-occurrence of substance P-like and Leu-enkephalin-like immunoreactivities in neurones and fibres of avian nervous system. Erichsen JT, et al. **Nature** 1982 Feb 4;295(5848):407–10

Fifty years of substance P [news] Jessell TM. **Nature** 1982 Feb 18; 295(5850):551–3

A survey of substance P, somatostatin, and neurotensin levels in aging in the rat and human central nervous system. Buck SH, et al. **Neurobiol Aging** 1981 Winter;2(4):257–64

The role of the N-terminal tetrapeptide in the histamine releasing action of substance P. Mazurek N, et al. **Neuropharmacology** 1981 Nov;

20(11):1025-7

Substance P decreases membrane conductance in neurons of the guinea pig hypothalamus in vitro. Ogata N, et al. **Neuropharmacology** 1982 Feb;21(2):187-9

Developmental changes in bombesin, substance P, somatostatin and vasoactive intestinal polypeptide in the rat brain. McGregor GP, et al. **Neurosci Lett** 1982 Jan 22;28(1):21-7

Localization of substance P-like immunoreactivity in cell bodies of the feline dorsal vagal nucleus. Maley B, et al. **Neurosci Lett** 1981 Dec 11;27(2):187-91

Depletion by capsaicin of substance P-immunoreactivity and acetylcholinesterase activity from nerve fibres in the guinea-pig heart. Papka RE, et al. **Neurosci Lett** 1981 Nov 18;27(1):47-53

Transplantation of irides or sensory ganglia to the anterior eye chamber of the rat: survival and sprouting of substance P-containing neurones. Skagerberg G, et al. **Neurosci Lett** 1982 Jan 22;28(1):29-34

Coexistence of substance P- and cholecystokinin-like immunoreactivity in neurons of the mesencephalic periaqueductal central gray. Skirboll L, et al. **Neurosci Lett** 1982 Jan 22;28(1):35-9

Peptidergic innervation of the mammalian sinus nodes: vasoactive intestinal polypeptide, neurotensin, substance P. Weihe E, et al. **Neurosci Lett** 1981 Nov 4;26(3):283-8

Localization of substance P-like immunoreactivity in the adult and developing goldfish retina. Brecha N, et al. **Neuroscience** 1981; 6(12):2737-46

Thermal analgesia and substance P depletion induced by capsaicin in guinea-pigs. Buck SH, et al. **Neuroscience** 1981;6(11):2217-22

The distribution of substrate P-like immunoreactive nerves in the guinea-pig heart. Wharton J, et al. **Neuroscience** 1981;6(11):2193-204

Mini review: smooth muscle pharmacology of substance P. Couture R, et al. **Pharmacology** 1982 Jan;24(1):1-25 (66 ref.)

Substance P levels in the rat forebrain after apomorphine and haloperidol treatment. Janicki P, et al. **Pol J Pharmacol Pharm** 1981; 33(5):499-502

[Duration of the normalizing effect of substance P in disturbances of the learning process after long-term exposure to noise] Hecht K, et al. **Pharmazie** 1981 Dec;36(12):859-60 **(Ger)**

[Neuropeptides in the rabbit eye. I. RIA for beta-endorphin, substance P and neurotensin in the aqueous humor, iris-ciliary body and retina (author's transl)] Baba S, et al. **Nippon Ganka Gakkai Zasshi** 1981 Sep 10;85(9):1267-72 (Eng. Abstr.) **(Jpn)**

[Effect of substance P on the mesenteric microcirculation system] Gorizontova MP, et al. **Biull Eksp Biol Med** 1981 Nov;92(11):515-7 (Eng. Abstr.) **(Rus)**

SYMPATHOMIMETICS

Effect of sympathomimetic substances and analogues on tail absorption of frog larva. Csaba G, et al. **Acta Biol Acad Sci Hung** 1981; 32(2):103-9

Suppression of mammotropic development and prolactin release by sympathomimetic drugs in rats. Shani J, et al. **Arch Farmacol Toxicol** 1981 Aug;7(2):201-8

Response of the isolated rabbit ciliary epithelium to adrenergic drugs following superior cervical ganglionectomy. Green K, et al. **Curr Eye Res** 1981;1(4):217-22

Effects of adrenergic drugs on raphe unit activity in freely moving cats. Heym J, et al. **Eur J Pharmacol** 1981 Sep 11;74(2-3):117-25

Effects of adrenergic drugs on miniature contractions of isolated dog urinary bladder. Ueda S, et al. **Eur Urol** 1982 Jan-Feb;8(1):37-41

Effects of parasympathomimetic and sympathomimetic drugs on the secretion and composition of rat sublingual saliva. Abe K, et al. **J Dent Res** 1982 Jan;61(1):52-6

Effects of intraventricular administration of sympathomimetic agents on metabolic, vasomotor and temperature responses in Taiwan monkeys. Chern YF, et al. **Jpn J Physiol** 1981;31(4):599-603

Development of stimulus-secretion coupling in salivary glands. Cutler LS, et al. **Methods Cell Biol** 1981;23:531-45

Shock demands drugs--but which one's best for your patient? Barrows JJ. **Nursing (Horsham)** 1982 Feb;12(2):34-41

SYNAPTIC RECEPTORS

Stereoselectivity of presynaptic autoreceptors modulating dopamine release. Arbilla S, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):345-51

Affinity of thiocolchicoside and thiocolchicoside analogues for the postsynaptic GABA receptor site. Biziere K, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):167-8

Endogenous GABA determines the characteristics of [3H]GABA-binding. Gardner CR, et al. **Eur J Pharmacol** 1981 Oct 22;75(2-3):83-92

Inhibition of [3H]GABA binding to postsynaptic receptors in human cerebellar synaptic membranes by carboxyl and amino derivatives of GABA. Breckenridge RJ, et al. **J Neurochem** 1981 Oct;37(4):837-44

Molecular interactions of etazolate with benzodiazepine and picrotoxinin binding sites. Ticku MK, et al. **J Neurochem** 1982 Apr;38(4):1180-2

Benzodizepines: biochemistry of function. Tallman JF. **Natl Inst Drug Abuse Res Monogr Ser** 1980;(33):4-11

Molecular size of benzodiazepine receptor in rat brain in situ: evidence for a functional dimer? Doble A, et al. **Nature** 1982 Feb 11; 295(5849):522-3

Non-dopaminergic fibres may regulate dopamine-sensitive adenylate cyclase in the prefrontal cortex and nucleus accumbens. Tassin JP, et al. **Nature** 1982 Feb 25;295(5851):696-8

Effect of lithium on circadian neurotransmitter receptor rhythms. Kafka MS, et al. **Neuropsychobiology** 1982 Jan-Feb;8(1):41-50

6 -Hydroxydopamine decreases benzodiazepine but not GABA receptor binding in rat cerebellum. Doble A, et al. **Neurosci Lett** 1981 Dec 11; 27(2):199-204

Changes in rat hippocampal benzodiazepine receptors and lack of changes in muscarinic receptors after fimbria-fornix lesions. Sábato UC, et al. **Neurosci Lett** 1981 Dec 11;27(2):193-7

Different synaptic location of mianserin and imipramine binding sites. Brunello N, et al. **Science** 1982 Feb 26;215(4536):1112-5

TESTOSTERONE

Responses of ram lambs to active immunization against testosterone and luteinizing hormone-releasing hormone. Schanbacher BD. **Am J Physiol** 1982 Mar;242(3):E201-5

Temporal relationship between the development of the self-priming effect of LHRH and changes in serum concentrations of testosterone and androstenedione during the sexual maturation of the male rat. Nazian SJ. **Biol Reprod** 1981 Dec;25(5):977-82

Induction of testicular gonadotropin-releasing hormone (GnRH) receptors by GnRH: effects of pituitary hormones and relationship to inhibition of testosterone production. Bourne GA, et al. **Endocrinology** 1982 Mar;110(3):727-33

Pituitary receptor sites for gonadotropin-releasing hormone: effect of castration and substitutive therapy with sex steroids in the male rat. Conne BS, et al. **Endocrinology** 1982 Jan;110(1):70-9

Effect of unilateral castration and unilateral cryptorchidism on gonadotropin and testosterone response to gonadotropin releasing hormone in the bull. Barnes MA, et al. **J Anim Sci** 1981 Nov; 53(5):1341-50

Sexual differentiation of hepatic metabolism of corticosterone and testosterone in the rat. Rahman R, et al. **J Biochem (Tokyo)** 1981 Dec; 90(6):1567-75

Plasma LH and testosterone responses to synthetic gonadotrophin-releasing hormone (GnRH) or dexamethasone-GnRH combined treatment and their relationship to semen output in bulls. Abdel Malak G, et al. **J Reprod Fertil** 1982 Jan;64(1):107-13

Comparison of steroid and LH-RH effects on the responsiveness of hemipituitary glands and dispersed pituitary cells. Speight A, et al. **Mol Cell Endocrinol** 1981 Dec;24(3):267-81

Dissociation of the effects of gonadal steroids on brain serotonin metabolism and sexual behavior in the male rat. Bradshaw WG, et al. **Neuroendocrinology** 1982 Jan;34(1):38-45

Serum testosterone concentrations during the 4-day estrous cycle in normal and adrenalectomized rats. Rush ME, et al. **Proc Soc Exp Biol Med** 1982 Feb;169(2):216-21

[A factor influencing in vitro the influx of 86Rb+ into erythrocytes as an impurity of a commercial preparation of testosterone (author's transl)] Schreiber V, et al. **Sb Lek** 1981;83(11-12):305-8 (Eng. Abstr.) **(Cze)**

[Studies on the feedback regulation of gonadotropin concentrations in male rats (I). The effects of hypothalamic implantation of testosterone and its metabolites on gonadotropin release in castrated male rats (author's transl)] Noguchi K. **Nippon Naibunpi Gakkai Zasshi** 1981 Aug 20;57(8):1139-47 (Eng. Abstr.) **(Jpn)**

[Changes in the blood level of certain hormones of immature rats after thermal burn] Kamilov FKh, et al. **Vopr Med Khim** 1982 Jan-Feb; 28(1):56-9 (Eng. Abstr.) **(Rus)**

THINKING

The flow of thought and the flow of substance in the brain. McIlwain H. **Biol Psychol** 1981 Mar-May;12(2-3):147-69

THIORIDAZINE

Disparate serum thioridazine concentrations: liquid chromatography versus radioreceptor assay. Linnoila M, et al. **Acta Pharmacol Toxicol (Copenh)** 1982 Jan;50(1):25-9

[Comparison of the effectiveness of tranylcypromine, nortriptyline, thioridazine and amitriptyline in two syndromological types of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981;77(4):245-52 (Eng. Abstr.) **(Cze)**

THIOTHIXENE

Serum level monitoring of thiothixene in schizophrenia: acute single-dose levels at fixed doses. Yesavage JA, et al. **Am J Psychiatry** 1982 Feb; 139(2):174-8

THIRST

Anygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst-motivated behavior. Lénárd L, et al. **Brain Res** 1982 Feb 4;233(1):115–32

THYROID HORMONES

Differences in the binding of thyroid hormones and indoles by rat alpha 1-fetoprotein and serum albumin. Hervé F, et al. **Eur J Biochem** 1982 Mar 1;122(3):609–12

The effect of antipyrine, phenobarbitol and rifampicin on thyroid hormone metabolism in man. Ohnhaus EE, et al. **Eur J Clin Invest** 1981 Oct; 11(5):381–7

Acute thyroid hormone increases noradrenergic responsiveness of rat atria in vitro. Eiden LE, et al. **Eur J Pharmacol** 1981 Aug 27;74(1):91–3

Thyroid proliferation, body weight, thyrotropin and thyroid hormones in chronic antithyroid (carbimazole) treatment in rats. Redmond O, et al. **J Anat** 1981 Aug;133(Pt 1):37–47

The effects of aging on thyroid hormone economy in man. Ingbar SH. **Prog Clin Biol Res** 1981;74:135–45 (42 ref.)

An inhibitor of the binding of thyroid hormones to serum proteins is present in extrathyroidal tissues. Chopra IJ, et al. **Science** 1982 Jan 22; 215(4531):407–9

[Age and changes in thyroid function and tissue metabolism of its hormones] Iasenchak SA, et al. **Fiziol Zh** 1982 Jan–Feb;28(1):25–9 **(Rus)**

[Effect of thyroid hormones on various indices of water–electrolyte and kidney function in rats] Mostovoi VS. **Fiziol Zh** 1981 Nov–Dec; 27(6):826–9 **(Rus)**

[Isoenzymatic spectra of lactate dehydrogenase in various areas of the rat brain and the influence of thyroidin on them] Kononenko VIa, et al. **Ukr Biokhim Zh** 1982;54(1):26–30 (Eng. Abstr.) **(Rus)**

[Changes in the blood level of certain hormones of immature rats after thermal burn] Kamilov FKh, et al. **Vopr Med Khim** 1982 Jan–Feb; 28(1):56–9 (Eng. Abstr.) **(Rus)**

[Effect of heparin on thyroid function indicators as determined by radioanalysis] Košlík S, et al. **Vnitr Lek** 1982 Feb;28(2):122–8 (Eng. Abstr.) **(Slo)**

THYROTROPIN

Studies on the mechanism of the GABAergic inhibition of TSH secretion in male rats. Mattila J. **Acta Pharmacol Toxicol (Copenh)** 1981 Apr; 48(4):320–5

Persistent elevation of thyroid-stimulating hormone in women with bipolar affective disorder. O'Shanick GJ, et al. **Am J Psychiatry** 1982 Apr;139(4):513–4

Effect of domperidone on prolactin (PRL)and thyrotrophin (TSH) secretion. Kaufman JM, et al. **Arch Int Pharmacodyn Ther** 1981 Dec; 254(2):293–303

Large single doses of oral TRH blockade the TSH response in children. Villalpando-Hernández S, et al. **Arch Invest Med (Mex)** 1981; 12(4):491–7 **(Eng, Spa)**

The extracerebral dopamine antagonist domperidone block the suppressive effect of bromocriptine on prolactin and TSH secretion in man. Švet-Moldavsky I, et al. **Biomedicine** 1981 Oct;35(5):142–4

Differential effects of pharmacological manipulations of central alpha 1- and alpha 2-adrenergic receptors on the secretion of thyrotropin and growth hormone in male rats. Krulich L, et al. **Endocrinology** 1982 Mar;110(3):796–804

Involvement of alpha 1-adrenergic receptors in the inhibitory effect of catecholamines on the thyrotropin-induced release of thyroxine by the mouse thyroid. Muraki T, et al. **Endocrinology** 1982 Jan;110(1):51–4

Influence of endogenous somatostatin on growth hormone and thyrotropin secretion in neonatal rats. Oliver C, et al. **Endocrinology** 1982 Mar; 110(3):1018–22

Possible involvement of nigrostriatal dopamine system in the inhibition of thyrotropin secretion in the rat. Männistö P, et al. **Eur J Pharmacol** 1981 Dec 17;76(4):403–9

Plasma triiodothyronine response to thyrotropin releasing hormone, thyrotropin and propranolol in old age. Szabolcs I, et al. **Exp Gerontol** 1981;16(4):309–16

Thyroid proliferation, body weight, thyrotropin and thyroid hormones in chronic antithyroid (carbimazole) treatment in rats. Redmond O, et al. **J Anat** 1981 Aug;133(Pt 1):37–47

The effect of TRH and its analogues, (Pro-NH-NH2)3TRH and (2-Picolyl)1-TRH on TSH level in rat serum. Ryżewska M, et al. **Mater Med Pol** 1980 Jan–Jun;12(1–2):136–9

[Effects of cyproheptadine on the secretion and pituitary content of thyrotropin in rats] Ulloa ER, et al. **Medicina (B Aires)** 1981; 41(3):333–6 (Eng. Abstr.) **(Spa)**

THYROXINE

Abnormal brown adipose tissue in genetically obese mice (ob/ob): effect of thyroxine. Hogan S, et al. **Am J Physiol** 1981 Dec; 241(6):E436–43

Thyroxine radioimmunoassay for population surveys using dried blood: modifications of a highly sensitive method. Obregón MJ. **Ann Clin Biochem** 1982 Jan;19(Pt 1):29–34

Treatment of intractable rapid-cycling manic-depressive disorder with levothyroxine. Clinical observations. Stancer HC, et al. **Arch Gen Psychiatry** 1982 Mar;39(3):311–2

Effects of thyroxine binding on the stability, conformation, and fluorescence properties of thyroxine-binding globulin. Grimaldi S, et al. **Biochemistry** 1982 Jan 5;21(1):145–51

Influence of growth hormone and thyroxine on thermotropic effects of respiration and 1-anilino-8-naphthalene sulfonate fluorescence and on lipid composition of cardiac membranes. Clejan S, et al. **Biochim Biophys Acta** 1981 Dec 4;678(2):250–6

Thyroxine-induced redistribution of isoenzymes of rabbit ventricular myosin. Martin AF, et al. **Circ Res** 1982 Jan;50(1):117–24

Enzyme immunoassay of thyroxin with a centrifugal analyzer. Izquierdo JM, et al. **Clin Chem** 1982 Jan;28(1):123–5

Covalent linkage of antisera to microparticulate cellulose using 1,1'-carbonyldiimidazole: a rapid, practical method with potential use in solid-phase immunoassay. Chapman RS, et al. **Clin Chim Acta** 1982 Jan 5;118(1):129–34

Insulin binding and response to insulin of adipocytes from thyroxine-treated rats. Heise E, et al. **Endocrinology** 1982 Mar; 110(3):955–60

Involvement of alpha 1-adrenergic receptors in the inhibitory effect of catecholamines on the thyrotropin-induced release of thyroxine by the mouse thyroid. Muraki T, et al. **Endocrinology** 1982 Jan;110(1):51–4

Regulation of mouse submaxillary gland renin by thyroxine. Wilson CM, et al. **Endocrinology** 1982 Mar;110(3):982–9

Lack of effect of cortisone, thyroxine and insulin on the developmental pattern of mouse intestinal glucose-6-phosphatase activity. Ménard D, et al. **Experientia** 1982 Jan 15;38(1):111–2

Seasonal plasma T4 titers in the hibernating lizard Cnemidophorus sexlineatus. Sellers JC, et al. **Gen Comp Endocrinol** 1982 Jan; 46(1):24–8

Direct and correlated responses to selection for plasma thyroxine levels in mice. Tilakaratne N, et al. **Genet Res** 1981 Oct;38(2):157–69

Early changes in brush border disaccharidase kinetics in rat jejunum following subcutaneous administration of tetraiodothyronine: a quantitative histochemical study on villi revealing normal morphology. Gutschmidt S, et al. **Histochemistry** 1981;73(1):151–60

Comparison of eleven commercially available kits for the radioimmunoassay of serum thyroxine. Elvers LH, et al. **J Clin Chem Clin Biochem** 1981 Jul;19(7):453–6

Increased immunological efficiency in young mice by short-term treatment with L-thyroxine. Basso A, et al. **J Endocrinol Invest** 1981 Oct–Dec;4(4):431–8

Inhibition of rat hepatic thyroxine 5'-monodeiodinase by propylthiouracil: relation to site of interaction of thyroxine and glutathione. Yamada T, et al. **J Endocrinol Invest** 1981 Oct–Dec;4(4):379–87

Ontogenesis of monoamine-synthesizing enzyme activities and biopterin levels in rat brain or salivary glands, and the effects of thyroxine administration. Kato T, et al. **J Neurochem** 1982 Apr;38(4):896–901

Neonatal hormone treatment and maturation of the pineal noradrenergic system: hydrocortisone and thyroxine. Yuwiler A, et al. **J Neurochem** 1981 Oct;37(4):985–92

Membrane immunoassay: a spin membrane immunoassay for thyroxine. Tan CT, et al. **Methods Enzymol** 1981;74 Pt C:152–61

Developmental changes in the activities of prolinase and prolidase in rat salivary glands, and the effect of thyroxine administration. Imai K, et al. **Mol Cell Biochem** 1982 Jan 16;42(1):31–6

Thyroxine only on Sundays [letter] Belton CH. **NZ Med J** 1981 Dec 23;94(698):470

Digoxin-like immunoreactivity of certain steroid and other hormones. Schreiber V, et al. **Physiol Bohemoslov** 1981;30(6):569–71

Interaction of thyroxine with lysozyme. Kramer KJ, et al. **Physiol Chem Phys** 1981;13(4):313–7

In vivo thyroxine release in day-old cockerels in response to acute stimulation by mammalian and avian pituitary hormones. MacKenzie DS. **Poult Sci** 1981 Sep;60(9):2136–43

Effect of high ambient temperature (35 degrees), and feed intake on plasma T4 levels in sheep. Valtorta S, et al. **Proc Soc Exp Biol Med** 1982 Feb; 169(2):260–5

An inhibitor of the binding of thyroid hormones to serum proteins is present in extrathyroidal tissues. Chopra IJ, et al. **Science** 1982 Jan 22; 215(4531):407–9

[Plasma T4: adaptation of a commercial radioimmunoassay for use in dogs] Garnier F, et al. **Ann Biol Clin (Paris)** 1981;39(6):369–70 **(Fre)**

[Basic and clinical evaluation of the method of free thyroxine levels in serum with radioimmunoassay (author's transl)] Masuoka T, et al. **Horumon To Rinsho** 1981 Aug;29(8):1025–9 **(Jpn)**

[Measurement of free thyroxine in serum using 'SPAC-T4' RIA kit (author's transl)] Usami H, et al. **Horumon To Rinsho** 1981 Sep; 29(9):1167–72 **(Jpn)**

[Radioimmunoassay of free thyroxine with microencapsulated anti-T4 specific antibody (author's transl)] Kasagi K, et al. **Kaku Igaku** 1981 Aug;18(7):973–83 **(Jpn)**

TRANQUILIZING AGENTS

Anxiety and other neurotic symptoms in patients suffering from dans la conception des états limitrophes et des mécanismes d'action clinique des tranquillisants. Skovronsky O, et al. **Agressologie** 1981 Oct; 22(C):25–6

Adverse reactions to benzodiazepine-tricyclic antidepressant compound. Beresford TP, et al. **J Clin Psychopharmacol** 1981 Nov;1(6):392–4

[New trends in the concept of border states and mechanisms of clinical action of tranquilizers] Alexandrovsky YA. **Agressologie** 1981 Oct; 22(C):19–24 **(Fre)**

[Hemorheological substantiation of transfusion therapy in acute exogenous poisoning] Kostin GM, et al. **Probl Gematol Pereliv Krovi** 1981 Oct; 26(10):37–41 (Eng. Abstr.) **(Rus)**

TRANQUILIZING AGENTS, MAJOR

Fluphenazine and flupenthixol decanoate in psychiatric outpatients practice. Coufal J, et al. **Act Nerv Super (Praha)** 1981;23(4):269–71

Further clinical experience with oxyprothepin–decanoate. Kalvach Z, et al. **Act Nerv Super (Praha)** 1981;23(4):271–2

Effects of lithium and neuroleptics and combinations of the two on renal function and structure in rats. Christensen S, et al. **Acta Pharmacol Toxicol (Copenh)** 1981 Sep;49(3):161–7

Anxiolytic properties of neuroleptic drugs. Balon R, et al. **Agressologie** 1981 Nov;22(D):9–10

Treatment of anxious depression with intravenous infusions of a combination of drugs. Krebs–Roubicek E, et al. **Agressologie** 1981 Nov; 22(D):25–6

Neuroleptics in the treatment of anxiety. Schmidt P. **Agressologie** 1981 Nov;22(D):19–20

Urinary incontinence and neuroleptics [letter] Ambrosini PJ, et al. **Am J Psychiatry** 1982 Apr;139(4):539

Stimulated lymphocytes in schizophrenia. Hirata–Hibi M, et al. **Arch Gen Psychiatry** 1982 Jan;39(1):82–7

Brain histamine H1– and H2–receptors and histamine–sensitive adenylate cyclase: effects of antipsychotics and antidepressants. Coupet J, et al. **Eur J Pharmacol** 1981 Sep 11;74(2–3):149–55

Hypophysectomy does not prevent development of striatal dopamine receptor supersensitivity induced by repeated neuroleptic treatment. Jenner P, et al. **Eur J Pharmacol** 1981 Nov 19;76(1):31–6

Des–tyr–gamma–endorphin (DT gamma E) and pineal levels of melatonin and arginine vasopressin (AVP). King MG, et al. **Eur J Pharmacol** 1981 Dec 3;76(2–3):271–4

Possible use of non–neuroleptic isomers of anti–psychotics in anti–sickling therapy. Ohnishi ST, et al. **Eur J Pharmacol** 1981 Oct 22; 75(2–3):121–5

Comparative effects of short– and long–term treatment with neuroleptics on behavioural activity as well as dopamine turnover in striatum. Rastogi RB, et al. **Gen Pharmacol** 1982;13(1):35–40

The treatment of refractory schizophrenia: pharmacotherapy and clinical implications of blood level measurement of neuroleptics. Pi EH, et al. **Int Pharmacopsychiatry** 1981;16(3):154–61

Antipsychotic drugs and the noninstitutionalized patient: a leap into the future or the past? Fried JM. **J Clin Psychopharmacol** 1981 Sep; 1(5):323–5

How capable of driving are hospitalized psychiatric patients under psycho–active drug therapy? Hobi V, et al. **J Int Med Res** 1981; 9(6):434–47

Effects of neuroleptic drugs on endogenous opioid peptides in the rat. Höllt V. **Mod Probl Pharmacopsychiatry** 1981;17:1–18

Neuroleptic–like and antipsychotic effects of gamma–type endorphins. Van Ree JM, et al. **Mod Probl Pharmacopsychiatry** 1981;17:266–78

Neuroleptic malignant syndrome caused by dopamine depleting drugs [letter] Login IS, et al. **Neurology (NY)** 1982 Feb;32(2):218–9

Site–specific blockade of dopamine receptors by neuroleptic agents in human brain. Borison RL, et al. **Neuropharmacology** 1981 Dec; 20(12B):1321–2

Pharmacokinetic aspects of new antipsychotic drugs. Dahl SG. **Neuropharmacology** 1981 Dec;20(12B):1299–302

Substituted benzamide drugs as selective neuroleptic agents. Jenner P, et al. **Neuropharmacology** 1981 Dec;20(12B):1285–93

Pharmacological properties of new antipsychotic agents: use of animal models. Puech AJ, et al. **Neuropharmacology** 1981 Dec; 20(12B):1279–84

Neuroleptics as antidepressants. Robertson MM, et al. **Neuropharmacology** 1981 Dec;20(12B):1335–6

Initial improvement as predictor of outcome of neuroleptic treatment. Nedopil N, et al. **Pharmacopsychiatria** 1981 Nov;14(6):205–7

Effect of neuroleptics on release on acetylcholine to the lateral cerebral ventricle in the rat. Plech A, et al. **Pol J Pharmacol Pharm** 1981; 33(4):393–400

Enhancement of the avoidance–suppressing effects of neuroleptic agents after repeated administration: changes in the discriminated avoidance response in rats. Kuribara H, et al. **Psychopharmacology (Berlin)** 1981; 75(2):148–51

Effect of single oral doses of various neuroleptic drugs on salivary secretion rate, pH, and buffer capacity in healthy subjects. Molander L, et al. **Psychopharmacology (Berlin)** 1981;75(2):114–8

Assessing pharmacologically induced dopamine receptor sensitivity changes with the Ungerstedt turning model. Siever L, et al. **Psychopharmacology (Berlin)** 1981;75(2):212–3

[Psychopharmacology and Research into Borderline states (author's transl)] Boleloucký Z, et al. **Cesk Psychiatr** 1981 Jun;77(3):148–52 (Eng. Abstr.) **(Cze)**

[Depot Neuroleptic preparations in psychiatric practice (author's transl)] Svestka J, et al. **Cesk Psychiatr** 1981 Jun;77(3):187–97 (Eng. Abstr.) **(Cze)**

[Conditions for prolonged prescription of neuroleptics with reference to several clinical cases] Tholose A. **Ann Med Psychol (Paris)** 1981; 139(8):894–9 **(Fre)**

[Acute renal failure caused by non–traumatic rhabdomyolysis (letter)] Deboscker Y, et al. **Nouv Presse Med** 1982 Jan 16;11(2):131 **(Fre)**

[Biologic therapy of schizophrenia] Lambert PA, et al. **Soins Psychiatr** 1981 Dec;(14):19–22 **(Fre)**

[Comparison between the effectiveness of fluphenazine decanoate and oxyprothepin decanoate in schizophrenia (double–blind crossover study)] Balon R, et al. **Zh Nevropatol Psikhiatr** 1982;82(1):116–8 (Eng. Abstr.) **(Rus)**

[Predicting the effect of psychopharmacotherapy in schizophrenic patients] Dikil NT. **Zh Nevropatol Psikhiatr** 1982;82(1):110–5 (Eng. Abstr.) **(Rus)**

TRANQUILIZING AGENTS, MINOR

Anxiolytics and beta blockers: evaluation of pharmacodynamics by quantitative EEG, psychometric and physiological variables. Saletu B, et al. **Agressologie** 1981 Oct;22(C):5–16

Prescribing of minor tranquillizers for emotional problems in a family practice. Bass MJ, et al. **Can Med Assoc J** 1981 Dec 1; 125(11):1225–6

Adverse effects of antianxiety drugs. Edwards JG. **Drugs** 1981 Dec; 22(6):495–514 (83 ref.)

Use of stimulant/depressant drugs by drug abuse clients in selected metropolitan areas. Brown BS, et al. **Int J Addict** 1981 Dec; 16(8):1473–90

Determination of the anxiolytic agent 8–chloro–6–(2–chlorophenyl)–4H–imidazo–[1,5–alpha] [1,4]–benzodiazepine–3–carboxamide in whole blood, plasma or urine by high–performance liquid chromatography. Puglisi CV, et al. **J Chromatogr** 1981 Nov 13;226(1):135–46

Recent advances in anxiolytic therapy. Rickels K. **J Clin Psychiatry** 1981 Nov;42(11 Pt 2):40–4

Anxiolytic properties of opiates and endogenous opioid peptides and their relationship to the actions of benzodiazepines. Millan MJ, et al. **Mod Probl Pharmacopsychiatry** 1981;17:123–41

Effects of anxiolytic drugs on the catecholamine and DOPAC (3, 4–dihydroxyphenylacetic acid) levels in brain cortical areas and on corticosterone and prolactin secretion in rats subjected to stress. Fekete MI, et al. **Psychoneuroendocrinology** 1981;6(2):113–20

A water lick conflict paradigm using drug experienced rats. Petersen EN, et al. **Psychopharmacology (Berlin)** 1981;75(3):236–9

Minor tranquilizers: prescribing practices of primary physicians. Rittelmeyer LF Jr. **Psychosomatics** 1982 Jan;23(1):23–6

[Psychopharmacology of anxiety. 1] **Agressologie** 1981 Oct;22(C):1–53 **(Fre)**

[Are benzodiazepines anxiolytics or hypnotics?] Porot M, et al. **Ann Med Psychol (Paris)** 1981;139(8):915–9 **(Fre)**

TRANYLCYPROMINE

[Comparison of the effectiveness of tranylcypromine, nortriptyline, thioridazine and amitriptyline in two syndromological types of endogenous depression (author's transl)] Náhunek K, et al. **Cesk Psychiatr** 1981;77(4):245–52 (Eng. Abstr.) **(Cze)**

TRIFLUOPERAZINE

Cyclic nucleotide phosphodiesterase of rat pancreatic islets. Effects of Ca2+, calmodulin and trifluoperazine. Sugden MC, et al. **Biochem J** 1981 Aug 1;197(2):459–64

Effects of trifluoperazine on human neutrophil function. Smith RJ, et al. **Immunology** 1981 Dec;44(4):677–84

Trifluoperazine inhibits phagocytosis in a macrophagelike cultured cell line. Horwitz SB, et al. **J Cell Biol** 1981 Dec;91(3 Pt 1):798–802

GLC analysis of trifluoperazine in human plasma. Javaid JI, et al. **J Pharm Sci** 1982 Jan;71(1):63–6

Drug management in chronic schizophrenia. Tune LE, et al. **Johns Hopkins Med J** 1982 Jan;150(1):45–8

TRYPTAMINES

Comparison of the cardiovascular responses to intracerebroventricular administration of tryptamine, 5-hydroxytryptamine, tryptophan and 5-hydroxytryptophan in rats. Krstić MK, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):385-91

Correlation of inhibitory activity of tryptamine derivatives on serotonin uptake in thrombocyte with van der Waals volume. Gupta SP, et al. **Arzneimittelforsch** 1981;31(12):2053-5

Behavioral effects and physiological disposition of some beta-hydroxylated indoleamines in the rat. Gentile NT, et al. **Biol Psychiatry** 1982 Jan;17(1):109-13

N, N-Diisopropyltryptamine (DIPT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT). Two orally active tryptamine analogs with CNS activity. Shulgin AT, et al. **Commun Psychopharmacol** 1980;4(5):363-9

Biosynthesis of some urinary trace amines in the rat and the human. Boulton AA, et al. **Res Commun Chem Pathol Pharmacol** 1981 Nov;34(2):295-310

TRYPTOPHAN

Effect of leucine on tryptophan metabolism [letter] Narasinga Rao BS, et al. **Am J Clin Nutr** 1982 Jan;35(1):178-80

Effect of tryptophan on transport properties of newborn rabbit jejunum. Cooke HJ, et al. **Am J Physiol** 1982 Apr;242(4):G308-12

Microdetermination of unbound tryptophan in plasma by a combination of ultrafiltration and high-performance liquid chromatography. Hijikata Y, et al. **Anal Biochem** 1981 Nov 15;118(1):10-6

Enrichment and high-performance liquid chromatography analysis of tryptophan metabolites in plasma. Morita I, et al. **Anal Biochem** 1981 Nov 15;118(1):142-6

New approach to tryptophan production by Escherichia coli: genetic manipulation of composite plasmids in vitro. Aiba S, et al. **Appl Environ Microbiol** 1982 Feb;43(2):289-97

The amino acid composition of secreted mouse prolactin, growth hormone, and hamster prolactin: the presence of one tryptophan in mouse prolactin. Colosi P, et al. **Arch Biochem Biophys** 1981 Dec;212(2):759-61

Comparison of the cardiovascular responses to intracerebroventricular administration of tryptamine, 5-hydroxytryptamine, tryptophan and 5-hydroxytryptophan in rats. Krstić MK, et al. **Arch Int Physiol Biochim** 1981 Nov;89(4):385-91

Quantitative autoradiographic study of tryptophane movement in guinea-pig submandibular glands. Matthews RW, et al. **Arch Oral Biol** 1981;26(11):911-4

Tryptophan pyrrolase in haem regulation. The mechanism of the opposite effects of tryptophan on rat liver 5-aminolaevulinate synthase activity and the haem saturation of tryptophan pyrrolase. Badawy AA, et al. **Biochem J** 1981 Aug 15;198(2):309-14

Measurement of urinary tryptophan metabolites by reverse-phase high-pressure liquid chromatography. Tarr JB. **Biochem Med** 1981 Dec;26(3):330-8

Chemical cleavage of tryptophanyl and tyrosyl peptide bonds via oxidative halogenation mediated by o-iodosobenzoic acid. Fontana A, et al. **Biochemistry** 1981 Nov 24;20(24):6997-7004

Quenching of enzyme-generated acetone phosphorescence by indole compounds: stereospecific effects of D- and L-tryptophan. Photochemical-like effects. Rivas-Suárez E, et al. **Biochemistry** 1981 Dec 22;20(26):7329-33

Interaction of tryptophan-modified analogues of cholecystokinin-octapeptide with cholecystokinin receptors on pancreatic acini. Adachi H, et al. **Biochim Biophys Acta** 1981 Dec 18;678(3):358-63

Tryptophan fluorescence of human hemoglobin. II. Effect of inositol hexaphosphate on the T-R transition. Mizukoshi H. et al. **Biochim Biophys Acta** 1982 Jan 18;700(2):143-7

A kinetic analysis of L-tryptophan transport in human red blood cells. Rosenberg R. **Biochim Biophys Acta** 1981 Dec 7;649(2):262-8

Effect of blue light on the urinary excretion of tryptophan metabolites in adult heterozygous and homozygous Gunn rats. Costa C, et al. **Boll Soc Ital Biol Sper** 1981 Oct 15;57(19):1969-75

Enzyme activities of tryptophan metabolism in heterozygous and homozygous Gunn rats before and after blue light exposure. De Antoni A, et al. **Boll Soc Ital Biol Sper** 1981 Oct 15;57(19):1976-80

Naturally occurring prototrophic strains of Salmonella typhi. Virgilio R, et al. **Can J Microbiol** 1981 Dec;27(12):1272-5

Effect of dl-3-pyridylalanine on serotonin concentration and tryptophan-serotonin metabolizing enzymes in rats. Shimeno H, et al. **Chem Pharm Bull (Tokyo)** 1981 Oct;29(10):2940-8

Stress-modulated alteration of brain biogenic amines in the rat: effects of L-tryptophan. Quirce CM, et al. **Commun Psychopharmacol** 1980;4(5):371-7

The mechanism of tryptophan binding to tryptophan synthase from Escherichia coli. Lane AN, et al. **Eur J Biochem** 1981 Nov;120(2):379-87

Effect of Nin-formylation of the tryptophan residue on gastrin (HG-13) binding and on gastric acid secretion. Magous R, et al. **Eur J Pharmacol** 1982 Jan 8;77(1):11-6

Modification of diazepam's antileptazol activity by endogenous tryptophan-like compounds. Vellucci SV, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):255-9

Construction of new vectors for cloning of promoters. Enger-Valk BE, et al. **Gene** 1981 Dec;15(4):297-305

Increased serotonin level via augmented tryptophan diet and its effect on escape learning. Yehuda S, et al. **Int J Neurosci** 1981;15(4):193-6

Regulation of tryptophan genes in Rhizobium leguminosarum. Holmgren E, et al. **J Bacteriol** 1982 Mar;149(3):1135-7

Effects of long-term low dietary tryptophan intake on determinants of 5-hydroxytryptamine metabolism in the brains of young rats. Ashley DV, et al. **J Neurochem** 1981 Dec;37(6):1385-93

Tryptophan overload in the pregnant rat: effect on brain amino acid levels in in vitro protein synthesis. Fando JL, et al. **J Neurochem** 1981 Oct;37(4):824-9

Simultaneous determination of 3,4-dihydroxyphenylalanine, 5-hydroxytryptophan, dopamine, 4-hydroxy-3-methoxyphenylalanine, norepinephrine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, serotonin, and 5-hydroxyindoleacetic acid in rat cerebrospinal fluid and brain by high-performance liquid chromatography with electrochemical detection. Wagner J, et al. **J Neurochem** 1982 May;38(5):1241-54

The complete nucleotide sequence of the tryptophan operon of Escherichia coli. Yanofsky C, et al. **Nucleic Acids Res** 1981 Dec 21;9(24):6647-68 (62 ref.)

Effect of tryptophan administration on spontaneous and P-CPA-induced muricidal aggression in laboratory rats. Valzelli L, et al. **Pharmacol Res Commun** 1981 Oct;13(9):891-7

Relative contributions of tryptophan and tyrosine to the phosphorescence emission of human serum albumin at low temperatures. Waldmeyer J, et al. **Photochem Photobiol** 1982 Mar;35(3):299-304

Learned aversions in rats fed a tryptophan-free diet. Treneer CM, et al. **Physiol Behav** 1981 Nov;27(5):757-60

[Mutagenicity of the reaction products of L-ascorbic acid and L-tryptophan (author's transl)] Kanamori H, et al. **Yakugaku Zasshi** 1981 Jul;101(7):596-604 (Eng. Abstr.) **(Jpn)**

[Role of tryptophan in the enzymatic activity of histidine decarboxylase from Micrococcus sp. n.] Gonchar NA, et al. **Biokhimiia** 1981 Nov;46(11):1970-80 (Eng. Abstr.) **(Rus)**

[Changes in the functional characteristics of the compound eye of the honeybee after mutations interfering with the metabolism of tryptophan] Gribakin FG, et al. **Neirofiziologiia** 1982;14(1):69-75 (Eng. Abstr.) **(Rus)**

[Changes in the properties of the protein and nucleic acid components of an artificial nucleotide as affected by gamma and UV radiation] Kalabukhova TN, et al. **Radiobiologiia** 1981 Nov-Dec;21(6):912-5 (Eng. Abstr.) **(Rus)**

TRYPTOPHAN HYDROXYLASE

Strain differences in kinetic and thermal stability of two mouse brain tryptophan hydroxylase activities. Knapp S, et al. **Brain Res** 1981 Dec 28;230(1-2):317-36

Purification and properties of tryptophan 5-monooxygenase from rat brain-stem. Nakata H, et al. **Eur J Biochem** 1982 Feb;122(1):41-7

Methamphetamine-induced depression of tryptophan hydroxylase: recovery following acute treatment. Bakhit C, et al. **Eur J Pharmacol** 1981 Dec 3;76(2-3):229-33

Cloning characterization of iaaM, a virulence determinant of Pseudomonas savastanoi. Comai L, et al. **J Bacteriol** 1982 Jan;149(1):40-6

Ontogenesis of monoamine-synthesizing enzyme activities and biopterin levels in rat brain or salivary glands, and the effects of thyroxine administration. Kato T, et al. **J Neurochem** 1982 Apr;38(4):896-901

[Express nonisotope method of determination of tryptophan hydroxylase activity in the brain] Kulikov AV. **Vopr Med Khim** 1982 Jan-Feb;28(1):135-9 **(Rus)**

TYROSINE

Formation of 3H-dopamine and 3H-noradrenaline from 3H-tyrosine in the canine saphenous vein. Boels PJ, et al. **Arch Int Pharmacodyn Ther** 1981 Oct;253(2):315-16

Chemical cleavage of tryptophanyl and tyrosyl peptide bonds via oxidative halogenation mediated by o-iodosobenzoic acid. Fontana A, et al. **Biochemistry** 1981 Nov 24;20(24):6997-7004

Study on the role of tyrosine side-chains at the active centre of emulsin beta-D-glucosidase. Kiss L, et al. **Biochim Biophys Acta** 1981 Dec 15;662(2):308-11

Modification of tyrosine residues in dihydrofolate reductase from Lactobacillus casei. Rosson D, et al. **Biochim Biophys Acta** 1982 Feb 4;701(1):49-56

Assay for plasma free phenylalanine and tyrosine by high-pressure liquid chromatography and field desorption mass spectrometry and its application to an in vivo study of the phenylalanine hydroxylating system in man. Lehmann WD, et al. **Biomed Mass Spectrom** 1981 Dec;8(12):598–605

An ultrastructural and cytochemical analysis of the cellular basis for tyrosine–derived collagen crosslinks in Leptogorgia virgulata (Cnidaria: Gorgonacea). Tidball JG. **Cell Tissue Res** 1982;222(3):635–45

Autoregulation of the tyrR gene. Camakaris H, et al. **J Bacteriol** 1982 Apr;150(1):70–5

Reactions of purified hog thyroid peroxidase with H2O2, tyrosine, and methylmercaptoimidazole (goitrogen) in comparison with bovine lactoperoxidase. Ohtaki S, et al. **J Biol Chem** 1982 Jan 25;257(2):761–6

Chemical modification of D–amino acid oxidase. Amino acid sequence of the tryptic peptides containing tyrosine and lysine residues modified by fluorodinitrobenzene. Swenson RP, et al. **J Biol Chem** 1982 Feb 25;257(4):1937–44

Stimulation of tyrosine–specific phosphorylation by platelet–derived growth factor. Ek B, et al. **Nature** 1982 Feb 4;295(5848):419–20

Relative contributions of tryptophan and tyrosine to the phosphorescence emission of human serum albumin at low temperatures. Waldmeyer J, et al. **Photochem Photobiol** 1982 Mar;35(3):299–304

Reaction of nitrite with tyrosine residues in digestive enzymes. Cheng CC, et al. **Taiwan I Hsueh Hui Tsa Chih** 1981 Nov;80(11):1186–92

[In vitro study of L–tyrosine as a possible substrate for energy metabolism of tissue sections (brain, liver) and its effect on isolated mitochondria of the rat brain] Bonifacj JF, et al. **Agressologie** 1981;22(6):241–4 (Eng. Abstr.) **(Fre)**

TYROSINE AMINOTRANSFERASE

Ontogeny of the glucocorticoid receptor and its relationship to tyrosine aminotransferase induction in cultured foetal hepatocytes. Cake MH, et al. **Biochem J** 1981 Aug 15;198(2):301–7

Enhancement of rat brain tyrosine aminotransferase activity by cortisol. Snape BM, et al. **Biochem J** 1981 Aug 15;198(2):417–20

Growth hormone inhibition of tyrosine aminotransferase in primary cultures of rat liver cells. Shires TK, et al. **Biochim Biophys Acta** 1982 Jan 12;714(1):170–2

Evidence for a dual effect of dibutyryl cyclic AMP on the synthesis of tyrosine aminotransferase in rat liver. Noguchi T, et al. **J Biol Chem** 1982 Mar 10;257(5):2386–90

[Characterization of tyrosine aminotransferase by an immunoadsorption technic. Application to the measurement of the specific messenger RNA] Santana MA, et al. **C R Soc Biol (Paris)** 1981;175(6):859–65 (Eng. Abstr.) **(Fre)**

TYROSINE HYDROXYLASE

Effect of chronic propranolol treatment and withdrawal on norepinephrine and tyrosine hydroxylase in sympathetic tissues. Atkins F, et al. **Arch Int Pharmacodyn Ther** 1981 Dec;254(2):271–81

Retinal amacrine cell system tyrosine hydroxylase: the development of responsiveness to light and neuroleptic drugs. Cohen J, et al. **Brain Res** 1982 Jan;255(1):160–3

The inheritance and genetic correlation of tyrosine hydroxylase activities in the substantia nigra and corpus striatum in the C x B recombinant inbred mouse strains. Vadasz C, et al. **Brain Res** 1982 Feb 18;234(1):1–9

Effect of des–Tyr1–gamma–endorphin and des–Tyr1–alpha–endorphin on alpha–MPT–induced catecholamine disappearance in rat brain nuclei: a dose––response study. Versteeg DH, et al. **Brain Res** 1982 Jan 14;231(2):343–51

Purification and some properties of tyrosine 3–monooxygenase from rat adrenal. Okuno S, et al. **Eur J Biochem** 1982 Feb;122(1):49–55

Ontogenesis of monoamine–synthesizing enzyme activities and biopterin levels in rat brain or salivary glands, and the effects of thyroxine administration. Kato T, et al. **J Neurochem** 1982 Apr;38(4):896–901

Short–term regulation of hydroxylase cofactor activity in rat brain. Mandell AJ, et al. **J Neurochem** 1981 Dec;37(6):1573–8

Tyrosine hydroxylase activity in rat brain synaptosomes: direct measurement using high performance liquid chromatography. Messripour M, et al. **J Neurochem** 1982 Apr;38(4):1139–43

Effect of cyclic AMP–dependent protein phosphorylating conditions on the pH–dependent activity of tyrosine hydroxylase from beef and rat striata. Pollock RJ, et al. **J Neurochem** 1981 Oct;37(4):855–60

Development and aging of noradrenergic cell bodies and axon terminals in the chicken. Yurkewicz L, et al. **J Neurosci Res** 1981;6(5):621–41

Regulation of tyrosine hydroxylase activity in retinal cell suspensions: effects of potassium and 8–bromo cyclic AMP. Iuvone PM, et al. **Life Sci** 1982 Jan 4;30(1):85–91

Tyrosine hydroxylase–like immunoreactive interplexiform cells in the rat retina. Nguyen–Legros J, et al. **Neurosci Lett** 1981 Dec 23;27(3):255–9

Dopaminergic dendrites in the pars reticulata of the rat substantia nigra and their striatal input. Combined immunocytochemical localization of tyrosine hydroxylase and anterograde degeneration. Wassef M, et al. **Neuroscience** 1981;6(11):2125–39

VASOPRESSINS

Vasopressins and other neuropeptides as CNS mental modulators. A review. Edelstein EL. **Isr J Psychiatr Relat Sci** 1981;18(3):229–36

Age–related failure of volume–pressure–mediated vasopressin release. Rowe JW, et al. **J Clin Endocrinol Metab** 1982 Mar;54(3):661–4

Central effects of dopamine and bromocriptine on vasopressin release and blood pressure. Kimura T, et al. **Neuroendocrinology** 1981 Dec;33(6):347–51

VASOTOCIN

Arginine vasotocin: effects on open field behavior, whole brain monoamines and plasma corticosterone. Golus P, et al. **Peptides (Fayetteville)** 1981 Winter;2(4):437–40

[Effect of arginine vasotocin, oxytocin and their fragments on the corticosterone content in the blood plasma of chickens of different ages] Sirotkin AV, et al. **Fiziol Zh SSSR** 1982 Jan;68(1):112–5 (Eng. Abstr.) **(Rus)**

VIOLENCE

The violent girl. Burquest B. **Adolescence** 1981 Winter;16(64):749–64

VISUAL PERCEPTION

Retinal amacrine cell system tyrosine hydroxylase: the development of responsiveness to light and neuroleptic drugs. Cohen J, et al. **Brain Res** 1982 Jan;255(1):160–3

Chlorpromazine reduces the perceptual ambiguity of a reversible visual figure. Harris JP, et al. **Neuropharmacology** 1981 Dec;20(12B):1337–8

Don Juan and the vision of Vision. Smith CU. **Perception** 1981;10(4):435–53

WAKEFULNESS

Effects of oxolinic acid on the sleep–wakefulness cycle of the rat. D'Angelo L, et al. **Br J Pharmacol** 1981 Oct;74(2):399–404

AUTHOR SECTION

A

Aaltonen L, Kanto J, Iisalo E, et al: The passage of flunitrazepam into cerebrospinal fluid in man. Acta Pharmacol Toxicol (Copenh) 1981 Apr; 48(4):364–8

Abdel Malak G, Thibier M: Plasma LH and testosterone responses to synthetic gonadotrophin-releasing hormone (GnRH) or dexamethasone-GnRH combined treatment and their relationship to semen output in bulls. J Reprod Fertil 1982 Jan;64(1):107–13

Abe K, Yokota Y, Dawes C: Effects of parasympathomimetic and sympathomimetic drugs on the secretion and composition of rat sublingual saliva. J Dent Res 1982 Jan;61(1):52–6

Abensour P, Jouvent R, Lecrubier Y: Noradrenergic drugs and affective disorders [letter] Am J Psychiatry 1982 Jan;139(1):142–3

Abernethy DR, Greenblatt DJ, Divoll M, et al: Impairment of diazepam metabolism by low-dose estrogen-containing oral-contraceptive steroids. N Engl J Med 1982 Apr 1;306(13):791–2

Abramowitz J, Iyengar R, Birnbaumer L: Guanine nucleotide and magnesium ion regulation of the interaction of gonadotropic and beta-adrenergic receptors with their hormones: a comparative study using a single membrane system. Endocrinology 1982 Feb;110(2):336–46

Abrams PH, Shah PJ, Stone R, et al: Bladder outflow obstruction treated with phenoxybenzamine. Prog Clin Biol Res 1981;78:269–75

Abroms GM: The diagnosis and treatment of hidden depression. Psychiatr Q 1981 Winter;53(4):235–41

Adachi H, Rajh HM, Tesser GI, et al: Interaction of tryptophan-modified analogues of cholecystokinin-octapeptide with cholecystokinin receptors on pancreatic acini. Biochim Biophys Acta 1981 Dec 18; 678(3):358–63

Adams ME, O'Shea M: Vacuolation of an identified peptidergic (proctolin-containing) neuron. Brain Res 1981 Dec 28;230(1–2):439–44

Advis JP, Krause JE, McKelvy JF: Luteinizing hormone-releasing hormone peptidase activities in discrete hypothalamic regions and anterior pituitary of the rat: apparent regulation during the prepubertal period and first estrous cycle at puberty. Endocrinology 1982 Apr; 110(4):1238–45

Agarwal R, Misra S, Satsangi RK, et al: Synthesis and CNS activity of N,N-disubstituted 1-(aminomethyl)-5-alkyl-3-(aryloxyacetylhydrazono)indolin-2-ones. Arch Pharm (Weinheim) 1982 Feb;315(2):142–6

Agrawal AK, Bondy SC: Characterization of catecholamine binding sites in the rat brain. Neurotoxicology (Park Forest Il) 1981 Oct;2(2):365–71

Aguilera G, Parker DS: Pituitary somatostatin receptors. Characterization by binding with a nondegradable peptide analogue. J Biol Chem 1982 Feb 10;257(3):1134–7

Ahlfors UG, Baastrup PC, Dencker SJ, et al: Flupenthixol decanoate in recurrent manic-depressive illness. A comparison with lithium. Acta Psychiatr Scand 1981 Sep;64(3):226–37

Aiba S, Tsunekawa H, Imanaka T: New approach to tryptophan production by Escherichia coli: genetic manipulation of composite plasmids in vitro. Appl Environ Microbiol 1982 Feb;43(2):289–97

Aimoto T, Kaida M, Numazaki K, et al: Development of tolerance to the stimulatory effect of neuroleptic butyrophenones on pituitary-adrenal activity in rats. J Pharmacobiodyn 1981 Nov; 4(11):827–32

Airapetiants MG, Mekhedova AIa: Effekty piratsetama v norme i pri éksperimental'nykh nevrozakh u sobak. Zh Vyssh Nerv Deiat 1981 Nov–Dec;31(6):1164–70 (Eng. Abstr.) **(Rus)**

Akasu T, Hirai K, Koketsu K: Increase of acetylcholine-receptor sensitivity by adenosine triphosphate: a novel action of ATP on ACh-sensitivity. Br J Pharmacol 1981 Oct;74(2):505–7

Akatsu E: The half-life of 87Rb. Radioisotopes 1981 Dec;30(12):647–8

Akopyan TN, Berger H, Mehlis B, et al: In vitro degradation of substance P: new rapid assay and distribution in rat brain. Acta Biol Med Ger 1981;40(6):779–84

Alam MR: Enhancement of motor-accelerating effect induced by repeated administration of methamphetamine in mice: involvement of environmental factors. Jpn J Pharmacol 1981 Dec;31(6):897–904

Albuquerque EX, Aguayo LG, Warnick JE, et al: The behavioral effects of phencyclidines may be due to their blockade of potassium channels. Proc Natl Acad Sci USA 1981 Dec;78(12):7792–6

Aldinio C, Balzano M, Savoini G, et al: Ontogeny of 3H-diazepam binding sites in different rat brain area. Effect of GABA. Dev Neurosci 1981; 4(6):461–6

Aleixandre A, Garcia de Jalón P, Martin I: Effect of enkephalins in the presence of the antibiotic bacitracin in the longitudinal muscle strip preparation from guinea-pig ileum. Experientia 1981 Dec 15; 37(12):1318–20

Alexandrovsky YA: Nouvelles tendances dans la conception des états limitrophes et des mécanismes d'action clinique des tranquillisants. Agressologie 1981 Oct;22(C):19–24 **(Fre)**

Algeri S, Altstein M, de Simone GM, et al: In vivo potentiation of [D-Ala2]Met-enkephalin amide central effects after administration of an enkephalinase inhibitor. Eur J Pharmacol 1981 Sep 11;74(2–3):261–2

Allen C, Sievers J, Berry M, et al: Experimental studies on cerebellar foliation. II. A morphometric analysis of cerebellar fissuration defects and growth retardation after neonatal treatment with 6-OHDA in the rat. J Comp Neurol 1981 Dec 20;203(4):771–83

Allikmets LKh, Nurk AM: Vliianie khronicheskogo vvedeniia khlorida litiia na razvitie giperchuvstvitel'nosti dofaminovykh retseptorov pri otmene morfina u krys. Biull Eksp Biol Med 1981 Nov;92(11):571–2 (Eng. Abstr.) **(Rus)**

Allikmets LKh, Vasar EE: Sensibilizatsiia apomorfinom krys-samtsov k aggressivnomu povedeniiu. Zh Vyssh Nerv Deiat 1982 Jan–Feb; 32(1):130–5 (Eng. Abstr.) **(Rus)**

Allman FD, Rogers EL, Caniano DA, et al: Selective chemical hepatic sympathectomy in the dog. Crit Care Med 1982 Feb;10(2):100–3

Almazan G, Sourkes TL: Effect of haloperidol on adrenal ornithine decarboxylase activity of the rat. Eur J Pharmacol 1981 Oct 22; 75(2–3):131–6

Almeida OF: Hypothalamic secretion of thyrotrophin releasing hormone is decreased in male Japanese quail exposed to long daily photoperiods. J Endocrinol 1982 Feb;92(2):261–5

Altstein M, Blumberg S, Vogel Z: Phosphoryl-Leu-Phe: a potent inhibitor of the degradation of enkephalin by enkephalinase. Eur J Pharmacol 1981 Dec 3;76(2–3):299–300

Ambrosini PJ, Nurnberg HG: Urinary incontinence and neuroleptics [letter] Am J Psychiatry 1982 Apr;139(4):539

Ames MM, Frank SK: Stereochemical aspects of para-chloroamphetamine metabolism. Rabbit liver microsomal metabolism of RS-, R(-)-. and S(para-chloroamphetamine. Biochem Pharmacol 1982 Jan 1;31(1):5–9

Amir S, Amit Z, Brown ZW: Stress, endorphins and psychosis. A hypothesis. Mod Probl Pharmacopsychiatry 1981;17:192–201

Amrein R, Cano JP, Eckert M, et al: Pharmakokinetik von Midazolam nach intravenöser Verabreichung. Arzneimittelforsch 1981; 31(12a):2202–5 (Eng. Abstr.) **(Ger)**

Amsterdam JD, Winokur A, Caroff S, et al: The effects of desmethylimipramine and lithium on human sperm function. Psychoneuroendocrinology 1981 Dec;6(4):359–63

Anderson DC, King SC, Parsons SM: Uncoupling of acetylcholine uptake from the Torpedo cholinergic synaptic vesicle ATPase. Biochem Biophys Res Commun 1981 Nov 30;103(2):422–6

Anderson EE, Clement PW, Oettinger L Jr: Methylphenidate compared with behavioral self-control in attention deficit disorder: preliminary report. JDBP 1981 Dec;2(4):137–41

Andersson K, Fuxe K, Eneroth P, et al: Rat prolactin and hypothalamic catecholamine nerve terminal systems. Evidence for rapid and discrete increases in dopamine and noradrenaline turnover in the hypophysectomized male rat. Eur J Pharmacol 1981 Dec 3; 76(2–3):261–5

André M, Grizard G, Boucher D: Etude de la validité du dosage radioimmunologique de la prolactine sérique et hypophysaire chez le rat mâle. Action de la bromocriptine et de la thyréolibérine (TRH). C R Soc Biol (Paris) 1981;175(6):792–800 (Eng. Abstr.) **(Fre)**

Andrén L, Lindstedt G, Björkman M, et al: Effect of noise on blood pressure and 'stress' hormones. Clin Sci 1982 Feb;62(2):137–41

Andrews CD, Hutson PH: A reliable multichannel commutator for making electrical contact with conscious, freely moving rats. J Neurosci Methods 1982 Jan;5(1–2):73–6

Andrews CD, Fernando JC, Curzon G: Differential involvement of dopamine-containing tracts in 5-hydroxytryptamine-dependent behaviours caused by amphetamine in large doses. Neuropharmacology 1982 Jan;21(1):63–8

Angeli S, Fougère P: A propos d'une observation de troubles ménopausiques rebelles traités par le véralipride. Sem Hop Paris 1982 Jan 14;58(2):111–2 (Eng. Abstr.) **(Fre)**

Anokhina IP, Kogan BM: Nekotorye osobennosti obmena dofamina pri shizofrenii. Zh Nevropatol Psikhiatr 1981;81(9):1343–7 (Eng. Abstr.) **(Rus)**

Antonelli de Gómez de Lima M, Rodríquez de Lores Arnaiz G: Tissue specificity of dopamine effects on brain ATPases. Neurochem Res 1981 Sep;6(9):969–77

Antoni FA, Makara GB, Rappay G: Growth hormone releasing activity persists in the deafferented medial-basal hypothalamus of the rat. J Endocrinol 1981 Dec;91(3):415–25

Aoki T, Narita T: Morphological evidence for the innervation of apocrine sweat glands in the general hairy skin of the goat. Cell Tissue Res 1981; 221(1):221–6

Apfelbaum ME: Basal and GnRH-induced release and synthesis of LH and FSH from incubated pituitary glands throughout the 4-day estrous cycle of the rat. Horm Res 1981;15(2):109–21

Appelbaum PS, Gutheil TG: The right to refuse treatment: the real issue is quality of care. Bull Am Acad Psychiatry Law 1981;9(3):199–202

Appleton WS: Fourth psychoactive drug usage guide. J Clin Psychiatry 1982 Jan;43(1):12–27

Araki K, Wakabayashi M, Sakimura K, et al: Decreased uptake of GABA by dorsal ganglia in methylmercury-treated rats. Neurotoxicology (Park Forest Il) 1981 Nov;2(3):557–66

Arap-Mengech HN: Practical therapeutics management of anxiety. East Afr Med J 1981 Sep;58(9):631–5

Aravich PF, Sclafani A, Leibowitz SF: Effects of hypothalamic knife cuts on feeding induced by paraventricular norepinephrine injections.

Pharmacol Biochem Behav 1982 Jan;16(1):101-11

Arbilla S, Kamal LA, Langer SZ: Inhibition by apomorphine of the potassium-evoked release of [3H]-gamma-aminobutyric acid from the rat substantia nigra in vitro. Br J Pharmacol 1981 Oct;74(2):389-97

Arbilla S, Langer SZ: Stereoselectivity of presynaptic autoreceptors modulating dopamine release. Eur J Pharmacol 1981 Dec 17; 76(4):345-51

Archer T, Ogren SO, Fuxe K, et al: On the interactive role of central noradrenaline neurons and corticosterone in two-way active avoidance acquisition in the rat. Neurosci Lett 1981 Dec 23;27(3):341-6

Areekul S, Srichairat S: Serum and red cell cholinesterase activities in pregnancy. J Med Assoc Thai 1981 Nov;64(11):584-8

Argiolas A, Mereu G, Serra G, et al: N-n-propyl-norapomorphine: an extremely potent stimulant of dopamine autoreceptors. Brain Res 1982 Jan 7;231(1):109-16

Argiolas A, Melis MR, Fadda F, et al: Evidence for dopamine autoreceptors controlling dopamine synthesis in the substantia nigra. Brain Res 1982 Feb 18;234(1):177-81

Arkhipov VI, Azarashvili AA: Role of cholinergic and monoaminergic brain systems in dissociated learning. Neurosci Behav Physiol 1981 May-Jun;11(3):226-9

Armstrong-James M, Fox K, Kruk ZL, et al: Quantitative ionophoresis of catecholamines using multibarrel carbon fibre microelectrodes. J Neurosci Methods 1981 Dec;4(4):385-406

Aronstam RS, Narayanan L: 3-Chlorodibenzazepine binding to cholinergic receptors and ion channels. Res Commun Chem Pathol Pharmacol 1981 Dec;34(3):551-4

Aronstam RS, Buccafusco JJ: Cholinergic actions of false neurotransmitters: acetyldiethylcholine. Neurosci Lett 1982 Jan 22; 28(1):51-6

Arushanian EB, Tolpyshev BA: Vliianie fenamina i galoperidola na stereotipnoe povedenie, voznikaiushchee u koshek pri élektricheskom razdrazhenii chernoĭ substantsii. Biull Eksp Biol Med 1981 Oct; 91(10):444-7 (Eng. Abstr.) **(Rus)**

Arutunian RA: Vliianie vnutrigipotalamicheskogo gamma-aminomaslianoĭ kisloty na temperaturu gipotalamusa i obshchuiu teploproduktsiiu organizma. Fiziol Zh SSSR 1981 Oct;67(10):1480-6 (Eng. Abstr.) **(Rus)**

Asarch KB, Shih JC, Kulscàr A: Decreased 3H-imipramine binding in depressed males and females. Commun Psychopharmacol 1980; 4(5):425-32

Asch RH, Eddy CA, Schally AV: Lack of luteolytic effect of D-Trp-6-LH-RH in hypophysectomized rhesus monkeys (Macaca mulatta). Biol Reprod 1981 Dec;25(5):963-8

Ashley DV, Curzon G: Effects of long-term low dietary tryptophan intake on determinants of 5-hydroxytryptamine metabolism in the brains of young rats. J Neurochem 1981 Dec;37(6):1385-93

Ashton D, Geerts R, Waterkeyn C, et al: Etomidate stereospecifically stimulates forebrain, but not cerebellar, 3H-diazepam binding. Life Sci 1981 Dec 21;29(25):2631-6

Asscher Y, Avnir D, Rotman A, et al: Active conformation of polycyclic antidepressants. J Pharm Sci 1982 Jan;71(1):122-4

Assimacopoulos-Jeannet FD, Blackmore PF, Exton JH: Studies of the interaction between glucagon and alpha-adrenergic agonists in the control of hepatic glucose output. J Biol Chem 1982 Apr 10; 257(7):3759-65

Atkins F, Nicolosi GL, Beck L: Effect of chronic propranolol treatment and withdrawal on norepinephrine and tyrosine hydroxylase in sympathetic tissues. Arch Int Pharmacodyn Ther 1981 Dec; 254(2):271-81

Augustine GJ, Fetterer R, Watson WH 3d: Amine modulation of the neurogenic Limulus heart. J Neurobiol 1982 Jan;13(1):61-74

Avdulov NA, Maisov NI: Atipichnye antidepressanty: vliianie na sinaptosomal'nyĭ zakhvat serotonina i GAMK. Biull Eksp Biol Med 1981 Nov;92(11):564-6 (Eng. Abstr.) **(Rus)**

Ayd FJ Jr: Diazepam dependency and withdrawal. Curr Psychiatr Ther 1981;20:263-73

Ayme J: Thérapetes et choix thérapeutiques. Encephale 1981;7(4 Suppl):507-11 (Eng. Abstr.) **(Fre)**

Azmitia EC, Perlow MJ, Brennan MJ, et al: Fetal raphe and hippocampal transplants into adult and aged C57BL/6N mice: a preliminary immunocytochemical study. Brain Res Bull 1981 Dec;7(6):703-10

Azmitia EC: Bilateral serotonergic projections to the dorsal hippocampus of the rat: simultaneous localization of 3H-5HT and HRP after retrograde transport. J Comp Neurol 1981 Dec 20;203(4):737-43

B

Baba S, Miyachi Y: [Neuropeptides in the rabbit eye. I. RIA for beta-endorphin, substance P and neurotensin in the aqueous humor, iris-ciliary body and retina (author's transl)] Nippon Ganka Gakkai Zasshi 1981 Sep 10;85(9):1267-72 (Eng. Abstr.) **(Jpn)**

Babeniuk IuD, Blium IaB, Tsudzevich BA, et al: Sravnenia atsetilirovaniia iadernykh belkov v pecheni i timuse krys pri luchevom porazhenii v usloviiakh zashchity serotoninom. Radiobiologiia 1982 Jan-Feb; 22(1):13-8 (Eng. Abstr.) **(Rus)**

Bach B, Hansen JM, Kampmann JP, et al: Disposition of antipyrine and phenytoin correlated with age and liver volume in man. Clin Pharmacokinet 1981 Sep-Oct;6(5):389-96

Bacopoulos NG: Acute changes in the state of dopamine receptors; in vitro monitoring with 3H-dopamine. Life Sci 1981 Dec 7;29(23):2407-14

Bacopoulos NG, Bustos G, Redmond DE Jr, et al: Chronic treatment with haloperidol or fluphenazine decanoate: regional effects on dopamine and serotonin metabolism in primate brain. J Pharmacol Exp Ther 1982 Apr;221(1):22-8

Badawy AA, Welch AN, Morgan CJ: Tryptophan pyrrolase in haem regulation. The mechanism of the opposite effects of tryptophan on rat liver 5-aminolaevulinate synthase activity and the haem saturation of tryptophan pyrrolase. Biochem J 1981 Aug 15;198(2):309-14

Badder EM, Seaton J, Harrison TS: Cardiac output, vascular resistance and catecholamine release in hemorrhaged anephric dogs. Trans Am Soc Artif Intern Organs 1981;27:330-5

Badr G, Matousek M: Intérêt de l'electroencéphalogramme quantitatif dans la dépression. Encephale 1981;7(4 Suppl):421-7 (Eng. Abstr.) **(Fre)**

Badzhinian SA, Gabrielian ES: Vliianie serotonina i prostaglandinov na pronitsaemost' model'nykh lipidnykh membran. Biull Eksp Biol Med 1981 Nov;92(11):557-9 (Eng. Abstr.) **(Rus)**

Bakalkin GIa, Taborko MM: Neĭropeptidy: istoriia izucheniia i perspektivy primeneniia v meditsine. Bol Serv Odontol Saint (Porto Alegre) 1981; 4(2):100-5 (Eng. Abstr.) **(Rus)**

Baker PC, Goodrich CA: The effects of the specific uptake inhibitor Lu 10-171 (citalopram) upon brain indoleamine stores in the maturing mouse. Gen Pharmacol 1982;13(1):59-61

Baker PF, Knight DE: Calcium control of exocytosis and endocytosis in bovine adrenal medullary cells. Philos Trans R Soc Lond [Biol] 1981 Dec 18;296(1080):83-103 (46 ref.)

Bakhit C, Morgan ME, Peat MA, et al: Long-term effects of methamphetamine on the synthesis and metabolism of 5-hydroxytryptamine in various regions of the rat brain. Neuropharmacology 1981 Dec;20(12A):1135-40

Bakhit C, Gibb JW: Methamphetamine-induced depression of tryptophan hydroxylase: recovery following acute treatment. Eur J Pharmacol 1981 Dec 3;76(2-3):229-33

Bakai SN, Redington TE, Hughes MJ: Antiestrogen-induced alterations of hypothalamic dopamine and norepinephrine levels in the female rat. Neuropharmacology 1981 Dec;20(12A):1163-7

Baldessarini RJ, Neumeyer JL, Campbell A, et al: An orally effective, long-acting dopaminergic prodrug: (-)-10,11-methylenedioxy-N-propylnoraporphine. Eur J Pharmacol 1982 Jan 8;77(1):87-8

Ball SG, Gunn IG, Douglas IH: Renal handling of dopa, dopamine, norepinephrine, and epinephrine in the dog. Am J Physiol 1982 Jan; 242(1):F56-62

Ballabio M, Caccia S, Garattini S, et al: Antileptazol activity and kinetics of clobazam and N-desmethyl-clobazam in the guinea-pig. Arch Int Pharmacodyn Ther 1981 Oct;253(2):192-9

Ballus C: Interactions entre dépression et angoisse. Encephale 1981;7(4 Suppl):335-7 (Eng. Abstr.) **(Fre)**

Balogh A, Fünfstück R, Demme U, et al: Dialysability of benzodiazepines by haemodialysis and controlled sequential ultrafiltration (CSU) in vitro. Acta Pharmacol Toxicol (Copenh) 1981 Sep;49(3):174-80

Balon R, Kabes J: Comparison of the dosage schedules during the administration of retarded lithium carbonate. Act Nerv Super (Praha) 1981;23(4):278-80

Balon R, Kabès J: Anxiolytic properties of neuroleptic drugs. Agressologie 1981 Nov;22(D):9-10

Balon R, Kabesh Ia, Papezhova G: Sravnenie éffektivnosti flufenazin-dekanoata i oksiprotepin-dekanoata pri shizofrenii (dvoĭnoe slepoe perekrestnoe issledovanie). Zh Nevropatol Psikhiatr 1982; 82(1):116-8 (Eng. Abstr.) **(Rus)**

Balster RL, Woolverton WL: Unlimited access intravenous drug self-administration in rhesus monkeys. Fed Proc 1982 Feb;41(2):211-5

Balster RL, Harris LS: Drugs as reinforcers in animals and humans: introduction. Fed Proc 1982 Feb;41(2):209-10

Ban TA, Wilson WH: Multicenter clinical trials: methodological aspects. Mod Probl Pharmacopsychiatry 1981;16:9-20

Bandman AL, Andriianov AI: Vliianie amizila i galantamina na povedencheskie éffekty apomorfina u krys. Biull Eksp Biol Med 1981 Nov;92(11):566-9 (Eng. Abstr.) **(Rus)**

Banerji A, Prasad C: The postnatal development of the pituitary thyrotropin-releasing hormone receptor in male and female rats. Endocrinology 1982 Feb;110(2):663-4

Banerji TK, Parkening TA, Collins TJ: Effects of aging on the activity of hypothalamic dopamine-beta-hydroxylase during various stages of the estrous cycle in C57BL/6 mice. Neuroendocrinology 1982 Jan; 34(1):14-9

Bank N, Lief PD, Aynedjian HS, et al: Studies of the urinary acidification defect induced by lithium. Am J Physiol 1982 Jan;242(1):F23-9

Bank RL, Bissell WG: Overdose of benzodiazepines [letter] JAMA 1982

AUTHOR SECTION

Jan 15;247(3):304

Bánki C: A depresszió biokémiájáról. Kiegészítés é korrekció. Orv Hetil 1982 Jan 17;123(3):187 (Hun)

Bannon MJ, Reinhard JF Jr, Bunney EB, et al: Unique response to antipsychotic drugs is due to absence of terminal autoreceptors in mesocortical dopamine neurones. Nature 1982 Apr 1;296(5856):444–6

Barber M, Bordoli RS, Garner GV, et al: Fast-atom-bombardment mass spectra of enkephalins. Biochem J 1981 Aug 1;197(2):401–4

Barbosa MC, Migliorini RH: Free fatty acid mobilization in rats following intracerebroventricular norepinephrine. Am J Physiol 1982 Apr; 242(4):E248–52

Bardhan KD: Sedation for upper gastrointestinal endoscopy [letter] Br J Anaesth 1981 Dec;53(12):1368

Barinov EF: Vliianie elektrostimuliatsii avezdchatogo gangliia i podkliucheniia nadpochechnikov na soderzhanie katekholaminov v izolirovannom serdtse. Fiziol Zh SSSR 1981 Oct;67(10):1501–5 (Eng. Abstr.) (Rus)

Barker LA, Glick SD, Green JP, et al: Acetylcholine metabolism in the rat hippocampus and striatum following one-trial passive training. Neuropharmacology 1982 Feb;21(2):183–5

Barkley RA: The use of psychopharmacology to study reciprocal influences in parent-child interaction. J Abnorm Child Psychol 1981 Sep;9(3):303–10

Barner HB, Jellinek M, Standeven JW, et al: Cold blood-diltiazem cardioplegia. Ann Thorac Surg 1982 Jan;33(1):55–63

Barnes MA, Boockfor FR, Bierley ST, et al: Effect of unilateral castration and unilateral cryptorchidism on gonadotropin and testosterone response to gonadotropin releasing hormone in the bull. J Anim Sci 1981 Nov;53(5):1341–50

Barnes RF, Raskind M, Gumbrecht G, et al: The effects of age on the plasma catecholamine response to mental stress in man. J Clin Endocrinol Metab 1982 Jan;54(1):64–9

Baron J, Redick JA, Guengerich FP: Effects of 3-methylcholanthrene, beta-naphthoflavone, and phenobarbital on the 3-methylcholanthrene-inducible isozyme of cytochrome P-450 within centrilobular, midzonal, and periportal hepatocytes. J Biol Chem 1982 Jan 25;257(2):953–7

Baron M, Perlman R, Levitt M, et al: Plasma copper and dopamine-beta-hydroxylase in schizophrenia. Biol Psychiatry 1982 Jan; 17(1):115–20

Barraclough CA, Wise PM: The role of catecholamines in the regulation of pituitary luteinizing hormone and follicle-stimulating hormone secretion. Endocr Rev 1982 Winter;3(1):91–119 (268 ref.)

Barrand MA, Dauncey MJ, Ingram DL: Changes in plasma noradrenaline and adrenaline associated with central and peripheral thermal stimuli in the pig. J Physiol (Lond) 1981 Jul;316:139–52

Barrett JE: Differential drug effects as a function of the controlling consequences. Natl Inst Drug Abuse Res Monogr Ser 1981 Jul; (37):159–81 (40 ref.)

Barrows JJ: Shock demands drugs—but which one's best for your patient? Nursing (Horsham) 1982 Feb;12(2):34–41

Barry RH, Weiss M, Johnson JB, et al: Stability of phenylpropanolamine hydrochloride in liquid formulations containing sugars. J Pharm Sci 1982 Jan;71(1):116–8

Bartfai G, Sas M, Morvay J, et al: Effects of LHRH and long-acting LHRH on serum LH and FSH levels of healthy women. J Endocrinol Invest 1981 Jul–Sep;4(3):359–62

Barthó L, Szolcsányi J: Opiate agonists inhibit neurogenic plasma extravasation in the rat. Eur J Pharmacol 1981 Jul 17;73(1):101–4

Bartholini G, Scatton B, Worms P, et al: Interactions between GABA, dopamine, acetylcholine, and glutamate-containing neurons in the extrapyramidal and limbic systems. Adv Biochem Psychopharmacol 1981;30:119–28

Baruk H: Psychanalyse ou blocage pharmacologique dans la culture des handicapés mentaux. Ann Med Psychol (Paris) 1981;139(3):335–8 (Fre)

Bass MJ, Baskerville JC: Prescribing of minor tranquillizers for emotional problems in a family practice. Can Med Assoc J 1981 Dec 1; 125(11):1225–6

Basso A, Mocchegiani E, Fabris N: Increased immunological efficiency in young mice by short-term treatment with L-thyroxine. J Endocrinol Invest 1981 Oct–Dec;4(4):431–8

Bateson P, Martin P, Young M: Effects of interrupting cat mother's lactation with bromocriptine on the subsequent play of their kittens. Physiol Behav 1981 Nov;27(5):841–5

Baturin VA: Vliianie bol'shikh doz fenamina na instrumental'nye oboronitel'nye refleksy intaktnykh i striatéktomirovannykh krys. Zh Vyssh Nerv Deiat 1981 Nov–Dec;31(6):1305–7 (Rus)

Bauer B, Ehinger B, Tornqvist K: Release of some neurotransmitters from the retina. Vision Res 1981;21(11):1665–72

Bauer R, Evey L: Differential effects of l-amphetamine on ontogeny of active avoidance, intertrial responses, and locomotor activity. Psychopharmacology (Berlin) 1981;75(3):299–304

Baum T, Becker FT: Modulation of reflex sympathetic discharge by the cholinergic agonist oxotremorine and by clonidine. Life Sci 1981 Nov 23;29(21):2181–7

Bazanova NV, Prokudina EA: Issledovanie prirody defitsita katekholaminov v gipotalamuse krys v otdalennye sroki posle luchevogo vozdeistviia. Radiobiologiia 1982 Jan–Feb;22(1):19–24 (Rus)

Beaulieu M, Coyle JT: Effects of fetal methylazoxymethanol acetate lesion on the synaptic neurochemistry of the adult rat striatum. J Neurochem 1981 Oct;37(4):878–87

Beaven MA, Soll AH, Lewin KJ: Histamine synthesis by intact mast cells from canine fundic mucosa and liver. Gastroenterology 1982 Feb; 82(2):254–62

Beckman JK, Owens K, Knauer TE, et al: Hydrolysis of sarcolemma by lysosomal lipases and inhibition by chlorpromazine. Am J Physiol 1982 Apr;242(4):H652–6

Bedford JA, Nail GL, Elsohly HN, et al: Comparative stimulus properties of two fractions of the coca leaf (E. coca). Pharmacol Biochem Behav 1981 Dec;15(6):907–9

Behar J, Kerstein M, Biancani P: Neural control of the lower esophageal sphincter in the cat: studies on the excitatory pathways to the lower esophageal sphincter. Gastroenterology 1982 Apr;82(4):680–8

Bélanger PM, Atitsé-Gbeassor A: The inhibitory effect of monoamine oxidase inhibitors on hepatic microsomal enzyme systems of rat liver. Pharmacol Res Commun 1981 Oct;13(9):819–28

Belin MF, Weisman-Nanopoulos D, Steinbusch H, et al: Mise en évidence de glutamate décarboxylase et de sérotonine dans un même neurone au niveau du noyau du raphé dorsalis du rat par des méthodes de double marquage immunocytochimique. C R Seances Acad Sci [III] 1981 Oct 19;293(6):337–41 (Fre)

Bell RD, Alexander GM, Schwartzman RJ, et al: The methylphenidate-induced stereotypy in the awake rat: local cerebral metabolism. Neurology (NY) 1982 Apr;32(4):377–81

Bellemann P: Amino acid transport and rubidium-ion uptake in monolayer cultures of hepatocytes from neonatal rats. Biochem J 1981 Sep 15; 198(3):475–83

Bellin SI, Ritter S: Disparate effects of infused nutrients on delayed glucoprivic feeding and hypothalamic norepinephrine turnover. J Neurosci 1981 Dec;1(12):1347–53

Belton CH: Thyroxine only on Sundays [letter] NZ Med J 1981 Dec 23;94(698):470

Ben-Ari Y, Krnjevic K, Reinhardt W, et al: Intracellular observations on the disinhibitory action of acetylcholine in the hippocampus. Neuroscience 1981;6(12):2475–84

Ben-Ari Y, Krnjevic K, Reiffenstein RJ, et al: Inhibitory conductance changes and action of gamma-aminobutyrate in rat hippocampus. Neuroscience 1981;6(12):2445–63

Ben-Jonathan N, Braw RH, Laufer N, et al: Norepinephrine in Graafian follicles is depleted by follicle-stimulating hormone. Endocrinology 1982 Feb;110(2):457–61

Benfenati F, Bernardi P, Cortelli P, et al: Possible mixed agonist—antagonist activity of D-sulpiride at dopamine receptor level in man. Neurosci Lett 1981 Nov 4;26(3):289–95

Bennett-Clarke C, Joseph SA: Immunocytochemical distribution of LHRH neurons and processes in the rat: hypothalamic and extrahypothalamic locations. Cell Tissue Res 1982;221(3):493–504

Benoit R, Böhlen P, Ling N, et al: Presence of somatostatin-28-(1-12) in hypothalamus and pancreas. Proc Natl Acad Sci USA 1982 Feb; 79(3):917–21

Berdysheva LV, Mukhammedov A, Putintseva TG, et al: Adaptatsiia perifericheskikh organov krys k nedostatku noradrenalina pri khronicheskoi desimpatizatsii. Fiziol Zh SSSR 1981 Nov;67(11):1636–42 (Eng. Abstr.) (Rus)

Berendsen HH, Nickolson VJ: Androgenic influences on apomorphine-induced yawning in rats. Behav Neural Biol 1981 Sep; 33(1):123–8

Beresford TP, Feinsilver DL, Hall RC: Adverse reactions to benzodiazepine-tricyclic antidepressant compound. J Clin Psychopharmacol 1981 Nov;1(6):392–4

Berga P, Beckett PR, Massó JL, et al: Comparación entre clebopride, domperidona, metopimacina y trimebutina como antieméticos e inductores de peristaltismo gastrointestinal. Arch Farmacol Toxicol 1981 Apr;7(1):189–92 (Spa)

Bergman U, Rane A, Sjöqvist F, et al: Digoxin and Phenytoin analyses as part of consultations in clinical pharmacology: a study on the use of drugs. Ther Drug Monit 1981;3(3):259–69

Berkenbosch F, Vermes I, Binnekade R, et al: Beta-adrenergic stimulation induces an increase of the plasma levels of immunoreactive alpha-MSH, beta-endorphin, ACTH and of corticosterone. Life Sci 1981 Nov 30; 29(22):2249–56

Berlin FS, Bergey GK, Money J: Periodic psychosis of puberty: a case report. Am J Psychiatry 1982 Jan;139(1):119–20

Berlin-Wahlén A, Evers H, Haegerstam G, et al: Systemic absorption of ketocaine following epicutaneous administration. Acta Pharm Suec 1981;18(3):113–8

Bernardi G, Marciani MG, Stanzione P, et al: Evidence in favour of GABA as an inhibitory transmitter in the rat striatum. Adv Biochem Psychopharmacol 1981;30:69–77

Bertilsson L, Asberg M, Lantto O, et al: Gradients of monoamine metabolites and cortisol in cerebrospinal fluid of psychiatric patients

AUTHOR SECTION

and healthy controls. Psychiatry Res 1982 Feb;6(1):77-83

Besson MJ, Gauchy C, Kemel ML, et al: In vivo release of 3H-GABA synthesized from 3H-Glutamine in the substantia nigra and the pallido entopeduncular nuclei in the cat. Adv Biochem Psychopharmacol 1981; 30:95-103

Bevan JA: Selective action of diltiazem on cerebral vascular smooth muscle in the rabbit: antagonism of extrinsic but not intrinsic maintained tone. Am J Cardiol 1982 Feb 18;49(3):519-24

Bhagat B, Burke WJ, Dhalla NS: Insulin-induced enhancement of uptake of noradrenaline in atrial strips. Br J Pharmacol 1981 Oct;74(2):325-32

Bhanot R, Wilkinson M: Treatment of pregnant rats with haloperidol delays the onset of sexual maturation in female offspring. Experientia 1982 Jan 15;38(1):137-9

Bhavsar VH, Dhumal VR, Kelkar VV: The effect of some anti-epilepsy drugs on enhancement of the monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. Eur J Pharmacol 1981 Sep 11;74(2-3):243-7

Bialos D, Giller E, Jatlow P, et al: Recurrence of depression after discontinuation of long-term amitriptyline treatment. Am J Psychiatry 1982 Mar;139(3):325-9

Bicknell RJ, Schofield JG: Inhibition by somatostatin of bovine growth hormone secretion following sodium channel activation. J Physiol (Lond) 1981 Jul;316:85-96

Biegon A, McEwen BS: Modulation by estradiol of serotonin receptors in brain. J Neurosci 1982 Feb;2(2):199-205

Bilitch M, Hauser RG, Goldman BS, et al: Performance of cardiac pacemaker pulse generators. PACE 1981 Nov;4(6):730-5

Bird ED, Anton AH: Phenothiazine biphasic effect on dopamine concentrations in the basal ganglia of subhuman primates. Psychiatry Res 1982 Feb;6(1):1-6

Bishop AE, Polak JM, Lake BD, et al: Abnormalities of the colonic regulatory peptides in Hirschsprung's disease. Histopathology 1981 Nov; 5(6):679-88

Bisschop A, van Rooijen LA, Derks HJ, et al: Induction of rat hepatic ornithine decarboxylase by the tumor promotors 12-O-tetradecanoylphorbol-13-acetate and phenobarbital in vivo; effect of retinyl-acetate. Carcinogenesis 1981;2(12):1283-7

Biswas NM, Ghosh PK, Neuhaus OW: Effect of corticosterone on serum concentrations of alpha 2 micro-globulin and on spermatogenesis in oestrogen-treated rats. J Endocrinol 1982 Feb;92(2):309-14

Biziere K, Huguet F, Narcisse G, et al: Affinity of thiocolchicoside and thiocolchicoside analogues for the postsynaptic GABA receptor site. Eur J Pharmacol 1981 Oct 22;75(2-3):167-8

Björklund A, Falck B, Lindvall O, et al: The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. 2. Model experiments. J Neurosci Methods 1980 Jun;2(3):301-18

Blackburn AM, Bloom SR, Edwards AV: Pancreatic endocrine responses to physiological changes in plasma neurotensin concentration in the calf. J Physiol (Lond) 1981 Sep;318:407-12

Blackburn IM, Bishop S, Glen AI, et al: The efficacy of cognitive therapy in depression: a treatment trial using cognitive therapy and pharmacotherapy, each alone and in combination. Br J Psychiatry 1981 Sep;139:181-9

Blackburn TP, Cox B, Heapy CG, et al: Possible mechanism of 5-methoxy-N,N-dimethyltryptamine-induced turning behaviour in DRN lesioned rats. Pharmacol Biochem Behav 1982 Jan;16(1):7-11

Blackwell RE, Boots LR, Potter HD Jr: Evaluation of Delestrogen and Parlodel as a luteolytic agent in humans. Fertil Steril 1982 Feb; 37(2):213-7

Blaiklock RG, Hirsh EM, Dapson S, et al: Epinephrine induced myocardial necrosis: effects of aminophylline and adrenergic blockade. Res Commun Chem Pathol Pharmacol 1981 Nov;34(2):179-92

Blain PG, Mucklow JC, Bacon CJ, et al: Pharmacokinetics of phenytoin in children. Br J Clin Pharmacol 1981 Nov;12(5):659-61

Blanco C, Ritzenthaler P, Mata-Gilsinger M: Cloning and endonuclease restriction analysis of uidA and uidR genes in Escherichia coli K-12: determination of transcription direction for the uidA gene. J Bacteriol 1982 Feb;149(2):587-94

Bleuler M: Missverständnisse zwischen Hirnforschern und Klinikern. Nervenarzt 1982 Jan;53(1):14-7 **(Ger)**

Block ER, Schoen FJ: Depression of serotonin uptake by rat lungs exposed to paraquat. J Pharmacol Exp Ther 1982 Apr;221(1):254-60

Bloom AS: Effect of delta9-tetrahydrocannabinol on the synthesis of dopamine and norepinephrine in mouse brain synaptosomes. J Pharmacol Exp Ther 1982 Apr;221(1):97-103

Blum JW, Froehli D, Kunz P: Effects of catecholamines on plasma free fatty acids in fed and fasted cattle. Endocrinology 1982 Feb;110(2):452-6

Boarder MR, Erdelyi E, Barchas JD: Opioid peptides in human plasma: evidence for multiple forms. J Clin Endocrinol Metab 1982 Apr; 54(4):715-20

Bobon DP: La dépression: définition, mesure et classification. Rev Med Liege 1982 Jan 1;37(1):8-13 **(Fre)**

Bobrowska J, Leroux P, Maliński E, et al: Thyrotropin releasing hormone and its analogues I. New syntheses and biological properties of TRH (Pro-NH-NH2)3-TRH and (2-Picolyl)-TRH. Mater Med Pol 1980 Jan-Jun;12(1-2):129-35

Böckler H, Steinlechner S, Heldmaier G: Complete cold substitution of noradrenaline-induced thermogenesis in the Djungarian hamster, Phodopus sungorus. Experientia 1982 Feb 15;38(2):261-2

Boebel KP, Baker DH: Comparative utilization of the isomers of phenylalanine and phenyllactic acid by chicks and rats. J Nutr 1982 Feb;112(2):367-76

Boels PJ, Vanhoutte PM: Formation of 3H-dopamine and 3H-noradrenaline from 3H-tyrosine in the canine saphenous vein. Arch Int Pharmacodyn Ther 1981 Oct;253(2):315-16

Boki K, Tanada S, Matsui T, et al: Intraparticle diffusivity of methylene blue into porous activated carbon. Bull Environ Contam Toxicol 1981 Nov;27(5):610-5

Bolaffi JL, Jackson IM: Regulation of thyrotropin-releasing hormone secretion from frog skin. Endocrinology 1982 Mar;110(3):842-6

Boleloucký Z, Plevová J: Psychofarmakologie a výzkum hraničních stavu. Cesk Psychiatr 1981 Jun;77(3):148-52 (Eng. Abstr.) **(Cze)**

Bolelouckу Z: Neuroleptics in neurotic anxiety. Agressologie 1981 Nov; 22(D):15-7

Boleloucký Z, Plevová J, Boriová M, et al: Personnalité, antidépresseur et névroses. Agressologie 1981 Nov;22(E):3-5 **(Fre)**

Boleloutskiĭ Z: Psikhofarmakologicheskiĭ podkhod k izucheniiu nekotorykh voprosov malprogredientnoĭ shizofrenii. Zh Nevropatol Psikhiatr 1982;82(1):105-10 (Eng. Abstr.) **(Rus)**

Bolles RC, Fanselow MS: Endorphins and behavior. Annu Rev Psychol 1982;33:87-101

Bolt DJ: Development of a homologous radioimmunoassay for ovine follicle stimulating hormone: studies after estrus, ovariectomy, estradiol and releasing hormone. J Anim Sci 1981 Sep;53(3):730-41

Boman H: Distribution of the E1 gene among Norwegian blood donors studied by an automated screening method. Hum Hered 1981; 31(5):308-11

Bonacossa A, Sterin-Speziale N, Gimeno MF, et al: Effect of corticosterone, hydrocortisone and prostaglandin fatty acid precursors on the spontaneous motility of the uterus isolated from ovariectomized rats. Prostaglandins 1982 Jan;23(1):113-28

Bonaventure N, Wioland N: Involvement of GABA in ganglion cell receptive field organization in the frog retina. Vision Res 1981; 21(11):1653-5

Bone S, Roose SP, Dunner DL, et al: Bioavailability of lithium carbonate: single versus multiple daily dosing. J Clin Psychopharmacol 1981 Nov; 1(6):390-1

Bonifacj JF, Laborit H: Etude in vitro de la L-tyrosine comme substrat possible du métabolisme énergétique des coupes de tissu (cerveau, foie) et de son action sur mitochondries isolées de cerveau de rat. Agressologie 1981;22(6):241-4 (Eng. Abstr.) **(Fre)**

Bonnet MH, Kramer M, Roth T: A dose response study of the hypnotic effectiveness of alprazolam and diazepam in normal subjects. Psychopharmacology (Berlin) 1981;75(3):258-61

Boren JL, Suarez SD, Gallup GG Jr: p-Chloroamphetamine: effects on tonic immobility, activity, and temperature in chickens. J Comp Physiol Psychol 1981 Dec;95(6):991-1002

Borenstein R, Kessler I, Ben-David M: Prolactin resistance to bromocryptine treatment: a case report. Int J Fertil 1981;26(4):287-9

Boriová M, Boleloucký Z, Plevová J, et al: Dothiepin, antianxiety effect in neurotic women. Agressologie 1981 Nov;22(E):9-10

Borison RL, Fields JZ, Diamond BI: Site-specific blockade of dopamine receptors by neuroleptic agents in human brain. Neuropharmacology 1981 Dec;20(12B):1321-2

Boufflioux R, Van de Velde G: Position des benzodiazépines parmi les psychotropes. Rev Med Brux 1982 Jan;3(1):55-61 (Eng. Abstr.) **(Fre)**

Boulton AA, Huebert ND: Biosynthesis of some urinary trace amines in the rat and the human. Res Commun Chem Pathol Pharmacol 1981 Nov;34(2):295-310

Bourne GA, Dockrill MR, Regiani S, et al: Induction of testicular gonadotropin-releasing hormone (GnRH) receptors by GnRH: effects of pituitary hormones and relationship to inhibition of testosterone production. Endocrinology 1982 Mar;110(3):727-33

Bove FC, Haarstad VB: Hemicholinium-3 and related ether analogues on the synthesis of acetylcholine by mouse brain (in vitro). Arch Int Pharmacodyn Ther 1981 Oct;253(2):278-93

Bowyer JF, Winters WD, Albertson TE: Pentylenetetrazol augmentation of developing kindled amygdaloid seizures. Neuropharmacology 1981 Dec;20(12A):1225-7

Bradshaw WG, Erskine MS, Baum MJ: Dissociation of the effects of gonadal steroids on brain serotonin metabolism and sexual behavior in the male rat. Neuroendocrinology 1982 Jan;34(1):38-45

Brambilla F, Genazzani AR, Facchinetti F, et al: beta-Endorphin and beta-lipotropin plasma levels in chronic schizophrenia, primary affective disorders and secondary affective disorders. Psychoneuroendocrinology 1981 Dec;6(4):321-30

Brandão F, Rodrigues-Pereira E, Monteiro JG, et al: A kinetic study of the release of noradrenaline by tyramine. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(2):83-7

Brantigan CO, Brantigan TA, Joseph N: Effect of beta blockade and beta stimulation on stage fright. Am J Med 1982 Jan;72(1):88-94

AUTHOR SECTION

ram SJ, Sweadner KJ, Patterson PH: Neuronal cell surfaces: distinctive glycoproteins of cultured adrenergic and cholinergic sympathetic neurons. J Neurosci 1981 Dec;1(12):1397–406

echa N, Sharma SC, Karten HJ: Localization of substance P-like immunoreactivity in the adult and developing goldfish retina. Neuroscience 1981;6(12):2737–46

eckenridge C, Pesant M, Durham HD, et al: A 30-day toxicity study of inhaled fenitrothion in the albino rat. Toxicol Appl Pharmacol 1982 Jan;62(1):32–43

eckenridge RJ, Nicholson SH, Nicol AJ, et al: Inhibition of [3H]GABA binding to postsynaptic receptors in human cerebellar synaptic membranes by carboxyl and amino derivatives of GABA. J Neurochem 1981 Oct;37(4):837–44

eckenridge RJ, Nicholson SH, Nicol AJ, et al: Inhibition of neuronal GABA uptake and glial beta-alanine uptake by synthetic GABA analogues. Biochem Pharmacol 1981 Nov 15;30(22):3045–9

emer KV, Gürtler H, Müller I: Auswirkungen einer Applikation von Adrenalin, Noradrenalin und Isoprenalin auf Parameter des Kohlenhydrat- und Fettstoffwechsels im Blutplasma von Schweinen. Arch Exp Veterinarmed 1981;35(5):697–706 (Eng. Abstr.) (Ger)

ight TP, Sandage BW Jr, Fletcher HP: Selected cardiac and metabolic responses to pseudoephedrine with exercise. J Clin Pharmacol 1981 Nov–Dec;21(11–12 Pt 1):488–92

inkman UA, Welling PL, de Vries G, et al: Liquid chromatography of demoxepam and phenothiazines using a post–column photochemical reactor and fluorescence detection. J Chromatogr 1981 Nov 6; 217:463–71

own BS, Chaitkin L: Use of stimulant/depressant drugs by drug abuse clients in selected metropolitan areas. Int J Addict 1981 Dec; 16(8):1473–90

own CD, Simmons NL: Catecholamine–stimulation of Cl- secretion in MDCK cell epithelium. Biochim Biophys Acta 1981 Dec 7; 649(2):427–35

own CM, Collis MG: Adenosine contracts the isolated rat tail artery by releasing endogenous 5–hydroxytryptamine. Eur J Pharmacol 1981 Dec 3;76(2–3):275–7

own MR, Fisher LA, Rivier J, et al: Corticotropin–releasing factor: effects on the sympathetic nervous system and oxygen consumption. Life Sci 1982 Jan 11;30(2):207–10

own OM, Palfai T, Wichlinski L: Effect of an amnesic dose of reserpine, syrosingopine or guanethidine on the levels of whole brain dopamine and norepinephrine in the mouse. Pharmacol Biochem Behav 1981 Dec; 15(6):911–4

own SJ, Gisolfi CV, Mora F: Temperature regulation and dopaminergic systems in the brain: does the substantia nigra play a role? Brain Res 1982 Feb 25;234(2):275–86

own WA, Laughren TP: Tolerance to the prolactin–elevating effect of neuroleptics. Psychiatry Res 1981 Dec;5(3):317–22

ückner–Schmidt R, Jackisch R, Hertting G: On the mechanism of noradrenaline–induced prostaglandin E2–Synthesis in primary cell cultures from rabbit splenic pulpa. Arch Int Pharmacodyn Ther 1981 Oct;253(2):266–77

unello N, Cheney DL, Costa E: Increase in exogenous choline fails to elevate the content or turnover rate of cortical, striatal, or hippocampal acetylcholine. J Neurochem 1982 Apr;38(4):1160–3

unello N, Chuang DM, Costa E: Different synaptic location of mianserin and imipramine binding sites. Science 1982 Feb 26;215(4536):1112–5

us K, Szkilnik R, Słomińska–Zurek J, et al: Studies on the behavioral and hypotensive effects of intraventricular prostacyclin (PGI2) in rats. Pol J Pharmacol Pharm 1981;33(4):467–74

ck SH, Deshmukh PP, Yamamura HI, et al: Thermal analgesia and substance P depletion induced by capsaicin in guinea–pigs. Neuroscience 1981;6(11):2217–22

ck SH, Miller MS, Burks TF: Depletion of primary afferent substance P by capsaicin and dihydrocapsaicin without altered thermal sensitivity in rats. Brain Res 1982 Feb 4;233(1):216–20

ck SH, Deshmukh PP, Burks TF, et al: A survey of substance P, somatostatin, and neurotensin levels in aging in the rat and human central nervous system. Neurobiol Aging 1981 Winter;2(4):257–64

ckett WR: The influence of a GABA transaminase inhibitor, gamma–vinyl GABA, on voluntary morphine consumption in the rat. Psychopharmacology (Berlin) 1981;75(2):214–6

ckingham JC: The hypophysiotrophic hormones. Prog Med Chem 1978; 15:165–210 (380 ref.)

da M, Gonon F, Cespuglio R, et al: In vivo electrochemical detection of catechols in several dopaminergic brain regions of anaesthetized rats. Eur J Pharmacol 1981 Jul 17;73(1):61–8

dd RD: Phencyclidine (PCP)–structure versus reactivity. Clin Toxicol 1981;18(9):1033–41

dd RD: The use of diazepam and of cocaine in combination with other drugs by Los Angeles County probationers. Am J Drug Alcohol Abuse 1981;8(2):249–55

ger R, Permanetter B, Sommer O, et al: Adaptive changes of pyruvate oxidation in perfused heart during adrenergic stimulation. Am J Physiol 1982 Jan;242(1):H30–6

rch JE, Roberts SG, Raddats MA: Binding of amitriptyline and nortriptyline in plasma determined from their equilibrium distributions between red cells and plasma, and between red cells and buffer solution. Psychopharmacology (Berlin) 1981;75(3):262–72

Burckart GJ, Hammond RW, Akers MJ: Stability of extemporaneous suspensions of carbamazepine. Am J Hosp Pharm 1981 Dec; 38(12):1929–31

Buriakov IE: Izmenenie soderzhaniia katekholaminov i sokratitel'noi funktsii miokarda pri ochagovom tsitotoksicheskom porazhenii serdtsa. Fiziol Zh 1981 Nov–Dec;27(6):780–5 (Eng. Abstr.) (Rus)

Burquest B: The violent girl. Adolescence 1981 Winter;16(64):749–64

Burrows GH, Barnea A: Copper stimulates the release of luteinizing hormone releasing hormone from isolated hypothalamic granules. Endocrinology 1982 Apr;110(4):1456–8

Burrows ME, Vanhoutte PM: Pharmacology of arterioles: some aspects of variability in response to norepinephrine, histamine, and 5–hydroxytryptamine. J Cardiovasc Pharmacol 1981 Nov–Dec; 3(6):1370–80

Burstein S, Hunter S: The biochemistry of the cannabinoids. Rev Pure Appl Pharmacol Sci 1981 Apr–Jun;2(2):155–226 (289 ref.)

Burstein S, Ozman K, Burstein E, et al: Prostaglandins and cannabis––XI. Inhibition of delta 1–tetrahydrocannabinol–induced hypotension by aspirin. Biochem Pharmacol 1982 Feb 15;31(4):591–2

Busby WH Jr, Youngblood WW, Humm J, et al: A review of the methods used for the measurement of thyrotropin–releasing hormone (TRH). J Neurosci Methods 1981 Dec;4(4):305–14 (31 ref.)

Buu NT, Duhaime J, Kuchel O, et al: The convulsive effects of dopamine sulfate conjugates in rat brain. Life Sci 1981 Nov 30;29(22):2311–6

Buvat J, Buvat–Herbaut M: Régulation de la fonction hypothalamo–hypophyso–ovarienne au cours du cycle menstruel de la femme normale. 1. Schéma d'ensemble et contrôle de la sécrétion–libération des gonadotrophines par le LH–RH et les oestrogènes. J Gynecol Obstet Biol Reprod (Paris) 1981;10(5):415–23 (55 ref.) (Eng. Abstr.) (Fre)

C

Caccia S, Dagnino G, Garattini S, et al: Kinetics of fenfluramine isomers in the rat. Eur J Drug Metab Pharmacokinet 1981;6(4):297–301

Caffrey JL, Hodges DH: Inhibition of the enzymatic degradation of Met–enkephalin by catecholamines. Endocrinology 1982 Jan; 110(1):291–3

Cake MH, Yeoh GC, Oliver IT: Ontogeny of the glucocorticoid receptor and its relationship to tyrosine aminotransferase induction in cultured foetal hepatocytes. Biochem J 1981 Aug 15;198(2):301–7

Calderini G, Bonetti AC, Aldinio A, et al: Functional interaction between benzodiazepine and GABA recognition sites in aged rats. Neurobiol Aging 1981 Winter;2(4):309–13

Calderón Narváez G: La depresión, problema de salud pública. Salud Publica Mex 1981 Sep–Oct;23(5):503–8 (Eng. Abstr.) (Spa)

Calil HM, Jostell KG, Cowdry RW, et al: Zimelidine and norzimelidine protein binding measured by equilibrium dialysis and cerebrospinal fluid. Clin Pharmacol Ther 1982 Apr;31(4):522–7

Callegaro L, Barbieri U, Denti E: Selective detoxification: hemoperfusion on antiphenobarbital antibody immobilized on solid phase. Trans Am Soc Artif Intern Organs 1981;27:566–9

Callery PS, Geelhaar LA, Nayar MS, et al: Pyrrolines as prodrugs of gamma–aminobutyric acid analogues. J Neurochem 1982 Apr; 38(4):1063–7

Calltorp J: Psykiarin i Kina. Tvekar inför Freud, blandar örtmediciner, och västerländska psykofarmaka. Lakartidningen 1981 Oct 21; 78(43):3788–91 (Eng. Abstr.) (Swe)

Camakaris H, Pittard J: Autoregulation of the tyrR gene. J Bacteriol 1982 Apr;150(1):70–5

Cannon JG, Long JP, Bhatnagar R: Future directions in dopaminergic nervous system and dopaminergic agonists. J Med Chem 1981 Oct; 24(10):1113–8 (66 ref.)

Cano J, Lobera B, Rodriguez–Echandia EL, et al: Influence of innervation on the levels of noradrenaline and serotonin in the circumvallate papilla of the rat. J Neurobiol 1982 Jan;13(1):1–7

Cano JP, Sumirtapura YC, Cautreels W, et al: Analysis of the metabolites of ethyl loflazepate by gas chromatography with electron–capture detection. J Chromatogr 1981 Dec 11;226(2):413–22

Carasikas S, Mizrahi J, D'Orléans–Juste P, et al: Antagonists of substance P. Eur J Pharmacol 1982 Jan;77(2–3):205–6

Cardinali DP, Fernández Pardal J, Gimeno MF, et al: Effects of estradiol on norepinephrine and prostaglandin efflux in medial basal hypothalamus of ovariectomized rats. J Neural Transm 1982;53(1):39–47

Carlà V, Dacke CG, Davidson N, et al: Taurine and thermoregulation: behavioral and cellular studies. Adv Exp Med Biol 1981;139:361–72

Carmeliet E, Saikawa T: Shortening of the action potential and reduction of pacemaker activity by lidocaine, quinidine, and procainamide in sheep cardiac purkinje fibers. An effect on Na or K currents? Circ Res 1982 Feb;50(2):257–72

Carpentier RG: The effect of harmine on the action potential of the guinea–pig atrial muscle depends on the external calcium concentration.

Br J Pharmacol 1981 Oct;74(2):415–8

Carraway R, Ruane SE, Feurle GE, et al: Amphibian neurotensin (NT) is not xenopsin (XP): dual presence of NT-like and XP-like peptides in various amphibia. Endocrinology 1982 Apr;110(4):1094–101

Carrillo Broatch A: Aspectos del linde de la psiquiatría y la terapéutica biológica. Rev Neuropsiquiatr 1980 Jun;43(2):87–96 (Eng. Abstr.) **(Spa)**

Carroll PT, Aspry JA: Spontaneous and potassium-induced release of acetylcholine from mouse forebrain minces. Neuroscience 1981; 6(12):2555–9

Cartaud A, Huchon D, Marot J, et al: Calmodulin is involved in the first step of oocyte maturation: effects of the antipsychotic drug fluphenazine and of anticalmodulin antibodies on the progesterone-induced maturation of xenopus laevis oocyte. Cell Differ 1981 Dec;10(6):357–63

Carter BL, Garnett WR, Pellock JM, et al: Effect of antacids on phenytoin bioavailability. Ther Drug Monit 1981;3(4):333–40

Carter DA, Pennington JM, Whitehead SA: In-vivo and in-vitro effects of domperidone on the release of prolactin and LH in male and female rats. J Reprod Fertil 1982 Jan;64(1):191–7

Carter DA, Whitehead SA: Pituitary sensitivity to gonadotrophin releasing hormone after hyperprolactinaemia induced with neuroleptics and domperidone in the rat. J Endocrinol 1981 Dec;91(3):439–46

Casais PL, Chermat R, Cuenca E, et al: Influencia de la N-(4-picolil)-3,5 dimetilbenzamida (M-14012-4) sobre la conducta estereotipada inducida por la apomorfina y la anfetamina en la rata y el ratón.
Arch Farmacol Toxicol 1981 Apr;7(1):65–72 **(Spa)**

Cascieri MA, Goldenberg MM, Liang T: Biological activity of substance P methyl ester. Mol Pharmacol 1981 Nov;20(3):457–9

Casper RF, Erickson GF, Rebar RW, et al: The effect of luteinizing hormone-releasing factor and its agonist on cultured human granulosa cells. Fertil Steril 1982 Mar;37(3):406–9

Castellani S, Adams PM, Giannini AJ: Physostigmine treatment of acute phencyclidine intoxication. J Clin Psychiatry 1982 Jan;43(1):10–1

Castellani S, Giannini AJ, Adams PM: Physostigmine and haloperidol treatment of acute phencyclidine intoxication. Am J Psychiatry 1982 Apr;139(4):508–10

Castelli A, Martorana GE, Frasca AM, et al: Confronto tra i metodi della 2,4-dinitrofenilidrazina e dell'acido fosfotungstico per la determinazione colorimetrica della vitamina C nel plasma. Acta Vitaminol Enzymol 1981;3(2):103–10 (Eng. Abstr.) **(Ita)**

Castracane VD, Goldzieher JW: The luteolytic and abortifacient potential of an estrogen-bromergocryptine regimen in the baboon.
Fertil Steril 1982 Feb;37(2):258–62

Caudill WL, Houck GP, Wightman RM: Determination of gamma-aminobutyric acid by liquid chromatography with electrochemical detection. J Chromatogr 1982 Feb 12;227(2):331–9

Ceriani C: Uso de psicotrópicos em odonyologia. Quintessencia 1981 Apr; 8(4):45–53 **(Por)**

Chan MY, Hung F: A study on the effect of chlorpromazine and desipramine on the activity of some adrenal enzymes.
Biochem Pharmacol 1981 Dec 15;30(24):3365–7

Chandra AV, Ali MM, Saxena DK, et al: Behavioral and neurochemical changes in rats simultaneously exposed to manganese and lead.
Arch Toxicol 1981 NOV;49(1):49–56

Chandra SV, Shukla GS: Effect of manganese on synthesis of brain catecholamines in growing rats. Acta Pharmacol Toxicol (Copenh) 1981 Apr;48(4):349–54

Chapler CK, Cain SM: Blood flow and O2 uptake in dog hindlimb with anemia, norepinephrine, and propranolol. J Appl Physiol 1981 Sep; 51(3):565–70

Chapman RS, Ratcliffe JG: Covalent linkage of antisera to microparticulate cellulose using 1,1'-carbonyldiimidazole: a rapid, practical method with potential use in solid-phase immunoassay.
Clin Chim Acta 1982 Jan 5;118(1):129–34

Chappel SC, Coutifaris C, Jacobs SJ: Studies on the microheterogeneity of follicle-stimulating hormone present within the anterior pituitary gland of ovariectomized hamsters. Endocrinology 1982 Mar; 110(3):847–54

Charles L, Schain R: A four-year follow-up study of the effects of methylphenidate on the behavior and academic achievement of hyperactive children. J Abnorm Child Psychol 1981 Dec;9(4):495–505

Charney DS, Heninger GR, Sternberg DE, et al: Adrenergic receptor sensitivity in depression. Effects of clonidine in depressed patients and healthy subjects. Arch Gen Psychiatry 1982 Mar;39(3):290–4

Chaturvedi AK, Rowell PP, Sastry BV: Relationships between chemical structure and cholinergic activities of furmethides and potentiation of these activities by physostigmine. Pharmacol Res Commun 1981 Oct; 13(9):829–45

Chauhan MS, Dakshinamurti K: Gas chromatographic method for the simultaneous determination of dopamine and norepinephrine metabolites. J Chromatogr 1982 Feb 12;227(2):323–30

Check WA: Endorphin-mental illness link far from proved [news]
JAMA 1982 Feb 5;247(5):570–1, 575–7

Chen GB: Role of the nervous system of the human body with regard to acupuncture analgesia. Acupunct Electrother Res 1981;6(1):7–17

Cheng CC, Lin JK: Reaction of nitrite with tyrosine residues in digestive enzymes. Taiwan I Hsueh Hui Tsa Chih 1981 Nov;80(11):1186–92

Cheng TO: Digoxin – quinidine interaction [letter] J Am Geriatr Soc 1982 Jan;30(1):79–80

Chéramy A, Leviel V, Daudet F, et al: Involvement of the thalamus in the reciprocal regulation of the two nigrostriatal dopaminergic pathways. Neuroscience 1981;6(12):2657–68

Chern YF, Lin MT: Effects of intraventricular administration of sympathomimetic agents on metabolic, vasomotor and temperature responses in Taiwan monkeys. Jpn J Physiol 1981;31(4):599–603

Chernyshevskaia IA: Gistokhimicheskoe izuchenie kholinésteraz razlichnykh formatsiĭ konechnogo mozga pozvonochnykh.
Zh Evol Biokhim Fiziol 1981 Nov–Dec;17(6):595–601 (Eng. Abstr.) **(Rus)**

Cherry N, Rodgers B, Venables H, et al: Acute behavioral effects of styrene exposure: a further analysis. Br J Ind Med 1981 Nov;38(4):346–50

Chevolet C, Carlier G, Rondia K, et al: Convulsant action of kainic acid after subcutaneous injection to the rat. Arch Int Pharmacodyn Ther 1981 Oct;253(2):319–20

Chida AM, Vital LM: Fundamentos biológicos da agressão.
Rev Paul Enferm 1981 Jul–Aug;(1):13–5 (Eng. Abstr.) **(Por)**

Childers JW, Schneider EG: Aldosterone and the enhanced natriuresis of hypertonic infusions in the dog. Am J Physiol 1982 Jan;242(1):F30–7

Childs G, Redfern PH: A circadian rhythm in passive avoidance behavior: the effect of phase shift and the benzodiazepines.
Neuropharmacology 1981 Dec;20(12B):1365–6

Chomicka LK, Domański E: Activity of noradrenergic neurons of preoptic-anterior hypothalamic area of female rabbits in some stages of reproduction. Mater Med Pol 1980 Jan–Jun;12(1–2):97–101

Chopra IJ, Solomon DH, Teco GN, et al: An inhibitor of the binding of thyroid hormones to serum proteins is present in extrathyroidal tissues. Science 1982 Jan 22;215(4531):407–9

Chou D, Polnaszek CF, Yost Y, et al: Application of spin labeling to drug assays. II. Determination of the binding of [14C]-phenytoin and spin-labeled phenytoins to albumin and human serum.
Mol Pharmacol 1981 Nov;20(3):674–80

Chow EH, Marshall JM: Effects of catecholamines on circular and longitudinal uterine muscle of the rat. Eur J Pharmacol 1981 Dec 3; 76(2–3):157–65

Christensen S, Kristensen AR, Faarup P: Effects of lithium and neuroleptics and combinations of the two on renal function and structure in rats. Acta Pharmacol Toxicol (Copenh) 1981 Sep;49(3):161–7

Christie MJ, Chesher GB, Bird KD: The correlation between swim-stress induced antinociception and [3H] leu-enkephalin binding to brain homogenates in mice. Pharmacol Biochem Behav 1981 Dec;15(6):853–7

Christie MJ, Zingarelli GJ, Chesher GB: Method of sacrifice influences leucine enkephalin binding to mouse brain.
Pharmacol Biochem Behav 1981 Dec;15(6):849–51

Chronister RB, Palmer GC, Defrance JF, et al: Histamine: correlative studies in nucleus accumbens. J Neurobiol 1982 Jan;13(1):23–37

Church AC, Bunney BS, Krieger NR: Neuronal localization of dopamine-sensitive adenylate cyclase within the rat olfactory tubercle.
Brain Res 1982 Feb 25;234(2):369–76

Chweh AY, Leslie SW: Phosphatidylserine enhancement of [3H]gamma-aminobutyric acid uptake by rat whole brain synaptosomes.
J Neurochem 1982 Mar;38(3):691–5

Cid E, Morán I, Monaris M, et al: Bioavailability of four brands of phenytoin. Biopharm Drug Dispos 1981 Oct–Dec;2(4):391–4

Clardy DO, Ragle JL: Stability of phencyclidine in stored blood.
Clin Toxicol 1981 Aug;18(8):929–34

Clark KE, Austin JE, Seeds AE: Effect of bisenoic prostaglandins and arachidonic acid on the uterine vasculature of pregnant sheep.
Am J Obstet Gynecol 1982 Feb 1;142(3):261–8

Clark MR: Stimulation of progesterone and prostaglandin E accumulation by luteinizing hormone-releasing hormone (LHRH) and LHRH analogs in rat granulosa cells. Endocrinology 1982 Jan;110(1):146–52

Clarke DE, Lyles GA, Callingham BA: A comparison of cardiac and vascular clorgyline-resistant amine oxidase and monoamine oxidase. Inhibition by amphetamine, mexiletine and other drugs.
Biochem Pharmacol 1982 Jan 1;31(1):27–35

Claustre J, Peyrin L: Free and conjugated catecholamines and metabolites in cat urine after hypoxia. J Appl Physiol 1982 Feb;52(2):304–8

Clayton RN, Popkin RM, Fraser HM: Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of gonadotropin-releasing hormone immunoneutralization.
Endocrinology 1982 Apr;110(4):1116–22

Clayton RN, Channabasavaiah K, Stewart JM, et al: Hypothalamic regulation of pituitary gonadotropin-releasing hormone receptors: effects of hypothalamic lesions and a gonadotropin-releasing hormone antagonist. Endocrinology 1982 Apr;110(4):1108–15

Clejan S, Jonas E, Collipp PJ, et al: Influence of growth hormone and thyroxine on thermotropic effects of respiration and 1-anilino-8-naphthalene sulfonate fluorescence and on lipid composition of cardiac membranes. Biochim Biophys Acta 1981 Dec 4;678(2):250–6

Clements-Jewery S, Robson PA: Are striatal [3H]spiperone radioreceptor assays indicative of multiple dopamine receptor interactions?

AUTHOR SECTION

Neuropharmacology 1981 Dec;20(12B):1295–8

Cohen J, Neff NH: Retinal amacrine cell system tyrosine hydroxylase: the development of responsiveness to light and neuroleptic drugs. Brain Res 1982 Jan;255(1):160–3

Cohen MS, Britt RH: Effects of sodium pentobarbital, ketamine, halothane, and chloralose on brainstem auditory evoked responses. Anesth Analg (Cleve) 1982 Apr;61(4):338–43

Cohen SL, Morley BJ, Snead OC: An EEG analysis of convulsive activity produced by cholinergic agents. Prog Neuropsychopharmacol 1981; 5(4):383–8

Colatsky TJ: Mechanisms of action of lidocaine and quinidine on action potential duration in rabbit cardiac Purkinje fibers. An effect on steady state sodium currents? Circ Res 1982 Jan;50(1):17–27

Cole KJ, Seller MJ: Gel electrophoresis of maternal and fetal serum cholinesterases from normal pregnancies and of those affected by neural tube defects. Clin Chim Acta 1982 Feb 26;119(1–2):1–6

Coleman JW, Holgate ST, Church MK, et al: Immunoglobulin E decapeptide–induced 5–hydroxytryptamine release from rat peritoneal mast cells. Comparison with corticotropin–(1–24)–peptide, polyarginine, polylysine and antigen. Biochem J 1981 Sep 15;198(3):615–9

Collingridge GL, Thompson PA, Davies J, et al: In vitro effect of tetanus toxin on GABA release form rat hippocampal slices. J Neurochem 1981 Oct;37(4):1039–41

Colosi P, Talamantes F: The amino acid composition of secreted mouse prolactin, growth hormone, and hamster prolactin: the presence of one tryptophan in mouse prolactin. Arch Biochem Biophys 1981 Dec; 212(2):759–61

Comai L, Kosuge T: Cloning characterization of iaaM, a virulence determinant of Pseudomonas savastanoi. J Bacteriol 1982 Jan; 149(1):40–6

Comar D, Maziere M, Cepeda C, et al: The kinetics and displacement of [11C]flunitrazepam in the brain of the living baboon. Eur J Pharmacol 1981 Oct 15;75(1):21–6

Comb M, Seeburg PH, Adelman J, et al: Primary structure of the human Met– and Leu–enkephalin precursor and its mRNA. Nature 1982 Feb 25;295(5851):663–6

Combie J, Blake JW, Nugent TE, et al: Morphine glucuronide hydrolysis: superiority of beta–glucuronidase from Patella vulgata. Clin Chem 1982 Jan;28(1):83–6

Commissaris RL, Semeyn DR, Rech RH: Dispositional without functional tolerance to the hypothermic effects of pentobarbital in the rat. J Pharmacol Exp Ther 1982 Mar;220(3):536–9

Commissaris RL, Semeyn DR, Moore KE, et al: The effects of 2,5–dimethoxy–4–methylamphetamine (DOM) on operant behavior: interactions with other neuroactive agents. Commun Psychopharmacol 1980;4(5):393–404

Cone RI, Davis GA, Goy RW: Effects of ovarian steroids on serotonin metabolism within grossly dissected and microdissected brain regions of the ovariectomized rat. Brain Res Bull 1981 Dec;7(6):639–44

Conne BS, Scaglioni S, Lang U, et al: Pituitary receptor sites for gonadotropin–releasing hormone: effect of castration and substitutive therapy with sex steroids in the male rat. Endocrinology 1982 Jan; 110(1):70–9

Consolazione A, Milstein C, Wright B, et al: Immunocytochemical detection of serotonin with monoclonal antibodies. J Histochem Cytochem 1981 Dec;29(12):1425–30

Cooke HJ, Cooke AR: Effect of tryptophan on transport properties of newborn rabbit jejunum. Am J Physiol 1982 Apr;242(4):G308–12

Cookson J: Oestrogens, dopamine and mood [letter] Br J Psychiatry 1981 Oct;139:365–6

Cooper GR, Shin SH: Somatostatin inhibits prolactin secretion in the estradiol primed male rat. Can J Physiol Pharmacol 1981 Oct; 59(10):1082–8

Coppen A, Abou–Saleh MT, Milln P, et al: Lithium continuation therapy following electroconvulsive therapy. Br J Psychiatry 1981 Oct; 139:284–7

Corbett AD, McKnight AT, Kosterlitz HW: Tetraethylammonium facilitates the stimulation–evoked loss of the enkephalins from the myenteric plexus of guinea–pig ileum. Proc R Soc Lond [Biol] 1981 Oct 14;213(1191):171–82

Corrent G, Eskin A, Kay I: Entrainment of the circadian rhythm from the eye of Aplysia: role of serotonin. Am J Physiol 1982 Mar; 242(3):R326–32

Corrent G, Eskin A: Transmitterlike action of serotonin in phase shifting a rhythm from the Aplysia eye. Am J Physiol 1982 Mar;242(3):R333–8

Corsini GU, Pitzalis GF, Bernardi F, et al: The use of dopamine agonists in the treatment of schizophrenia. Neuropharmacology 1981 Dec; 20(12B):1309–13

Costa C, De Antoni A, Baccichetti F, et al: Effect of blue light on the urinary excretion of tryptophan metabolites in adult heterozygous and homozygous Gunn rats. Boll Soc Ital Biol Sper 1981 Oct 15; 57(19):1969–75

Costa JL, Murphy DL, Stark H: Applicability of models for carrier–mediated serotonin transport to pools of serotonin in intact human platelets. J Physiol (Lond) 1981 Jul;316:153–61

Costa JL, Dobson CM, Fay DD, et al: Nuclear magnetic resonance studies of amine storage in pig platelets. FEBS Lett 1981 Dec 28;136(2):325–8

Costa T, Russell L, Pert CB, et al: Halide– and gamma–aminobutyric acid–induced enhancement of diazepam receptors in rat brain. Reversal by disulfonic stilbene blockers of anion channels. Mol Pharmacol 1981 Nov;20(3):470–6

Cotton BR, Smith G, Fell D: Effect of oral diazepam on lower oesophageal sphincter pressure. Br J Anaesth 1981 Nov;53(11):1147–50

Cottrell GA: FMRFamide neuropeptides simultaneously increase and decrease K+ current in an identified neurone. Nature 1982 Mar; 296(5852):87–9

Coudray–Lucas C, Prioux–Guyonneau M, Tassel A, et al: Influence of intoxication by anticholinesterase agents on core temperature in rats: relationships between hypothermia and acetylcholinesterase inhibition in different brain areas. Acta Pharmacol Toxicol (Copenh) 1981 Sep; 49(3):215–22

Coufal J, Novotný M: Fluphenazine and flupenthixol decanoate in psychiatric outpatients practice. Act Nerv Super (Praha) 1981; 23(4):269–71

Coupar IM: Evidence against the involvement of prostaglandins in the vasoconstrictor action of calcium ion in rat mesenteric blood vessels. Br J Pharmacol 1981 Oct;74(2):477–84

Coupet J, Rauh CE, Lippa AS, et al: The effects of acute administration of diazepam on the binding of [3H]–diazepam and [3H]–gaba to rat cortical membranes. Pharmacol Biochem Behav 1981 Dec;15(6):965–8

Coupet J, Szucha–Myers VA: Brain histamine H1– and H2–receptors and histamine–sensitive adenylate cyclase: effects of antipsychotics and antidepressants. Eur J Pharmacol 1981 Sep 11;74(2–3):149–55

Coutifaris C, Chappel SC: Intraventricular injection of follicle–stimulating hormone (FSH) during proestrus stimulates the rise in serum FSH on estrus in phenobarbital–treated hamsters through a central nervous system–dependent mechanism. Endocrinology 1982 Jan;110(1):105–13

Couture R, Regoli D: Mini review: smooth muscle pharmacology of substance P. Pharmacology 1982 Jan;24(1):1–25 (66 ref.)

Coy DH, Horvath A, Nekola MV, et al: Peptide antagonists of LH–RH: large increases in antiovulatory activities produced by basic D–amino acids in the six position. Endocrinology 1982 Apr;110(4):1445–7

Craig TJ, Behar R: Changes in the prescription of anticholinergic drugs (1970–1977) in a state hospital. Int Pharmacopsychiatry 1981;16(2):84–91

Craven PA, DeRubertis FR: Effects of vasopressin and urea on Ca2+–calmodulin–dependent renal prostaglandin E. Am J Physiol 1981 Dec;241(6):F649–58

Crawley JN, Hays SE, Paul SM, et al: Cholecystokinin reduces exploratory behavior in mice. Physiol Behav 1981 Sep;27(3):407–11

Crawley JN, Marangos PJ, Stivers J, et al: Chronic clonazepam administration induces benzodiazepine receptor subsensitivity. Neuropharmacology 1982 Jan;21(1):85–9

Crevoisier C, Eckert M, Heizmann P, et al: Relation entre l'effet clinique et la pharmacocinétique du midazolam après administration i.v. et i.m. 2ème communcation: Aspects pharmacocinétiques. Arzneimittelforsch 1981;31(12a):2211–5 (Eng. Abstr.) (Fre)

Crome P: Erreurs thérapeutiques et toxicité. Encephale 1981;7(4 Suppl):499–506 (Eng. Abstr.) (Fre)

Crow TJ: Positive and negative schizophrenia symptoms and the role of dopamine. Br J Psychiatry 1981 Sep;139:251–4

Crowley WR, Terry LC, Johnson MD: Evidence for the involvement of central epinephrine systems in the regulation of luteinizing hormone, prolactin, and growth hormone release in female rats. Endocrinology 1982 Apr;110(4):1102–7

Csaba G, Szalkó A, Kapa E: Effect of sympathomimetic substances and analogues on tail absorption of frog larva. Acta Biol Acad Sci Hung 1981;32(2):103–9

Cuenca E: Rôle des récepteurs noradrénergiques post–synaptiques dans le mode d'action des antidépresseurs. Encephale 1981;7(4 Suppl):397 (Fre)

Cumming R, Reaves TA Jr, Hayward JN: Ultrastructural immunocytochemical localization of enkephalin in the goldfish preoptic nucleus. Neurosci Lett 1981 Dec 23;27(3):313–8

Cutler LS, Christian CP, Bottaro B: Development of stimulus–secretion coupling in salivary glands. Methods Cell Biol 1981;23:531–45

Cutnell JD, La Mar GN, Dallas JL, et al: High–field 1H NMR studies of synthetic analogs of somatostatin. Structural features involving aromatic residues in an active eight–membered ring analog. Biochim Biophys Acta 1982 Jan 4;700(1):59–66

D

Dahl SG: Pharmacokinetic aspects of new antipsychotic drugs. Neuropharmacology 1981 Dec;20(12B):1299–302

Dahlgren N, Lindvall O, Nobin A, et al: Cerebral circulatory response to hypercapnia: effects of lesions of central dopaminergic and serotoninergic neuron systems. Brain Res 1981 Dec 28;230(1–2):221–33

Dahlgren N, Ingvar M, Siesjö BK: Effect of propranolol on local cerebral blood flow under normocapnic and hypercapnic conditions. J Cereb Blood Flow Metab 1981;1(4):429–36

Dalsgaard CJ, Hökfelt T, Johansson O, et al: Somatostatin immunoreactive cell bodies in the dorsal horn and the parasympathetic intermediolateral nucleus of the rat spinal cord. Neurosci Lett 1981 Dec 23;27(3):335–9

Dalterio S, Badr F, Bartke A, et al: Cannabinoids in male mice: effects on fertility and spermatogenesis. Science 1982 Apr 16;216(4543):315–6

Dam M, Pizzolato G, Merlo D, et al: Liposome–induced changes in the uptake of GABA and glutamate in mouse brain in vitro. Ital J Neurol Sci 1981 Dec;2(4):375–7

Damian E, Ianăș O, Bădescu I: Reduction of pituitary nucleic acids, proteins, LH and FSH by melatonin–free pineal extract in rats stimulated with gonadotropin releasing hormone. Endocrinologie 1981 Oct–Dec; 19(4):227–30

D'Angelo L, Monti JM: Effects of oxolinic acid on the sleep–wakefulness cycle of the rat. Br J Pharmacol 1981 Oct;74(2):399–404

Daniel W, Adamus A, Melzacka M, et al: Cerebral pharmacokinetics of imipramine in rats after single and multiple dosages. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov;317(3):209–13

Danilov GE, Khaliullina KhV: Izmenenie vnutriglaznogo davleniia pri lokal'nom vvedenii katekholaminov v gipotalamus. Fiziol Zh SSSR 1981 Oct;67(10):1487–92 (Eng. Abstr.) **(Rus)**

Danner DJ, Sewell ET, Elsas LJ: Clofibric acid and phenylpyruvic acid as biochemical probes for studying soluble bovine liver branched chain ketoacid dehydrogenase. J Biol Chem 1982 Jan 25;257(2):659–62

Das G: Digoxin—quinidine interaction [letter] Am J Cardiol 1982 Feb 1;49(2):495

Das Gupta V, Stewart KR: Stability of haloperidol in 5% dextrose injection. Am J Hosp Pharm 1982 Feb;39(2):292–4

Dauthier C, Gaudy JH, Bonnet P: Etude comparée du diazépam et du fentanyl sur les seuils du réflexe de clignement chez l'homme normal éveillé (étude préliminaire). Ann Anesthesiol Fr 1981;22(4):317–21 (Eng. Abstr.) **(Fre)**

Davi H, Dupont P, Jeanniot JP, et al: The biotransformation of [14C]minaprine in man and five animals species. Xenobiotica 1981 Nov; 11(11):735–47

Davis BJ, Burd GD, Macrides F: Localization of methionine–enkephalin, substance P, and somatostatin immunoreactivities in the main olfactory bulb of the hamster. J Comp Neurol 1982 Feb 1;204(4):377–83

Davis JM, Fredman D: The new generation of antidepressants. Curr Psychiatr Ther 1981;20:293–7

Davis M, Astrachan DI: Spinal modulation of acoustic startle: opposite effects of clonidine and d–amphetamine. Psychopharmacology (Berlin) 1981;75(3):219–25

Davis NM, Brookes S, Gray JA, et al: Chlordiazepoxide and resistance to punishment. Q J Exp Psychol [B] 1981 Nov;33(Pt 4):227–39

Daw NW, Ariel M: Effect of synaptic transmitter drugs on receptive fields of rabbit retinal ganglion cells. Vision Res 1981;21(11):1643–7

Dawbarn D, Pycock CJ: Motor effects following application of putative excitatory amino acid antagonists to the region of the mesencephalic dopamine cell bodies in the rat. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(2):100–4

Dawling S, Crome P, Heyer EJ, et al: Nortriptyline therapy in elderly patients: dosage prediction from plasma concentration at 24 hours after a single 50 mg dose. Br J Psychiatry 1981 Nov;139:413–6

Dayton MA, Ewing AG, Wightman RM: Evaluation of amphetamine–induced in vivo electrochemical response. Eur J Pharmacol 1981 Oct 22;75(2–3):141–4

De Antoni A, Costa C, Baccichetti F, et al: Enzyme activities of tryptophan metabolism in heterozygous and homozygous Gunn rats before and after blue light exposure. Boll Soc Ital Biol Sper 1981 Oct 15;57(19):1976–80

de Arriaga D, Soler J, Cadenas E: Effect of Na+, K+ and Li+ on pH dependence of in situ beta–galactosidase from E. coli. Int J Biochem 1982;14(1):47–52

Deas JE, Lee LT: Competitive inhibition by soluble erythrocyte glycoproteins of penetration by Plasmodium falciparum. Am J Trop Med Hyg 1981 Nov;30(6):1164–7

Deboscker Y, Laurent JM, Lemaire V, et al: Insuffisance rénale aiguë par rhabdomyolyse non traumatique. Nouv Presse Med 1982 Jan 16; 11(2):131 **(Fre)**

de Buck RP: Analyse des études contrôlées comparant la miansérine et la clomipramine. Encephale 1981;7(4 Suppl):455–72 (Eng. Abstr.) **(Fre)**

De Carvalho LP, Zornetzer SF: Enhanced responsiveness of alpha–noradrenergic receptors following discrete electrolytic lesions of the nucleus locus coeruleus: a behavioral demonstration. J Neural Transm 1982;53(1):23–37

Dees JH, Masters BS, Muller–Eberhard U, et al: Effect of 2,3,7,8–tetrachlorodibenzo–p–dioxin and phenobarbital on the occurrence and distribution of four cytochrome P–450 isozymes in rabbit kidney, lung, and liver. Cancer Res 1982 Apr;42(4):1423–32

Deeter WT 3d, Mueller GP: Differential effects of warm– and cold–ambient temperature on blood levels of beta–endorphin and prolactin in the rat. Proc Soc Exp Biol Med 1981 Dec;168(3):369–72

DeFeudis FV: Time–dependent environmentally–induced changes in cerebral and extra–cerebral morphology and chemistry—the basis of learning, memory and behavior. Gen Pharmacol 1982;13(1):1–9 (97 ref.)

Deimling MJ, Schnell RC: Manganese prolongation of pentobarbital hypnosis in the male rat. Experientia 1981 Dec 15;37(12):1322–3

Delanoy RL, Kramarcy NR, Dunn AJ: ACTH 1–24 and lysine vasopressin selectively activate dopamine synthesis in frontal cortex. Brain Res 1982 Jan 7;231(1):117–29

De Lean A, Kilpatrick BF, Caron MG: Guanine nucleotides regulate both dopaminergic agonist and antagonist binding in porcine anterior pituitary. Endocrinology 1982 Mar;110(3):1064–6

Del Fiacco M, Paxinos G, Cuello AC: Neostriatal enkephalin–immunoreactive neurones project to the globus pallidus. Brain Res 1982 Jan 7;231(1):1–17

Dello Russo NM, Temple HV: Cocaine effects on gingiva [letter] J Am Dent Assoc 1982 Jan;104(1):13

del Villar E, Sanchez E, Letelier ME, et al: Differential inhibition by diazepam and nitrazepam of UDP–glucuronyltransferase activities in rats. Res Commun Chem Pathol Pharmacol 1981 Sep;33(3):433–47

Den Hertog A: Calcium and the alpha–action of catecholamines on guinea–pig taenia caeci. J Physiol (Lond) 1981 Jul;316:109–25

DeNoble VJ, Svikis DS, Meisch RA: Orally delivered pentobarbital as a reinforcer for rhesus monkeys with concurrent access to water: effects of concentration, fixed–ratio size, and liquid positions. Pharmacol Biochem Behav 1982 Jan;16(1):113–7

DePalatis LR, Fiorindo RP, Ho RH: Substance P immunoreactivity in the anterior pituitary gland of the guinea pig. Endocrinology 1982 Jan; 110(1):282–4

DePaolo LV, McCann SM, Negro–Vilar A: A sex difference in the activation of hypothalamic catecholaminergic and luteinizing hormone–releasing hormone peptidergic neurons after acute castration. Endocrinology 1982 Feb;110(2):531–9

DePaolo LV, Negro–Vilar A: Neonatal monosodium glutamate treatment alters the response of median eminence luteinizing hormone–releasing hormone nerve terminals to potassium and prostaglandin E2. Endocrinology 1982 Mar;110(3):835–41

Depue RA, Evans R: The psychobiology of depressive disorders: from pathophysiology to predisposition. Prog Exp Pers Res 1981;10:1–114 (436 ref.)

Dereux JF: Miansérine, récepteur présypnatique et schéma de Tissot. Encephale 1981;7(4 Suppl):399–400 (Eng. Abstr.) **(Fre)**

Désormeaux Y, Ballak M, Benchimol S, et al: Synthesis and migration of proteins and glycoproteins in juxtaglomerular cells of sodium–deficient rats. An ultrastructural radioautographic study. Cell Tissue Res 1982 Jan;222(1):53–67

De Souza EB, Van Loon GR: Stress–induced inhibition of the plasma corticosterone response to a subsequent stress in rats: a nonadrenocorticotropin–mediated mechanism. Endocrinology 1982 Jan; 110(1):23–33

Deupree JD, Weaver JA, Downs DA: Catecholamine content of chromaffin granule 'ghosts' isolated from bovine adrenal glands. Biochim Biophys Acta 1982 Feb 25;714(3):471–8

Deutsch SI, Stanley M, Banay–Schwartz M, et al: The effect of lithium on rat brain and erythrocyte glycine levels. Eur J Pharmacol 1981 Oct 15;75(1):75–6

de Villard R, Dallery J, Maillet J, et al: Etude en ouvert de la minaprine en pédopsychiatrie. Neuropsychiatr Enfance Adolesc 1981 Apr–May; 29(4–5):255–8 (Eng. Abstr.) **(Fre)**

De Vries J, Jansen JD, Kroese ED, et al: Protection against paracetamol–induced glutathione depletion following a paracetamol–acetylsalicylic acid mixture or benorilate in phenobarbital–treated rats. Toxicol Lett 1981 Dec;9(4):345–7

DeWald HA, Lobbestael S, Poschel BP: Pyrazolodiazepines. 3. 4–Aryl–1,6,7,8–tetrahydro–1,3–dialkylpyrazolo[3,4–e][1,4]diazepines as antidepressant agents. J Med Chem 1981 Aug;24(8):982–7

de Wildt DJ, Porsius AJ: Central cardiovascular effects of physostigmine in the cat; possible cholinergic aspects of blood pressure regulation. Arch Int Pharmacodyn Ther 1981 Sep;253(1):22–39

de Wildt DJ, Porsius AJ: The influence of physostigmine on sympathetic outflow and haemodynamics by an action upon the pontomedullary region of the cat. Arch Int Pharmacodyn Ther 1981 Sep;253(1):40–51

de Wit H, Stewart J: Reinstatement of cocaine–reinforced responding in the rat. Psychopharmacology (Berlin) 1981;75(2):134–43

D'Haenen H: Les fonctions du moi. Un objectif psychanalytique en recherche psychopharmacologique? Une revue de la littérature. Acta Psychiatr Belg 1981 Sep–Oct;81(5):452–9 (Eng. Abstr.) **(Fre)**

d'Hollander A, Primo G, Hennart D, et al: Compared efficacy of dobutamine and dopamine in association with calcium chloride on termination of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1982 Feb;83(2):264–71

Di Carlo R, Muccioli G: Changes in prolactin binding sites in the rabbit hypothalamus induced by physiological and pharmacological variations of prolactin serum levels. Brain Res 1981 Dec 28;230(1–2):445–50

Di Chiara G, Porceddu ML, Imperato A, et al: Role of GABA neurons in the expression of striatal motor functions. Adv Biochem Psychopharmacol 1981;30:129–63 (77 ref.)

Dickinson SL, Longman DA, Slater P: A method for measuring drug–induced changes in limb muscle tone in the rat. J Neurosci Methods 1982 Jan;5(1–2):195–200

Dickstein ES: Digitalis toxicity mistaken for jaundice. Geriatrics 1982 Apr; 37(4):133, 137–8

AUTHOR SECTION

Dietch JT: Steroid psychosis and tricyclic antidepressants [letter] Arch Gen Psychiatry 1982 Feb;39(2):236

DiFiglia M, Aronin N, Leeman SE: Immunoreactive substance P in the substantia nigra of the monkey: light and electron microscopic localization. Brain Res 1982 Feb 11;233(2):381–8

DiFiglia M, Aronin N, Martin JB: Light and electron microscopic localization of immunoreactive Leu–enkephalin in the monkey basal ganglia. J Neurosci 1982 Mar;2(3):303–20

Digregorio GJ, Ruch E, Piraino AJ: Detection and quantitation of phencyclidine in rat parotid saliva and plasma. Drug Alcohol Depend 1981 Sep;8(2):169–73

DiGregorio GJ, Piraino AJ, Ruch EK, et al: Investigation of digoxin, quinidine, and disopyramide interactions in rats utilizing parotid saliva, blood, and other tissues. J Pharm Sci 1982 Feb;71(2):211–3

Dikii NT: Prognozirovanie éffekta psikhofarmakoterapii u bol'nykh shizofreniei. Zh Nevropatol Psikhiatr 1982;82(1):110–5 (Eng. Abstr.) **(Rus)**

Dileepan KN, Khawaja AM, Wagle SR: Studies on the mechanism of action of somatostatin on renal gluconeogenesis: evidence for the involvement of alpha 1–adrenergic stimuli. Arch Biochem Biophys 1982 Jan; 213(1):169–76

Dish TN: Correlation between retention of defensive conditioned reflexes and brain acetylcholinesterase activity in rats. Neurosci Behav Physiol 1981 May–Jun;11(3):230–3

Divers WA, Babaknia A, Hopper BR, et al: Fetal lung maturation: amniotic fluid catecholamines, phospholipids, and cortisol. Am J Obstet Gynecol 1982 Feb 15;142(4):440–4

Divoll M, Greenblatt DJ, Ciraulo DA, et al: Clobazam kinetics: intrasubject variability and effect of food on adsorption. J Clin Pharmacol 1982 Jan;22(1):69–73

Dix GE: Realism and drug refusal: a reply to Appelbaum and Gutheil. Bull Am Acad Psychiatry Law 1981;9(3):180–98

Dixey R, Rein G: 3H–noradrenaline release potentiated in a clonal nerve cell line by low–intensity pulsed magnetic fields. Nature 1982 Mar 18; 296(5854):253–6

Dixon R, Marin D: Tricyclic antidepressants: a simplified approach for the routine clinical monitoring of parent drug and metabolites in plasma using HPLC. Res Commun Chem Pathol Pharmacol 1981 Sep; 33(3):537–45

Djamgoz MB, Reynolds SH, Rowe JS, et al: Control of retinal S–potentials in dark adapted and bleached retinae. Vision Res 1981;21(11):1581–4

Dluzen DE, Ramirez VD: Presence and localization of immunoreactive luteinizing hormone–releasing hormone (LHRH) within the olfactory bulbs of adult male and female rats. Peptides (Fayetteville) 1981 Winter; 2(4):493–6

D'Mello GD: A comparison of some behavioural effects of amphetamine and electrical brain stimulation of the mesolimbic dopamine system in rats. Psychopharmacology (Berlin) 1981;75(2):184–92

Doble A, Iversen LL, Bowery NG, et al: 6 –Hydroxydopamine decreases benzodiazepine but not GABA receptor binding in rat cerebellum. Neurosci Lett 1981 Dec 11;27(2):199–204

Doble A, Iversen LL: Molecular size of benzodiazepine receptor in rat brain in situ: evidence for a functional dimer? Nature 1982 Feb 11; 295(5849):522–3

Dobrzański T, Rychta T, Zurowski S, et al: Chronoendocrinological studies in athletes. III. Certain psychoendocrinological correlations. Acta Physiol Pol 1981 Sep–Oct;32(5):521–7

Doherty PC, Bartke A, Smith MS: Differential effects of bromocriptine treatment on LH release and copulatory behavior in hyperprolactinemic male rats. Horm Behav 1981 Dec;15(4):436–50

Dolgun ZS, Meshcheriakova SA, Belakovskii MS, et al: Izuchenie obmena serotonina i gistamina u kosmonavtov. Kosm Biol Aviakosm Med 1982 Jan–Feb;16(1):89–91 **(Rus)**

Domański E: Przekazywanie neurohormonów podwzgórzowych do gruczołowej części przysadki, regulujących jej funkcję. Acta Physiol Pol 1981;32(5 Suppl 23):59–78 (68 ref.) **(Pol)**

Domino EF: Central cholinergic mechanisms related to psychotropic drug action. Jpn J Pharmacol 1981;31 Suppl:21P–26P

Donoso AO, Zárate MB, Banzan AM: Nontraditional neurotransmitters and prolactin release. Prog Clin Biol Res 1981;74:219–28 (35 ref.)

Donovan CM: Problems of psychiatric practice in community mental health centers. Am J Psychiatry 1982 Apr;139(4):456–60

Doody MC, Gotto AM Jr, Smith LC: 5-(dimethylamino)naphthalene–1–sulfonic acid, a fluorescent probe of the medium chain fatty acid binding site of serum albumin. Biochemistry 1982 Jan 5;21(1):28–33

Doongaji DR, Sheth AS, Apte JS, et al: Penfluridol in chronic schizophrenia. Acta Psychiatr Belg 1981 Jul–Aug;81(4):407–15

Doongaji DR, Sheth AS, Apte JS, et al: Pimozide versus chlordiazepoxide in anxiety neurosis. Acta Psychiatr Belg 1981 Jul–Aug;81(4):416–23

Dörner G: Sex hormones and neurotransmitters as mediators for sexual differentiation of the brain. Endokrinologie 1981 Dec;78(2–3):129–38 (31 ref.)

Dosch HM, Jason J, Gelfand EW: Transient antibody deficiency and abnormal t–suppressor cells induced by phenytoin. N Engl J Med 1982 Feb 18;306(7):406–9

Dourish CT: Behavioural effects of acute and chronic beta–phenylethylamine administration in the rat: evidence for the involvement of 5–hydroxytryptamine. Neuropharmacology 1981 Nov; 20(11):1067–72

Dourish CT, Boulton AA: The effects of acute and chronic administration of beta–phenylethylamine on food intake and body weight in rats. Prog Neuropsychopharmacol 1981;5(4):411–4

Dourish CT, Cooper SJ: Suppression of drinking and induction of sedation by a dopamine agonist is blocked by small doses of spiperone. Neuropharmacology 1982 Jan;21(1):69–72

Dowson JH: Pharmacological treatment of chronic cognitive deficit: a review. Compr Psychiatry 1982 Jan–Feb;23(1):85–98

Dremova VP, Inglom DL, Markina VV, et al: Issledovaniia éffektivnosti repellentnogo deistviia i perspektivnosti ispol'zovaniia odezhdy s khimicheski prisoedinennym karboksidom. Med Parazitol (Mosk) 1982 Jan–Feb;51(1):39–44 (Eng. Abstr.) **(Rus)**

Drop SL, Frohn–Mulder IM, Visser HK, et al: The effect of ACTH stimulation on plasma steroids in two patients with congenital hypoaldosteronism and in their relatives. Acta Endocrinol (Copenh) 1982 Feb;99(2):245–50

Drødal S, Burvald S, Bredesen JE, et al: Diazepam (Diazemuls 'Vitrum' og veneskader. Tidsskr Nor Laegeforen 1981 Sep 20;101(26):1477–8 **(Nor)**

Dubovsky SL, Franks RD, Lifschitz M, et al: Effectiveness of verapamil in the treatment of a manic patient. Am J Psychiatry 1982 Apr; 139(4):502–4

Dubuc PU, Leshin LS, Willis PL: Glucose and endocrine responses to hypothalamic electrical stimulation in rats. Am J Physiol 1982 Mar; 242(3):R220–6

Dudley CA, Jamison TS, Moss RL: Inhibition of lordosis behavior in the female rat by intraventricular infusion of prolactin and by chronic hyperprolactinemia. Endocrinology 1982 Feb;110(2):677–9

Dudley CA, Vale W, Rivier J, et al: The effect of LHRH antagonist analogs and an antibody to LHRH on mating behavior in female rats. Peptides (Fayetteville) 1981 Winter;2(4):393–6

Dudley SD: Prepubertal ontogeny of responsiveness to estradiol in female rat central nervous system. Neurosci Biobehav Rev 1981 Winter; 5(4):421–35 (238 ref.)

Dugas JE, Weber SS: Amoxapine (Asendin, Lederle Laboratories). Drug Intell Clin Pharm 1982 Mar;16(3):199–204 (34 ref.)

Dumas JP, Guilland JC, Braud ML, et al: Réactions cardio–vasculaires et sympathico–médullosurrénaliennes à l'intoxication tabagique aiguë. C R Soc Biol (Paris) 1981;175(6):866–9 (Eng. Abstr.) **(Fre)**

Dunn BM, Pham C, Raney L, et al: Interaction of alpha–dansylated peptide inhibitors with porcine pepsin: detection of complex formation by fluorescence energy transfer and chromatography and evidence for a two–step binding scheme. Biochemistry 1981 Dec 8;20(25):7206–11

Dunnette J, Weinshilboum R: Radioimmunoassay and immunotitration of human serum dopamine beta–hydroxylase. Methods Enzymol 1981;74 Pt C:370–80

Duplaix M, Williams J, Mongin P: Effects of an intermittent lighting schedule on the time of egg–laying and the levels of luteinizing hormone, progesterone and corticosterone in the plasma of the domestic hen. J Endocrinol 1981 Dec;91(3):375–83

Dupont A, Savard P, Mérand Y, et al: Age–related changes in central nervous system enkephalins and substance P. Life Sci 1981 Nov 30; 29(22):2317–22

Dupont A, Barden N, Ferland L, et al: Physiological role of endorphins in neuroendocrinology. Acta Physiol Pol 1981;32(5 Suppl 23):37–57 (45 ref.)

Dutt JE: On the clinical response/plasma level relationship for clomipramine [letter] Br J Psychiatry 1982 Jan;140:105

Dvornik D, Kraml M, Dubuc J, et al: Comparative bioavailability of propranolol: twice–daily versus four times–daily administration. J Clin Pharmacol 1981 Nov–Dec;21(11–12 Pt 1):472–6

Dychko EN, Sirota GI, Sukmanskii OI, et al: Vliianie povrezhdeniia verkhnego sheĭnogo simpaticheskogouzla u krolikov na mikrotsirkuliatsiiu i soderzhanie katekholaminov v tkaniakh innerviruemykh im slizistykh obolochek. Fiziol Zh 1982 Jan–Feb; 28(1):15–9 (Eng. Abstr.) **(Rus)**

Dychko EN, Mirtovskaia VN, Sirota GI, et al: Ekskretsiia 5–oksiindoliluksusnoĭ kisloty u bol'nykh s sindromom glossalgii. Stomatologiia (Mosk) 1982 Jan–Feb;61(1):34–5 (Eng. Abstr.) **(Rus)**

Dychko EN: Kharakter ékskretsii katekholaminov s mocholĭ pri sindrome glossalgii. Vrach Delo 1981 Dec;(12):93–5 **(Rus)**

E

Ebara T, Nakayama K, Otsuki S, et al: Effects of lithium on rat tail nerve conduction velocity. Int Pharmacopsychiatry 1981;16(3):129–37

Echizen H, Freed CR: Long–term infusion of L–5–hydroxytryptophan increases brain serotonin turnover and decreases blood pressure in normotensive rats. J Pharmacol Exp Ther 1982 Mar;220(3):579–84

Eddie LW, Baker HW, Higginson RE, et al: Gonadotrophin releasing hormone causes a biphasic secretion of luteinizing hormone and follicle stimulating hormone by cultures of rat anterior pituitary cells. Acta Endocrinol (Copenh) 1982 Jan;99(1):44–9

Edelstein EL: Vasopressins and other neuropeptides as CNS mental modulators. A review. Isr J Psychiatr Relat Sci 1981;18(3):229–36

Edvinsson L, McCulloch J: Effects of pentobarbital on contractile responses of feline cerebral arteries. J Cereb Blood Flow Metab 1981; 1(4):437–40

Edvinsson L, McCulloch J, Uddman R: Substance P: immunohistochemical localization and effect upon cat pial arteries in vitro and in situ. J Physiol (Lond) 1981 Sep;318:251–8

Edwards JG: Adverse effects of antianxiety drugs. Drugs 1981 Dec; 22(6):495–514 (83 ref.)

Edwards MW, Cawthorne MA, Williamson DH: Impairment of effects of vasopressin on [1-14C]oleate metabolism in hepatocytes from obese (ob/ob) mice. Biochem J [illegible] Jul 15;198(1):239–42

Egbe PC: The involvement of the catecholaminergic system in physostigmine-induced hyperactivity in rats. Arzneimittelforsch 1982; 32(1):27–9

Ehinger B, Hansson C, Tornqvist K: 5-Hydroxytryptamine in the retina of some mammals. Exp Eye Res 1981 Dec;33(6):663–72

Ehinger B, Florén, Tornqvist K: Autoradiography of (3H)-5-hydroxytryptamine uptake in the retina of some mammals. Graefes Arch Clin Exp Ophthalmol 1982;218(1):1–8

Eiden LE, Ruth JA: Acute thyroid hormone increases noradrenergic responsiveness of rat atria in vitro. Eur J Pharmacol 1981 Aug 27; 74(1):91–3

Eisenberg GC, Hilliard JT, Gutheil TG: Ethical aspects of the right to refuse medication: a clinicolegal dilemma for the psychiatrist and patient. Psychiatr Q 1981 Summer;53(2):93–9

Eisner DA, Richards DE: The interaction of potassium ions and ATP on the sodium pump of resealed red cell ghosts. J Physiol (Lond) 1981; 319:403–18

Ek B, Westermark B, Wasteson A, et al: Stimulation of tyrosine-specific phosphorylation by platelet-derived growth factor. Nature 1982 Feb 4;295(5848):419–20

Ekholm C, Clark MR, Magnusson C, et al: Ovulation induced by a gonadotropin releasing hormone analog in hypophysectomized rats involves prostaglandins. Endocrinology 1982 Jan;110(1):288–90

Elekes I, Láng T, Csányi E, et al: Absorption, distribution, elimination and metabolism of tofizopam, a new 2,3-benzodiazepine derivative, in animal experiments. Farmaco [Prat] 1981 Dec;36(12):542–52

Elfvin LG, Forsman C: Plasticitet och transmittorval i sympatiska ganglieceller. Lakartidningen 1981 Oct 28;78(44):3909–12 (15 ref.) (Eng. Abstr.) **(Swe)**

Elkind-Hirsch K, King JC, Gerall AA, et al: The luteinizing hormone-releasing hormone (LHRH) system in normal and estrogenized neonatal rats. Brain Res Bull 1981 Dec;7(6):645–54

Ellison G, Morris W: Opposed stages of continuous amphetamine administration: parallel alterations in motor stereotypies and in vivo spiroperidol accumulation. Eur J Pharmacol 1981 Sep 11;74(2–3):207–14

Elmazar MM, Sullivan FM: Effect of prenatal phenytoin administration on postnatal development of the rat: a behavioral teratology study. Teratology 1981 Oct;24(2):115–24

Elvers LH, Koedam JC, Loeber JG: Comparison of eleven commercially available kits for the radioimmunoassay of serum thyroxine. J Clin Chem Clin Biochem 1981 Jul;19(7):453–6

Embil K, Torosian G: Solubility and ionization characteristics of doxepin and desmethyldoxepin. J Pharm Sci 1982 Feb;71(2):191–3

Embree LJ, Roubein IF, Jackson DW, et al: Aging effect on the noradrenaline content of rat brain microvessels. Exp Aging Res 1981 Fall;7(3):215–24

Emel'ianov NA, Bagaeva TR: Vliianie gidrokortizona na dykhanie srezov kory mozga krys v sredakh s pirovinogradnoí ili beta-gidroksimaslianoí kislotoí. Fiziol Zh SSSR 1981 Oct;67(10):1468–71 (Eng. Abstr.) **(Rus)**

Emrich HM, Zaudig M, v. Zerssen D, et al: Action of [Des-Tyr1]-gamma-endorphin in schizophrenia. Mod Probl Pharmacopsychiatry 1981;17:279–86

Emson PC, Goedert M, Horsfield P, et al: The regional distribution and chromatographic characterisation of neurotensin-like immunoreactivity in the rat central nervous system. J Neurochem 1982 Apr;38(4):992–9

Endo M: [Neural origin and modulation by hypothalamic catecholamines of pulsatile secretion of luteinizing hormone in ovariectomized rats (author's transl)] Hokkaido Igaku Zasshi 1981 Mar;56(2):185–98 (Eng. Abstr.) **(Jpn)**

Enger-Valk BE, van Rotterdam J, Kos A, et al: Construction of new vectors for cloning of promoters. Gene 1981 Dec;15(4):297–305

Enz A: Biphasic influence of a 8 alpha-amino ergoline, CU 32-085, on striatal dopamine synthesis and turnover in vivo in the rat. Life Sci 1981 Nov 23;29(21):2227–34

Epelbaum J, Arancibia LT, Herman JP, et al: Topography of median eminence somatostatinergic innervation. Brain Res 1981 Dec 28; 230(1–2):412–6

Epstein O, Schoenfeld N, Greenblat Y, et al: The influence of propranolol on the concentration of heme and on the activity of delta aminolevulinate synthase in monolayers of chick embryo liver cells. Biochem Pharmacol 1982 Feb 15;31(4):485–9

Erdö SL, Rosdy B, Szporny L: Higher GABA concentrations in fallopian tube than in brain of the rat. J Neurochem 1982 Apr;38(4):1174–6

Erichsen JT, Reiner A, Karten HJ: Co-occurrence of substance P-like and Leu-enkephalin-like immunoreactivities in neurones and fibres of avian nervous system. Nature 1982 Feb 4;295(5848):407–10

Erinosho OA, Ayonrinde A: A cross-national comparison of patterns of utilization and psychiatric care. Int J Soc Psychiatry 1981 Winter; 27(4):289–96

Eristavi TM, Dzhaparidze ZO, Charkviani GG: Issledovanie lokalizatsii metalloaktseptornykh tsentrov, spetsificheski sviazyvaiushchikh dvukhvalentnye kationy v molekule miozina. Biofizika 1981 Sep-Oct; 26(5):931–2 (Eng. Abstr.) **(Rus)**

Esler M, Turbott J, Schwarz R, et al: The peripheral kinetics of norepinephrine in depressive illness. Arch Gen Psychiatry 1982 Mar; 39(3):295–300

Ettenberg A, White N: Pimozide attenuates conditioned taste preferences induced by self-stimulation in rats. Pharmacol Biochem Behav 1981 Dec;15(6):915–9

F

Facchinetti F, Bagnoli F, Bracci R, et al: Plasma opioids in the first hours of life. Pediatr Res 1982 Feb;16(2):95–8

Falch E, Krogsgaard-Larsen P: The binding of the GABA agonist [3H]THIP to rat brain synaptic membranes. J Neurochem 1982 Apr; 38(4):1123–9

Fallon JH: Collateralization of monoamine neurons: mesotelencephalic dopamine projections to caudate, septum, and frontal cortex. J Neurosci 1981 Dec;1(12):1361–8

Fan SG, Shutt AJ, Vogt M: The importance of 5-hydroxytryptamine turnover for the analgesic effect of morphine in the chicken. Neuroscience 1981;6(11):2223–7

Fando JL, Dominguez F, Herrera E: Tryptophan overload in the pregnant rat: effect on brain amino acid levels in in vitro protein synthesis. J Neurochem 1981 Oct;37(4):824–9

Fant ME, Harbison RD: Syncytiotrophoblast membrane vesicles: a model for examining the human placental cholinergic system. Teratology 1981 Oct;24(2):187–99

Fantini F, Morace G, Porciani MC, et al: Effects of isoproterenol on vectorcardiographic pattern of 'early repolarization syndrome'. G Ital Cardiol 1981;11(6):797–802

Farah JM Jr, Malcolm DS, Mueller GP: Dopaminergic inhibition of pituitary beta-endorphin-like immunoreactivity secretion in the rat. Endocrinology 1982 Feb;110(2):657–9

Faravelli C, Marchetti G, Benvenuti P, et al: Il litio nella prevenzione delle turbe cicliche dell'affettività (efficacia dei bassi livelli plasmatici e fattori di previsione dell'esito della terapia). Riv Patol Nerv Ment 1980 Nov-Dec;101(6):261–71 (Eng. Abstr.) **(Ita)**

Fassoulaki A: Postoperative effects of methylphenidate [letter] Br J Anaesth 1981 Dec;53(12):1365–6

Fauchère JL, Do KQ, Schwyzer R, et al: Interaction of p-nitrophenylalanine enkephalins with mu-, delta- and kappa-subtypes of the opiate receptor. Eur J Pharmacol 1982 Feb 5;77(4):339–42

Fedan JS, Ma J, Fromell G, et al: Effect of Mount St. Helens ash on the response of rat trachea to smooth muscle agonists. Environ Res 1981 Dec;26(2):497–502

Fedortsov VI: Depressii v pozdnem vozraste. Med Sestra 1982 Jan; 41(1):14–7 **(Rus)**

Feely J, Robertson D, Island DP, et al: Cimetidine alters plasma catecholamine levels and cortisol and aldosterone excretion [letter] N Engl J Med 1982 Apr 29;306(17):1054

Feger J: Electrophysiological studies of GABAergic neurons in the basal ganglia: nigro-collicular, nigro-thalamic, and pallido-subthalamic neurons. Adv Biochem Psychopharmacol 1981;30:53–68

Fekete MI, Szentendrei T, Kanyicska B, et al: Effects of anxiolytic drugs on the catecholamine and DOPAC (3, 4-dihydroxyphenylacetic acid) levels in brain cortical areas and on corticosterone and prolactin secretion in rats subjected to stress. Psychoneuroendocrinology 1981; 6(2):113–20

Felber W: Rezidivprophylaxe affektiver Erkrankungen mit Lithium und ihre Auswirkungen. Psychiatr Clin (Basel) 1981;14(3):161–6 (Eng. Abstr.) **(Ger)**

Felix D, Ehrenberger K: The action of putative neurotransmitter substances in the cat labyrinth. Acta Otolaryngol (Stockh) 1982 Jan-Feb; 93(1–2):101–5

Felten DL, Hallman H, Jonsson G: Evidence for a neurotropic role of noradrenaline neurons in the postnatal development of rat cerebral cortex. J Neurocytol 1982 Feb;11(1):119–35

Ferkany JW, Andree TH, Clarke DE, et al: Neurochemical effects of kojic amine, a GABAmimetic and its interaction with benzylamine oxidase. Neuropharmacology 1981 Dec;20(12A):1177–82

Ferrara P, Li CH: Opiate receptor-binding activity of [D-Thr2,Thz5]-and [D-Met2,Thz5]-enkephalinamides. Eur J Pharmacol 1981 Jul 17; 73(1):69–73

Ferri S, Cocchi D, Locatelli V, et al: ACTH1-24 counteracts the

AUTHOR SECTION

prolactin-releasing effect of an opioid. Eur J Pharmacol 1982 Jan; 77(2-3):143-5

Ferron A, Descarries L, Reader TA: Altered neuronal responsiveness to biogenic amines in rat cerebral cortex after serotonin denervation or depletion. Brain Res 1982 Jan 7;231(1):93-108

Ferruzza N, Farinella E: The influence of LiCL on animal halves isolated from ascidian eggs. Acta Embryol Morphol Exp 1981 Aug;2(1):57-67

Feuerstein C, Demenge P, Barrette G, et al: Long-term effects of nigro-striatal denervation of striatal [3H]haloperidol binding. Eur J Pharmacol 1981 Dec 17;76(4):457-60

Feuerstein G, Adelberg S, Kopin IJ, et al: Central cardiovascular effects of prostacyclin. Neuropharmacology 1981 Nov;20(11):1085-90

Filip V, Sladka R, Dostalova J, et al: A double-blind, placebo-controlled study with tofizopam in anxiety neurosis. Agressologie 1981 Oct; 22(C):27-30

Fietto JF: La psychotherapie de groupe des schizophrenes chroniques en milieu externe. Can J Psychiatry 1981 Dec;26(8):558-61 (Eng. Abstr.) **(Fre)**

Finger TE: Enkephalin-like immunoreactivity in the gustatory lobes and visceral nuclei in the brains of goldfish and catfish. Neuroscience 1981; 6(12):2747-58

Finlayson RE, Martin LM: Recognition and management of depression in the elderly. Mayo Clin Proc 1982 Feb;57(2):115-20

Finley JC, Maderdrut JL, Roger LJ, et al: The immunocytochemical localization of somatostatin-containing neurons in the rat central nervous system. Neuroscience 1981;6(11):2173-92

Fiók J, Acs Z, Stark E: Possible inhibitory influence of gamma-aminobutyric acid on growth hormone secretion in the rat. J Endocrinol 1981 Dec;91(3):391-7

Fischer-Colbrie R, Schachinger M, Zangerle R, et al: Dopamine beta-hydroxylase and other glycoproteins from the soluble content and the membranes of adrenal chromaffin granules: isolation and carbohydrate analysis. J Neurochem 1982 Mar;38(3):725-32

Fischman MW, Schuster CR: Cocaine self-administration in humans. Fed Proc 1982 Feb;41(2):241-6

Fisher SK, Frey KA, Agranoff BW: Loss of muscarinic receptors and of stimulated phospholipid labeling in ibotenate-treated hippocampus. J Neurosci 1981 Dec;1(12):1407-13

Fitzpatrick D, Johnson RP: Enkephalin-like immunoreactivity in the mossy fiber pathway of the hippocampal formation of the tree shrew (Tupaia glis). Neuroscience 1981;6(12):2485-94

Flaten O: The effect of adrenoceptor blockade on the release of gastric inhibitory polypeptide after intraduodenal glucose in humans. Scand J Gastroenterol 1981;16(5):641-5

Flaten O, Bohman T, Myren J: Serum concentration of pancreatic polypeptide after infusion of histamine and the effect of cimetidine, trimipramine, and atropine in man. Scand J Gastroenterol 1981; 16(8):989-91

Fleck S, Johnson D: The comprehensive treatment of schizophrenics. Curr Psychiatr Ther 1981;20:313-27

Fleming R, Adam AH, Barlow DH, et al: A new systematic treatment for infertile women with abnormal hormone profiles. Br J Obstet Gynaecol 1982 Jan;89(1):80-3

Flerkó B, Sétáló G, Vigh S, et al: Recent immunohistological findings on the LH-RH neuron system of the rat. Mater Med Pol 1980 Jan-Jun; 12(1-2):119-23

Fletcher A, Fowler LJ: A regional study of 4-aminobutyrate metabolism and amino acid levels in rat brain following chronic oral administration of ethanolamine O-sulphate. J Neurochem 1982 Apr;38(4):1022-8

Fletcher DR, Blackburn AM, Adrian TE, et al: Effect of neurotensin on pancreatic function in man. Life Sci 1981 Nov 23;29(21):2157-61

Flicker C, Geyer MA: Behavior during hippocampal microinfusions I. Norepinephrine and diversive exploration. Brain Res 1982 Mar; 257(1):79-103

Flick JR, Pitt BR, Hammond GL, et al: Selective effect of microembolization on pulmonary removal of biogenic amines. J Appl Physiol 1982 Feb;52(2):421-7

Flint RS, Rea MA, McBride WJ: In vitro release of endogenous amino acids from granule cell-, stellate cell-, and climbing fiber-deficient cerebella. J Neurochem 1981 Dec;37(6):1425-30

Fokina AA, Klimov PK, Shvachkin IuP, et al: Vliianie somatostatina na sekretsiiu podzheludochnoi zhelezy u sobak. Fiziol Zh SSSR 1981 Nov; 67(11):1737-9 **(Rus)**

Folks DG, King LD, Dowdy SB, et al: Carbamazepine treatment of selected affectively disordered inpatients. Am J Psychiatry 1982 Jan;139(1):115-7

Fong JC, Okada K, Goldstein M: The effect of GTP on benzodiazepine receptors. Eur J Pharmacol 1982 Jan 8;77(1):57-9

Fonnum F, Henke H: The topographical distribution of alanine, aspartate, gamma-aminobutyric acid, glutamate, glutamine, and glycine in the pigeon optic tectum and the effect of retinal ablation. J Neurochem 1982 Apr;38(4):1130-4

Fontana A, Dalzoppo D, Grandi C, et al: Chemical cleavage of tryptophanyl and tyrosyl peptide bonds via oxidative halogenation mediated by o-iodosobenzoic acid. Biochemistry 1981 Nov 24; 20(24):6997-7004

Forchetti CM, Marco EJ, Meek JL: Serotonin and gamma-aminobutyric acid turnover after injection into the median raphe of substance P and D-ala-met-enkephalin amide. J Neurochem 1982 May;38(5):1336-41

Forman LJ, Sonntag WE, Van Vugt DAU, et al: Immunoreactive beta-endorphin in the plasma, pituitary and hypothalamus of young and old male rats. Neurobiol Aging 1981 Winter;2(4):281-4

Fornal C, Radulovacki M: Sleep suppressant action of quipazine: relation to central serotonergic stimulation Pharmacol Biochem Behav 1981 Dec;15(6):937-44

Forni C: Realization of a new multifiber electrochemical device allowing continuous in vivo measurements of neuromediators. J Neurosci Methods 1982 Jan;5(1-2):167-71

Foster SD: MCN pharmacopoeia. Bromocriptine: suppressing lactation. MCN 1982 Mar-Apr;7(2):99

Fouks L: Le lorazépam. Bilan d'une large utilisation. Agressologie 1981 Oct;22(C):51-3 **(Fre)**

Fowler CJ, Tipton KF: Deamination of 5-hydroxytryptamine by both forms of monoamine oxidase in the rat brain. J Neurochem 1982 Mar; 38(3):733-6

Frankel BJ, Heldt AM, Grodsky GM: Effects of K+ and arginine on insulin, glucagon, and somatostatin release from the in vitro perfused rat pancreas. Endocrinology 1982 Feb;110(2):428-31

Fraser HM: Effect of oestrogen on gonadotrophin release in stumptailed monkeys (Macaca arctoides) treated chronically with an agonist analogue of luteinizing hormone releasing hormone. J Endocrinol 1981 Dec;91(3):525-30

Fraser HM: A new class of contraceptives? [news] Nature 1982 Apr 1; 296(5856):391-2

Freedman SB, Mustafa AA, Poat JA, et al: A study on the localization of [3H]sulpiride binding sites in rat striatal membranes. Neuropharmacology 1981 Dec;20(12A):1151-5

Freedman SB, Poat JA, Woodruff GN: [3H]Sulpiride, a ligand for neuroleptic receptors. Neuropharmacology 1981 Dec;20(12B):1323-6

Freedman SB, Poat JA, Woodruff GN: Influence of sodium and sulphydryl groups on [3H]sulpiride binding sites in rat striatal membranes. J Neurochem 1982 May;38(5):1459-65

Freeman WK, Rorie DK, Tyce GM: Effects of 5-hydroxytryptamine on neuroeffector junction in human pulmonary artery. J Appl Physiol 1981 Sep;51(3):693-8

Fried JM: Antipsychotic drugs and the noninstitutionalized patient: a leap into the future or the past? J Clin Psychopharmacol 1981 Sep;1(5):323-5

Fuchs V, Coper H: Modification of the drug talking behavior in rats by interference in the metabolism of 5-hydroxytryptamine and catecholamines. Drug Alcohol Depend 1981 Nov;8(3):235-44

Fuder H, Rink D, Muscholl E: Sympathetic Nerve Stimulation on the perfused rat heart. Affinities of N-methylatropine and pirenzepine at pre- and postsynaptic muscarine receptors. Naunyn Schmiedebergs Arch Pharmacol 1982 Feb;318(3):210-9

Fujimoto M, Hirai K, Okabayashi T: Comparison of the effects of GABA and chloride ion on the affinities of ligands for the benzodiazepine receptor. Life Sci 1982 Jan 4;30(1):51-7

Fujimoto S, Sasa M, Takaori S: Dopaminergic inhibition from substantia nigra of caudate neurons activated by cortical stimulation. Jpn J Pharmacol 1981 Dec;31(6):1037-42

Fujioka H, Tan T: Biopharmaceutical studies on hydantoin derivatives. I. Physico-chemical properties of hydantoin derivatives and their intestinal absorption. J Pharmacobiodyn 1981 Oct;4(10):759-70

Fujita P: Treatment of tricyclic poisoning [letter] Pediatrics 1981 Dec; 68(6):912

Fuller RW, Snoddy HD: Repeated administration of pergolide to rats attenuates the acute elevation of serum corticosterone by pergolide. Pharmacol Biochem Behav 1981 Dec;15(6):933-6

G

Gabryelewicz A, Prokopowicz J, Hnidec O, et al: Wpływ przewlekłego stosowania somatostatyny na układ hemostazy u psa. Przegl Lek 1981; 38(10):719-21 (Eng. Abstr.) **(Pol)**

Gaitonde MK, Lewis LP, Evans G, et al: The effect of 6-aminonicotinamide on the levels of brain amino acids and glucose, and their labeling with 14C after injection of [U-14C] glucose. Neurochem Res 1981 Oct;6(10):1159-67

Gal EM: Cerebral fluoride in mania and the effect of lithium: a hypothesis. Commun Psychopharmacol 1980;4(5):405-9

Gale K: Evidence for GABA receptors on serotonergic afferent terminals in the substantia nigra aad on nigral efferent projections to the caudal mesencephalon. Brain Res 1982 Jan 7;231(1):209-15

Gallicchio VS, Chen MG: Influence of lithium on proliferation of hematopoietic stem cells. Exp Hematol 1981 Aug;9(7):804-10

Gambert SR, Garthwaite TL, Pontzer CH, et al: Running elevates plasma beta-endorphin immunoreactivity and ACTH in untrained human subjects. Proc Soc Exp Biol Med 1981 Oct;168(1):1-4

Gandhi DN, Gulati OD, Hemavathi KG: Blockade of 5-hydroxytryptamine-induced responses of rat seminal vesicle by lithium-possible mediation through calcium exchange.. Arch Int Pharmacodyn Ther 1981 Oct;253(2):220-32

AUTHOR SECTION

Garattini S: Central mechanisms of fenfluramine and related anorectic drugs. Jpn J Pharmacol 1981;31 Suppl:29P–35P (26 ref.)

García Sacristán A, Vela R, Illera M: Respuesta ureteral por estimulación adrenérgica a la acción de la progesterona y el estradiol. Arch Farmacol Toxicol 1981 Apr;7(1):129–32 **(Spa)**

Gardner CR, Klein J, Grove J: Endogenous GABA determines the characteristics of [3H]GABA–binding. Eur J Pharmacol 1981 Oct 22; 75(2–3):83–92

Gardner CR, Roberts CJ, Walker RJ, et al: The activity of cis and trans –2– (aminomethyl) cyclopropane carboxylic acids on GABA – related mechanisms in the central nervous system of Limulus and Periplanata and of mammals. Neuropharmacology 1982 Feb;21(2):197–200

Garnier F, Benoit E: T4 plasmatique: adaptation au chien d'un dosage radio–immunologique du commerce. Ann Biol Clin (Paris) 1981; 39(6):369–70 **(Fre)**

Garreau B, Domenech J, Martineau J, et al: HVA and MHPG in urine of premature infants. Psychiatry Res 1981 Dec;5(3):323–30

Gasanov GG, Melikov EM, Ibragimov RS: Effect of serotonin injected into the amygdala on conditioned and unconditioned food reflexes and the EEG in cats. Neurosci Behav Physiol 1981 May–Jun;11(3):207–12

Gasco MR, Trotta M, Carlotti ME: Effect of carboxylic acids on permeation of chlorpromazine through dimethyl polysiloxane membrane. J Pharm Sci 1982 Feb;71(2):239–41

Gascon–Barré M, Delvin EE, Glorieux FH, et al: Influence of vitamin D3 status, phenobarbital, and diphenylhydantoin treatment on the plasma 25–hydroxyvitamin D3 concentrations in the rat. Can J Physiol Pharmacol 1981 Oct;59(10):1073–81

Gasparro FP, Kochevar IE: Investigation of protriptyline photoproducts which cause cell membrane disruption. Photochem Photobiol 1982 Mar; 35(3):351–8

Gaugas JM: Potent inhibition of diamine oxidase with the hydroxybenzyloxamines NSD–1039, NSD–1531 and NSD–1024. Biochem Pharmacol 1981 Nov 15;30(22):3121–2

Gautron JP, Pattou E, Kordon C: Occurrence of higher molecular forms of LHRH in fractionated extracts from rat hypothalamus, cortex and placenta. Mol Cell Endocrinol 1981 Oct;24(1):1–15

Gawienowski AM, Chatterjee D, Anderson PJ, et al: Effect of delta 9–tetrahydrocannabinol on monoamine oxidase activity in bovine eye tissues, in vitro. Invest Ophthalmol Vis Sci 1982 Apr;22(4):482–5

Gayte–Sorbier A, Airaudo CB: Etude spectrofluorimétrique des dérivés de la phénothiazine. II. Dérivés non substitués en 2 et portant en 10 une substitution alkylhétérocyclique. Ann Pharm Fr 1981;39(5):435–43 (Eng. Abstr.) **(Fre)**

Geary LE, Wiley KS, Scott WL, et al: Degradation of exogenous enkephalin in the guinea–pig ileum: relative importance of aminopeptidase, enkephalinase and angiotensin converting enzyme activity. J Pharmacol Exp Ther 1982 Apr;221(1):104–11

Gębala A, Szajner–Milart I, Zajączkowska M: Role of some biogenic amines in the pathomechanism of glomerulonephritis. II. Adrenaline, noradrenaline and serotonin in acute serum sickness in rabbits. Acta Physiol Pol 1981;32(4):363–73

Geffaru M, Gaffori O, Chauveau J, et al: Dramatic increase in pineal melatonin levels in the rat after subcutaneous injection of Des–tyrosine1–gamma–endorphin. Neurosci Lett 1981 Dec 23; 27(3):329–34

Geller I, Hartmann RJ, Messiha FS: Blockade of 5–HTp reduction of ethanol drinking with the decarboxylase inhibitor, ro 4–4602. Pharmacol Biochem Behav 1981 Dec;15(6):871–4

Geller JL: Sustaining treatment with the hospitalized patient who refuses treatment. Am J Psychiatry 1982 Jan;139(1):112–3

Gemberling GA, Domjan M: Selective associations in one–day–old rats: taste–toxicosis and texture–shock aversion learning. J Comp Physiol Psychol 1982 Feb;96(1):105–13

Genazzani AR, Facchinetti F, Ricci–Danero MG, et al: Beta–lipotropin and beta–endorphin in physiological and surgical menopause. J Endocrinol Invest 1981 Oct–Dec;4(4):375–8

Gentile NT, Friedman HA, Vogel WH: Behavioral effects and physiological disposition of some beta–hydroxylated indoleamines in the rat. Biol Psychiatry 1982 Jan;17(1):109–13

Gentsch C, Lichtsteiner M, Feer H: 3H–Diazepam binding sites in Roman high– and low–avoidance rats. Experientia 1981 Dec 15;37(12):1315–6

George SR, Van Loon GR: Characterization of high affinity dopamine uptake into the dopamine neurons of the hypothalamus. Brain Res 1982 Feb 25;234(2):339–55

George ST, Balasubramanian AS: The aryl acylamidases and their relationship to cholinesterases in human serum, erythrocyte and liver. Eur J Biochem 1981 Dec;121(1):177–86

Geraci JR, Skirnisson K, St. Aubin DJ: A safe method for repeatedly immobilizing seals. J Am Vet Med Assoc 1981 Dec 1;179(11):1192–3

Gerdin B: Use of 125I–labeled human serum albumin for quantitation of microvascular permeability in rat skin: reevaluation of an old method for studies on substances with an enhancing effect on microvascular permeability. J Pharmacol Methods 1981 Nov;6(3):167–75

Gereliuk IP: Vzaimosviaz' mezhdu soderzhaniem svobodnykh zhirnykh kislot v krovi i nakopleniem trombotsitov v krovenosnom rusle miokarda pri vvedenii adrenalina. Biull Eksp Biol Med 1981 Dec;92(12):661–3 (Eng. Abstr.) **(Rus)**

Gerritsen ME, Morgan DO, Parks TP, et al: A proposed role for prostaglandins in the modulation of the relaxation response to urotensin I in isolated rat arteries. Prostaglandins 1981 Dec;22(6):873–92

Gershon MD, Sherman DL: Identification of and interactions between noradrenergic and serotonergic neurites in the myenteric plexus. J Comp Neurol 1982 Feb 1;204(4):407–21

Gershon MD, Tamir H: Release of endogenous 5–hydroxytryptamine from resting and stimulated enteric neurons. Neuroscience 1981;6(11):2277–86

Gespach C, Bataille D, Dutrillaux MC, et al: The interaction of glucagon, gastric inhibitory peptide and somatostatin with cyclic AMP production systems present in rat gastric glands. Biochim Biophys Acta 1982 Feb 10;720(1):7–16

Getsova VM: Effect of serotonin on formation and fixation of various conditioned reflexes. Neurosci Behav Physiol 1981 May–Jun;11(3):280–5

Ghetti B, Fuller RW, Sawyer BD, et al: Purkinje cell loss and the noradrenergic system in the cerebellum of pcd mutant mice. Brain Res Bull 1981 Dec;7(6):711–4

Ghiselli G, Bernini F, Musanti R, et al: Effect of L–propranolol on the binding, Internalization and degradation of 125I–low density lipoproteins by human skin fibroblasts. Biochem Biophys Res Commun 1981 Dec 15;103(3):1060–8

Giammona G, Patti F, Sambataro V, et al: Effetti di differenti dosi di apomorfina sull'attività glutamato decarbossilasi nella sostanza nera e nell'ipotalamo medio basale. Boll Soc Ital Biol Sper 1981 Oct 30; 57(20):2074–9 (Eng. Abstr.) **(Ita)**

Gibberd FB, Spencer KM, Webley M, et al: A comparison of the bioavailability of two brands of phenytoin. Br J Clin Pharmacol 1982 Mar;13(3):455–6

Gibson GE, Peterson C: Aging decreases oxidative metabolism and the release and synthesis of acetylcholine. J Neurochem 1981 Oct; 37(4):978–84

Gibson GE, Peterson C: Decreases in the release of acetylcholine in vitro with low oxygen. Biochem Pharmacol 1982 Jan 1;31(1):111–5

Gielsdorf W, Schubert K: Zum Stoffwechsel des Doxylamin: Isolierung, Identifizierung und Syntheseeiniger Metabolite. J Clin Chem Clin Biochem 1981 Jul;19(7):485–90 (Eng. Abstr.) **(Ger)**

Giger U, Meyer UA: Role of haem in the induction of cytochrome P-450 by phenobarbitone. Studies in chick embryos in ovo and in cultured chick embryo hepatocytes. Biochem J 1981 Aug 15;198(2):321–9

Giguère V, Côtoé J, Labrie F: Specific inhibition by glucocorticoids of the alpha 2–adrenergic stimulation of adrenocorticotropin release in rat anterior pituitary cells. Endocrinology 1982 Apr;110(4):1225–30

Gilbert RF, Bennett GW, Marsden CA, et al: The effects of 5–hydroxytryptamine–depleting drugs on peptides in the ventral spinal cord. Eur J Pharmacol 1981 Dec 3;76(2–3):203–10

Giller E, Bialos D, Riddle M, et al: Monoamine oxidase inhibitor–responsive depression. Psychiatry Res 1982 Feb;6(1):41–8

Gingerich DA, Mia AS: Clinical toxicosis and erythrocyte cholinesterase inhibition of trichlorfon combined with mebendazole in horses. Am J Vet Res 1981 Sep;42(9):1645–50

Giorgi O, Rubio MC: Decreased 3H–L–quinuclidinyl benzilate binding and muscarine receptor subsensitivity after chronic gamma–butyrolactone treatment. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(1):14–8

Gitsch E, Schneider WH, Schmid R, et al: Die hypophysäre Reaktionslage unter oralen Kontrazeptiva. Wien Klin Wochenschr 1981 Oct 16; 93(19):599–601 (Eng. Abstr.) **(Ger)**

Gledhill B, Fraser HM, Donovan BT: Effect of passive immunization against LH–RH on gonadotropin secretion in the ferret. J Reprod Fertil 1982 Jan;64(1):19–23

Glennon RA, Rosecrans JA, Young R: Behavioral properties of psychoactive phenylisopropylamines in rats. Eur J Pharmacol 1981 Dec 17;76(4):353–60

Glennon RA, Young R, Benington F, et al: Hallucinogens as discriminative stimuli: a comparison of 4–OMe DMT and 5–OMe DMT with their methythio counterparts. Life Sci 1982 Feb 1;30(5):465–7

Glick SD, Ross DA, Hough LB: Lateral asymmetry of neurotransmitters in human brain. Brain Res 1982 Feb 18;234(1):53–63

Glickman RD, Adolph AR, Dowling JE: Inner plexiform circuits in the carp retina: effects of cholinergic agonists, GABA, and substance P on the ganglion cells. Brain Res 1982 Feb 18;234(1):81–99

Globus M, Lerer B, Hamburger R, et al: Chronic electroconvulsive shock and chronic haloperidol administration are not additive in effects on dopamine receptors. Neuropharmacology 1981 Nov;20(11):1125–8

Glöckner R, Klinger W: Influence of puromycin and chloramphenicol on aminoketone synthesis (delta–aminolevulinic acid synthesis) induction by allylisopropylacetamide in rat liver. Exp Pathol 1981;20(4):215–20

Glossmann H, Lübbecke F, Bellemann P, et al: Cation sensitivity of [125I]heat binding to alpha 1–adrenoceptors in rat cerebral cortex membranes. Eur J Pharmacol 1981 Oct 22;75(2–3):149–53

Glover JC, Kramer AP: Serotonin analog selectively ablates indentified neurons in the leech embryo. Science 1982 Apr 16;216(4543):317–9

Gode JD, Singh HC, Chandel AS, et al: Effect of immobilization stress & ascorbic acid on acetylcholine & plasma cortisol in albino rats. Indian J Exp Biol 1981 Dec;19(12):1175–6

AUTHOR SECTION

Goedert M, Otten U, Metz H: Endogenous opioid peptides. Bull Soc Sci Med Grand Duche Luxemb 1981;118(1):7–17

Goetze U, Tölle R: Antidepressive Wirkung des partiellen Schlafentzuges während der 1. Hälfte der Nacht. Psychiatr Clin (Basel) 1981; 14(3):129–49 (Eng. Abstr.) **(Ger)**

Goldberg D: Cognitive therapy for depression [editorial] Br Med J [Clin Res] 1982 Jan 16;284(6310):143–4

Goldhaber P, Rabadjija L: Effect of promethazine hydrochloride on bone resorption in tissue culture. Proc Soc Exp Biol Med 1982 Jan; 169(1):105–9

Goldstein BJ: Interaction of antacids with psychotropics. Hosp Community Psychiatry 1982 Feb;33(2):96

Goldszer F, Tindell GL, Walle UK, et al: Chemical trapping of labile aldehyde intermediates in the metabolism of propranolol and oxprenolol. Res Commun Chem Pathol Pharmacol 1981 Nov;34(2):193–205

Golus P, King MG: Arginine vasotocin: effects on open field behavior, whole brain monoamines and plasma corticosterone. Peptides (Fayetteville) 1981 Winter;2(4):437–40

Gomez-Sanchez CE, Gomez-Sanchez EP, Shackleton CH, et al: Identification of 19-hydroxydeoxycorticosterone, 19-oxo-deoxycorticosterone, and 19-oic-deoxycorticosterone as products of deoxycorticosterone metabolism by rat adrenals. Endocrinology 1982 Feb;110(2):384–9

Gonchar NA, Grebenshchikova OG, Komarova NV: Izuchenie roli triptofana v fermentativnoĭ aktivnosti gistidindekarboksilazy iz Micrococcus sp. n. Biokhimiia 1981 Nov;46(11):1970–80 (Eng. Abstr.) **(Rus)**

Goncharenko EN, Graevskaia EE, Sobolev AS, et al: Issledovanie vysvobozhdeniia serotonina in vivo tuchnymi kletkami pod vliianiem MEA. Radiobiologiia 1982 Jan–Feb;22(1):94–6 **(Rus)**

Gonzalez JL, Carpene C, Berlan M, et al: Discrepancy in the regulatory effects of sodium and guanine nucleotides on adrenaline and clonidine binding to alpha 2-adrenoceptors in human fat cell membranes. Eur J Pharmacol 1981 Dec 3;76(2–3):289–93

Good TJ, Andrews JS: The use of bonded-phase extraction columns for rapid sample preparation of benzodiazepines and metabolites from serum for HPLC analysis. J Chromatogr Sci 1981 Nov;19(11):562–6

Goode DJ, Manning AA, Middleton JF, et al: Fine motor performance before and after treatment in schizophrenic and schizoaffective patients. Psychiatry Res 1981 Dec;5(3):247–55

Goodnick PJ, Evans HE, Dunner DL, et al: Lithium and amino acids [letter] Am J Psychiatry 1982 Apr;139(4):538–9

Goodwin FK, Prange AJ Jr, Post RM, et al: Potentiation of antidepressant effects by L-triiodothyronine in tricyclic nonresponders. Am J Psychiatry 1982 Jan;139(1):34–8

Gordon CJ, Heath JE: Effect of beta-endorphin on the thermal excitability of preoptic neurons in the unanesthetized rabbit. Peptides (Fayetteville) 1981 Winter;2(4):397–401

Gorelick DA, Catlin DH, Gerner RH: beta-Endorphin studies in psychiatric patients. Mod Probl Pharmacopsychiatry 1981;17:236–45

Gorizontova MP, Gomazkov OA, Ignat'eva IR, et al: Vliianie veshchestva 'P' na sistemu mikrotsirkuliatsii bryzhelki. Biull Eksp Biol Med 1981 Nov;92(11):515–7 (Eng. Abstr.) **(Rus)**

Górny D, Miszczak M: Brain level and synthesis of acetylcholine during exposure to vibration and organic-phosphorus and phenol-derived pesticides. Acta Physiol Pol 1981;32(4):469–76

Gorsline J, Holmes WN: Effects of petroleum on adrenocortical activity and on hepatic naphthalene-metabolizing activity in mallard ducks. Arch Environ Contam Toxicol 1981 Nov;10(6):765–77

Goshima Y, Kaiho M, Misu Y: Dobutamine-induced facilitation of norepinephrine efflux from spiral strips of guinea pig pulmonary arteries. Jpn J Pharmacol 1981 Dec;31(6):1091–4

Göthert M, Huth H, Schlicker E: Characterization of the receptor subtype involved in alpha-adrenoceptor-mediated modulation of serotonin release from rat brain cortex slices. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov;317(3):199–203

Göthert M: ACTH1-24 increases stimulation-evoked noradrenaline release from sympathetic nerves by acting on presynaptic ACTH receptors. Eur J Pharmacol 1981 Dec 3;76(2–3):295–6

Goto M, Nakamura T, Ishii D: Micro high-performance liquid chromatographic system with micro precolumn and dual electrochemical detector for direct injection analysis of catecholamines in body fluids. J Chromatogr 1981 Nov 13;226(1):33–42

Goto M, Urata M, Yatani A, et al: Interaction of adenosine and acetylcholine on the bullfrog atrium. Jpn J Physiol 1981;31(4):501–13

Graber P, Hollan O, Kalahanis NG, et al: The effect of propranolol on insulin-stimulated gastric secretion in dogs. Scand J Gastroenterol 1981;16(8):1067–72

Grabowska-Hibner J, Stiasna I, Szukalski B: The influence of amitriptyline, imipramine and chlorpromazine on activity of arginase in rat's brain and liver. Mater Med Pol 1981 Jan–Mar;13(1):54–7

Graefe KH: The disposition of 3H-(–)noradrenaline in the perfused cat and rabbit heart. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec; 318(2):71–82

Gramsch C, Höllt V, Pasi A, et al: Immunoreactive dynorphin in human brain and pituitary. Brain Res 1982 Feb 4;233(1):65–74

Grandison L, Cavagnini F, Schmid R, et al: gamma-Aminobutyric acid- and benzodiazepine-binding sites in human anterior pituitary tissue. J Clin Endocrinol Metab 1982 Mar;54(3):597–601

Grant SJ, Redmond DE Jr: The Neuroanatomy and pharmacology of the nucleus locus coeruleus. Prog Clin Biol Res 1981;71:5–27

Grasela TH, Winter ME: Phenytoin pharmacokinetics: inappropriate data analysis. Am J Hosp Pharm 1982 Jan;39(1):41–3

Grau EG, Nishioka RS, Bern HA: Effects of somatostatin and urotensin II on tilapia pituitary prolactin release and interactions between somatostatin, osmotic pressure Ca++, and adenosine 3',5'-monophosphate in prolactin release in vitro. Endocrinology 1982 Mar;110(3):910–5

Gray JA: Anxiety as a paradigm case of emotion. Br Med Bull 1981 May; 37(2):193–7 (46 ref.)

Gray NM, Lu MC, Bhargava HN: The effects of stereoisomers of 2- and 9- aminobenzonorbornenes on food intake, brain serotonin concentration and monoamine oxidase activity in the rat. J Pharmacol Exp Ther 1982 Apr;221(1):58–62

Grecksch G, Matthies H: The role of dopaminergic mechanisms in the rat hippocampus for the consolidation in a brightness discrimination. Psychopharmacology (Berlin) 1981;75(2):165–8

Grecksch G, Schweigert C, Matthies H: Evidence for analgesic activity of beta-casomorphin in rats. Neurosci Lett 1981 Dec 23;27(3):325–8

Green K, Roth M: Ocular effects of topical administration of delta 9-tetrahydrocannabinol in man. Arch Ophthalmol 1982 Feb; 100(2):265–7

Green K, Lollis G: Response of the isolated rabbit ciliary epithelium to adrenergic drugs following superior cervical ganglionectomy. Curr Eye Res 1981;1(4):217–22

Greenberg RN, Murad F, Guerrant RL: Lanthanum chloride inhibition of the secretory response to Escherichia coli heat-stable enterotoxin. Infect Immun 1982 Feb;35(2):483–8

Greenblatt DJ, Divoll M, Puri SK, et al: Clobazam kinetics in the elderly. Br J Clin Pharmacol 1981 Nov;12(5):631–6

Greenblatt DJ, Divoll M, Harmatz JS, et al: Pharmacokinetic comparison of sublingual lorazepam with intravenous, intramuscular, and oral lorazepam. J Pharm Sci 1982 Feb;71(2):248–52

Greenwood DT, Kemp JD, Middlemiss DN: Stereospecificity of behavioural effects of viloxazine in bulbectomized rats does not correlate with its 5-HT-releasing action in vitro. J Pharm Pharmacol 1982 Jan; 34(1):38–41

Gribakin FG, Chesnokova EG: Izmenenie funktsional'nykh kharakteristik slozhnogo glaza medonosnoĭ pchely vsledstvie mutatsiĭ, narushaiushchikh obmen triptofana. Neirofiziologiia 1982;14(1):69–75 (Eng. Abstr.) **(Rus)**

Griffith SG, Crowe R, Lincoln J, et al: Regional differences in the density of perivascular nerves and varicosities, noradrenaline content and responses to nerve stimulation in the rabbit ear artery. Blood Vessels 1982 Jan–Feb;19(1):41–52

Griffiths EC, McDermott JR, Smith AI: Inactivation of thyrotropin-releasing hormone (TRH) and (3Me-His) TRH by brain peptidases studied by high-performance liquid chromatography. Neurosci Lett 1982 Jan 22;28(1):61–5

Griffiths RR, Ator NA: Benzodiazepine self-administration in animals and humans: a comprehensive literature review. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):22–36 (40 ref.)

Griffiths RR, Lukas SE, Bradford LD, et al: Self-injection of barbiturates and benzodiazepines in baboons. Psychopharmacology (Berlin) 1981; 75(2):101–9

Grimaldi S, Edelhoch H, Robbins J: Effects of thyroxine binding on the stability, conformation, and fluorescence properties of thyroxine-binding globulin. Biochemistry 1982 Jan 5;21(1):145–51

Gromova EA, Isabaeva VA, Semenova TP, et al: Izmeneniia aktivnosti monoaminergicheskikh sistem mozga v usloviiakh adaptatsii k vysokogor'iu. Dokl Akad Nauk SSSR 1982;262(1):245–7 **(Rus)**

Gromova EA, Katkov IuA, Kalmykov VL, et al: Obuchenie krys s razlichnoĭ émotsional'noĭ reaktivnost'iu i ee s monoaminami mozga. Zh Vyssh Nerv Deiat 1981 Nov–Dec;31(6):1238–46 (Eng. Abstr.) **(Rus)**

Grosman N: Histamine release from human basophils and isolated rat mast cells induced by ketobemidone, pethidine and the spasmolytic A29. Acta Pharmacol Toxicol (Copenh) 1982 Jan;50(1):78–80

Gross G, Göthert M, Ender HP, et al: 3H-Imipramine binding sites in the rat brain. Selective localization on serotoninergic neurones. Naunyn Schmiedebergs Arch Pharmacol 1981;317(4):310–4

Gross HA, Ebert MH, Faden VB, et al: A double-blind controlled trial of lithium carbonate primary anorexia nervosa. J Clin Psychopharmacol 1981 Nov;1(6):376–81

Gross SJ: Detection of tetrahydrocannabinol in blood [letter] J Anal Toxicol 1981 Sep–Oct;5(5):257–8

Grossman SH, Davis D, Kitchell BB, et al: Diazepam and lidocaine plasma protein binding in renal disease. Clin Pharmacol Ther 1982 Mar; 31(3):350–7

Grote B, Doenicke A, Kugler J, et al: Intramuskuläre Applikation von Midazolam. Wirkung auf ZNS und Atmung. Arzneimittelforsch 1981; 31(12a):2224–5 (Eng. Abstr.) **(Ger)**

AUTHOR SECTION

Grote B, Doenicke A, Kugler J, et al: Die antagonistische Wirkung von Physostigmin auf die Sedierung durch Lormetazepam. Anaesthesist 1981 Dec;30(12):627-32 (Eng. Abstr.) (Ger)

Grundström N, Andersson RG, Wikberg JE: Investigations on possible presynaptic effect of adenosine and noradrenaline on cholinergic neurotransmission in guinea pig trachea.
Acta Pharmacol Toxicol (Copenh) 1981 Aug;49(2):158-60

Grynszpan-Winograd O: Close relationship of mitochondria with intercellular junctions in the adrenaline cells of the mouse adrenal gland. Experientia 1982 Feb 15;38(2):270-1

Grzesiczak A, Ladwicki H, Ostrowska Z: Badanie uwalniania substancji czynnych z podłoży czopkowych. Acta Pol Pharm 1981;38(4):493-7 (Eng. Abstr.) (Pol)

Gualtieri CT, Kanoy R, Hawk B, et al: Growth hormone and prolactin secretion in adults and hyperactive children: relation to methylphenidate serum levels. Psychoneuroendocrinology 1981 Dec;6(4):331-9

Gubler U, Seeburg P, Hoffman BJ, et al: Molecular cloning establishes proenkephalin as precursor of enkephalin-containing peptides.
Nature 1982 Jan 21;295(5846):206-8

Guensberger E, Molcan J: A propos de la psychopathologie de l'anxiété. Agressologie 1981 Oct;22(C):31-3 (Eng. Abstr.) (Fre)

Guerrero-Muñoz F, Adames C, Fearon Z, et al: Calcium-opiate antagonism in the periaqueductal grey (PGA) region. Eur J Pharmacol 1981 Dec 17;76(4):417-9

El-Guindy MM, Neder AC, Gomes CB: 2,4-Dinitrophenol—mechanism of action. Cell Mol Biol 1981;27(5):399-402

Güllner HG, Lakatua DJ, Bartter FC: Effect of inhibition of prostaglandin synthesis on urinary free dopamine excretion in women. Clin Sci 1982 Feb;62(2):209-13

Gupta C, Yaffe SJ: Reproductive dysfunction in female offspring after prenatal exposure to phenobarbital: critical period of action.
Pediatr Res 1981 Dec;15(12):1488-91

Gupta SP, Singh P, Bindal MC: Correlation of inhibitory activity of tryptamine derivatives on serotonin uptake in thrombocyte with van der Waals volume. Arzneimittelforsch 1981;31(12):2053-5

Gutschmidt S, Emde C: Early changes in brush border disaccharidase kinetics in rat jejunum following subcutaneous administration of tetraiodothyronine: a quantitative histochemical study on villi revealing normal morphology. Histochemistry 1981;73(1):151-60

H

Haapanen EJ, Pellinen TJ: Hemoperfusion in quinidine intoxication.
Acta Med Scand 1981;210(6):515-6

Habermann E: Tetanus toxin and botulinum A neurotoxin inhibit and at higher concentrations enhance noradrenaline outflow from particulate brain cortex in batch. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(2):105-11

Hadjian AJ, Guidicelli C, Chambaz EM: Cholinergic muscarinic stimulation of steroidogenesis in bovine adrenal cortex fasciculata cell suspensions. Biochim Biophys Acta 1982 Jan 12;714(1):157-63

Hahn RA, Hynes MD, Fuller RW: Apomorphine-induced aggression in rats chronically treated with oral clonidine: modulation by central serotonergic mechanisms. J Pharmacol Exp Ther 1982 Feb; 220(2):389-93

Hailey DM, Lea AR, Coles DM, et al: Absorption of quinidine and dihydroquinidine in humans. Eur J Clin Pharmacol 1981;21(3):195-9

Hainer V, Urbánek J, Malec B, et al: The effect of TRH, cyproheptadine and pimozide on the growth hormone response to intramuscular glucagon. Horm Metab Res 1981 Aug;13(8):451-3

Halas ES, Wallwork JC, Sandstead HH: Mild zinc deficiency and undernutrition during the prenatal and postnatal periods in rats: effects on weight, food consumption, and brain catecholamine concentrations.
J Nutr 1982 Mar;112(3):542-51

Hall ED, Braughler JM: Thyrotropin-releasing hormone for spinal trauma [letter] N Engl J Med 1982 Feb 18;306(7):429-30

Hall TR: Neurotransmitter effects on release of prolactin and growth hormone in vitro from pituitary glands of the pigeon, Columba livia.
J Endocrinol 1982 Feb;92(2):303-8

Hallett MB, Luzio JP, Campbell AK: Stimulation of Ca2+-dependent chemiluminescence in rat polymorphonuclear leucocytes by polystyrene beads and the non-lytic action of complement. Immunology 1981 Nov; 44(3):569-76

Hällgren R, Venge P, Wistedt B: Elevated serum levels of lactoferrin and eosinophil cationic protein in schizophrenic patients.
Br J Psychiatry 1982 Jan;140:55-60

Hallstrom C, Treasaden I, Edwards JG, et al: Diazepam, propranolol and their combination in the management of chronic anxiety.
Br J Psychiatry 1981 Nov;139:417-21

Hammer JA 3d, Rannels DE: Protein turnover in pulmonary macrophages. Utilization of amino acids derived from protein degradation.
Biochem J 1981 Jul 15;198(1):53-65

Hammond DL, Yaksh TL, Tyce GM: Presence of conjugated 5-hydroxytryptamine in in vivo superfusates of rat spinal cord.
J Neurochem 1981 Oct;37(4):1068-71

Hammond JR, Paterson AR, Clanachan AS: Benzodiazepine inhibition of site-specific binding of nitrobenzylthioinosine, an inhibitor of adenosine transport. Life Sci 1981 Nov 23;29(21):2207-14

Hammond WP, Dale DC: Cyclic hematopoiesis: effects of lithium on colony-forming cells and colony-stimulating activity in grey collie dogs. Blood 1982 Jan;59(1):179-84

Hammonds RG Jr, Hammonds AS, Ling N, et al: beta-Endorphin and deletion peptides. A correlation of opiate receptor affinity with helix potential. J Biol Chem 1982 Mar 25;257(6):2990-5

Hanew K, Sasaki A, Yoshinaga K: Evidence for endogenous dopaminergic control of GH release in man. Tohoku J Exp Med 1981 Sep;135(1):103-8

Hanin I, Mallinger AG, Kopp U, et al: Mechanism of lithium-induced elevation in red blood cell choline content: an in vitro analysis.
Commun Psychopharmacol 1980;4(5):345-55

Haning RV Jr, Choi L, Kiggens AJ, et al: Effects of dibutyryl cAMP, LHRH, and aromatase inhibitor on simultaneous outputs of prostaglandin F2 alpha, and 13,14-dihydro-15-keto-prostaglandin F2 alpha by term placental explants. Prostaglandins 1982 Jan;23(1):29-40

Hansen BC, Schielke GP, Jen KL, et al: Rapid fluctuations in plasma catecholamines in monkeys under undisturbed conditions.
Am J Physiol 1982 Jan;242(1):E40-6

Hansen HE, Mogensen CE, Sørensen JL, et al: Albumin and beta 2-microglobulin excretion in patients on long-term lithium treatment. Nephron 1981;29(5-6):229-32

Hansen HE: Renal toxicity of lithium. Drugs 1981 Dec;22(6):461-76 (96 ref.)

Harasiewicz A, Kolasiewicz W: Thalamic mediation of impulses arriving from the substantia nigra. Pol J Pharmacol Pharm 1981;33(4):421-9

Hardcastle J, Hardcastle PT, Redfern JS: Action of 5-hydroxytryptamine on intestinal ion transport in the rat. J Physiol (Lond) 1981 Nov; 320:41-55

Hardin TC, Conrath FC: Desipramine-induced agranulocytosis. A case report. Drug Intell Clin Pharm 1982 Jan;16(1):62-3

Hardt W, Schmidt-Gollwitzer M, von der Ohe M, et al: Der Einfluss der Dauer-medikation des LH-RH-Analogons Buserelin auf die Zyklusregulation. Geburtshilfe Frauenheilkd 1981 Nov;41(11):791-6 (Eng. Abstr.) (Ger)

Hardy WT, Westbrook RF: Lithium-induced polydipsia in birds: a comparative study and analysis of electrolyte excretion.
Physiol Behav 1981 Oct;27(4):575-83

Harmar A, Keen P: Synthesis, and central and peripheral axonal transport of substance P in a dorsal root ganglion-nerve preparation in vitro. Brain Res 1982 Jan 14;231(2):379-85

Harris JP, Phillipson OT: Chlorpromazine reduces the perceptual ambiguity of a reversible visual figure. Neuropharmacology 1981 Dec; 20(12B):1337-8

Harris RN, Anders MW: 2-Propanol treatment induces selectively the metabolism of carbon tetrachloride to phosgene. Implications for carbon tetrachloride hepatotoxicity. Drug Metab Dispos 1981 Nov-Dec; 9(6):551-6

Harrison DE, Ashcroft SJ: Effects of Ca2+, calmodulin and cyclic AMP on the phosphorylation of endogenous proteins by homogenates of rt islets of langerhans. Biochim Biophys Acta 1982 Feb 2;714(2):313-9

Harrison GA, Palmer CD, Jenner DA, et al: Associations between rates of urinary catecholamine excretion and aspects of lifestyle among adult women in some Oxfordshire villages. Hum Biol 1981 Dec;53(4):617-33

Harrison J: Endorphins and legal issues. J Leg Med (Chicago) 1981 Dec; 2(4):543-68

Harsing LG Jr, Yang HY, Costa E: Evidence for a gamma-aminobutyric acid (GABA) mediation in the benzodiazepine inhibition of the release of Met5-enkephalin elicited by depolarization.
J Pharmacol Exp Ther 1982 Mar;220(3):616-20

Harsing LG Jr, Yang HY, Govoni S, et al: Elevation of Met5-enkephalin and beta-endorphin hypothalamic content in rats receiving anorectic drugs: differences between D-fenfluramine and D-amphetamine.
Neuropharmacology 1982 Feb;21(2):141-5

Harvey DJ: The mass spectra of the trimethylsilyl derivatives of the hydroxy and acid metabolites of delta 1- and delta 6-tetrahydrocannabinol. Biomed Mass Spectrom 1981 Dec;8(12):579-88

Hasan F, Leonard BE: Studies on the action of (+/-)sulpiride on dopamine receptors in the rat brain in vivo. Neuropharmacology 1981 Dec;20(12B):1327-30

Hasan MK, Mooney RP: Establishing lithium clinics in office practice. Postgrad Med 1982 Feb;71(2):182, 186, 190

Hashimoto K, Ohno N, Aoki Y, et al: Distribution and characterization of corticotropin-releasing factor and arginine vasopressin in rat hypothalamic nuclei. Neuroendocrinology 1982 Jan;34(1):32-7

Hassler R, Haug P, Nitsch C, et al: Effect of motor and premotor cortex ablation on concentrations of amino acids, monoamines, and acetylcholine and on the ultrastructure in rat striatum. A confirmation of glutamate as the specific cortico-striatal transmitter.
J Neurochem 1982 Apr;38(4):1087-98

Haubrich DR, Martin GE, Pflueger AB, et al: Neurotensin effects on brain dopaminergic systems. Brain Res 1982 Jan 7;231(1):216-21

Haubrich DR, Williams M, Yarbrough GG, et al: 2-chloroadenosine inhibits brain acetylcholine turnover in vivo.

AUTHOR SECTION

Can J Physiol Pharmacol 1981 Nov;59(11):1196-8

Haug T, Götestam KG: Two opposite effects of diazepam on fear by differential training in the CER-paradigm. Psychopharmacology (Berlin) 1981;75(2):110-3

Haugeto OK, Schrøder KE, Mair IW: Secretory otitis media, oral decongestant and antihistamine. J Otolaryngol 1981 Oct;10(5):359-62

Hauser G, Smith TL: Characteristics of the norepinephrine-stimulated phosphatidylinositol turnover in rat pineal cell dispersions. Neurochem Res 1981 Oct;6(10):1067-79

Hayashi H, Ohsumi K, Ueda N, et al: Effect of spinal ganglionectomy on substance P-like immunoreactivity in the gastroduodenal tract of cats. Brain Res 1982 Jan 28;232(1):227-30

Hayashi Y, Watanabe H, Okudaira N, et al: [The effects of butoctamide hydrogen succinate (BAHS) on the sleep of the aged people (author's transl)] No To Shinkei 1981 Dec;33(12):1243-50 (Eng. Abstr.) **(Jpn)**

Haynes LW, Smyth DG, Zakarian S: Immunocytochemical localization of beta-endorphin (lipotropin C-fragment) in the developing rat spinal cord and hypothalamus. Brain Res 1982 Jan 28;232(1):115-28

Heal DJ, Atterwill CK: Repeated administration of triiodothyronine (T3) to rats enhances nigrostriatal and mesolimbic dopaminergic behavioural responses. Neuropharmacology 1982 Feb;21(2):159-62

Heaslip RJ, Rahwan RG: Evidence for the existence of two distinct pools of intracellular calcium in the rat aorta accessible to mobilization by norepinephrine. J Pharmacol Exp Ther 1982 Apr;221(1):7-13

Hecht K, Oehme P, Ljowschina IP, et al: Zur Wirkungsdauer des normalisierenden Effektes von Substanz P bei Lernstörungen nach chronischer Lärmbelastung. Pharmazie 1981 Dec;36(12):859-60 **(Ger)**

Hecker LI, McClusky GA: Comparison of the in vitro metabolism of N-nitrosohexamethyleneimine by rat liver and lung microsomal fractions. Cancer Res 1982 Jan;42(1):59-64

Hede AR, Post C: Halothane inhibits the pulmonary clearance of 5-hydroxytryptamine in isolated perfused rat lungs [letter] Acta Pharmacol Toxicol (Copenh) 1981 Sep;49(3):239-40

Hedner J, Hedner T, Jonason J, et al: GABA-ergic mechanisms in central respiratory control in the anesthetized rat. Naunyn Schmiedebergs Arch Pharmacol 1981;317(4):315-20

Heggli DE, Aamodt A, Malthe-Sørenssen D: Kainic acid neurotoxicity; effect of systemic injection on neurotransmitter markers in different brain regions. Brain Res 1981 Dec 28;230(1-2):253-62

Heicklen J, Meagher JF, Weaver J, et al: Toxicological testing of rats subjected to inhalation of diethylhydroxylamine, nitroethane, and diethylamine hydrogen sulfite. Environ Res 1981 Dec;26(2):258-73

Heikkila RE, Cabbat FS, Manzino L: Differential inhibitory effects of ascorbic acid on the binding of dopamine agonists and antagonists to neostriatal membrane preparations: correlations with behavioral effects. Res Commun Chem Pathol Pharmacol 1981 Dec;34(3):409-21

Heikkila RE, Cabbat FS, Manzino L: Inhibitory effects of ascorbic acid on the binding of [3H]dopamine antagonists to neostriatal membrane preparations: relationship to lipid peroxidation. J Neurochem 1982 Apr;38(4):1000-6

Heise E, Joost HG, Hasselblatt A: Insulin binding and response to insulin of adipocytes from thyroxine-treated rats. Endocrinology 1982 Mar;110(3):955-60

Heizmann P, Ziegler WH: Excretion and metabolism of 14C-midazolam in humans following oral dosing. Arzneimittelforsch 1981;31(12a):2220-3

Hellegouarch A, DeFeudis FV, Clostre F: A regional difference in the in vitro response of the rabbit vena cava to norepinephrine. Gen Pharmacol 1982;13(1):41-3

Helm G, Owman C, Sjöberg NO, et al: Motor activity of the human Fallopian tube in vitro in relation to plasma concentration of oestradiol and progesterone, and the influence of noradrenaline. J Reprod Fertil 1982 Jan;64(1):233-42

Helman CG: 'Tonic', 'fuel' and 'food': social and symbolic aspects of the long-term use of psychotropic drugs. Soc Sci Med [B] 1981 Oct;15(4):521-33

Hemminki E, Pesonen T, Bruun K: Sales of psychotropic drugs in the Nordic countries. Soc Sci Med [a] 1981 Sep;15(5):589-97

Hemminki E: Problems in the measurement of psychotropic drug consumption. Am J Hosp Pharm 1982 Feb;39(2):325-9

Hempel K, Ullrich H, Philippu G: Quantitative investigation on the urinary excretion and metabolism of 3,4-dimethoxyphenylethylamine in schizophrenics and normal individuals. Biol Psychiatry 1982 Jan;17(1):49-59

Henkel JG, Sikand N, Makriyannis A, et al: Synthesis and adrenoceptor affinity of some highly polar beta-substituted catecholamines. J Med Chem 1981 Oct;24(10):1258-60

Henneberg M, Serówka E, Zrubek H, et al: Degradacja fenobarbitalu przez łożysko ludzkie w doświadczeniu in vitro na łożyskach perfundowanych. Ginekol Pol 1981;52(10):863-7 (Eng. Abstr.) **(Pol)**

Henrich RT, Nogawa T, Morishima A: In vitro induction of segregational errors of chromosomes by natural cannabinoids in normal human lymphocytes. Environ Mutagen 1980;2(2):139-47

Herink J, Fusek J, Vičar J: EEG changes in the limbic system after the administration of leu5-enkephalin. Act Nerv Super (Praha) 1981;23(4):290-2

Herling S, Winger G: Selective blockade of the discriminative stimulus effects of pentobarbital in pigeons. Psychopharmacology (Berlin) 1981;75(3):321-3

Herman ZS, Plech A, Bień E, et al: Effects of cholinomimetics, cholinolytics and atypical antidepressants in the behavioral despair test in the rat. Pol J Pharmacol Pharm 1981;33(5):485-9

Hermansen K: Tolbutamide, glucose, calcium, and somatostatin secretion. Acta Endocrinol (Copenh) 1982 Jan;99(1):86-93

Hervé F, Grigorova AM, Rajkowski K, et al: Differences in the binding of thyroid hormones and indoles by rat alpha 1-fetoprotein and serum albumin. Eur J Biochem 1982 Mar 1;122(3):609-12

Heym J, Trulson ME, Jacobs BL: Effects of adrenergic drugs on raphe unit activity in freely moving cats. Eur J Pharmacol 1981 Sep 11;74(2-3):117-25

Higashi H, Ueda N, Nishi S, et al: Chemoreceptors for serotonin (5-HT), acetylcholine (ACh), bradykinin (BK), histamine (H) and gamma-aminobutyric acid (GABA) on rabbit visceral afferent neurons. Brain Res Bull 1982 Jan;8(1):23-32

Hijikata Y, Hara K, Egawa H, et al: Microdetermination of unbound tryptophan in plasma by a combination of ultrafiltration and high-performance liquid chromatography. Anal Biochem 1981 Nov 15;118(1):10-6

Hillier K, Templeton WW: Stimulation of prostaglandin synthesis in rat cerebral cortex via a beta-adrenoceptor. Gen Pharmacol 1982;13(1):21-5

Hippius H, Matussek N: Comments on multicenter trials of antidepressant drugs. Mod Probl Pharmacopsychiatry 1981;16:95-9

Hirata K, Nagasaka T: Enhancement of calorigenic response to cold and to norepinephrine in physically trained rats. Jpn J Physiol 1981;31(5):657-65

Hirata T, Kai M, Kohashi K, et al: Determination of phenylpyruvic acid in urine and serum by high-performance liquid chromatography with fluorescence detection. J Chromatogr 1981 Nov 13;226(1):25-31

Hirata Y, Goto A, Takeda T, et al: [The effects of the angiotensin converting enzyme inhibitor, captopril, on catecholamine concentrations in rat plasma, heart, brain and kidneys (author's transl)] Nippon Naibunpi Gakkai Zasshi 1981 Aug 20;57(8):1097-108 (Eng. Abstr.) **(Jpn)**

Hirata-Hibi M, Higashi S, Tachibana T, et al: Stimulated lymphocytes in schizophrenia. Arch Gen Psychiatry 1982 Jan;39(1):82-7

Hisayama T, Takayanagi I: Physiological calcium ion concentration and a cholinergic drug on activity of particulate guanylate cyclase in guinea pig taenia caecum. J Pharmacobiodyn 1981 Sep;4(9):738-41

Hoagland TA, Diekman MA, Malven PV: Failure of stress and supplemental lighting to affect release of prolactin in swine. J Anim Sci 1981 Aug;53(2):467-72

Hobi V, Kielholz P, Gilsdorf U: How capable of driving are hospitalized psychiatric patients under psycho-active drug therapy? J Int Med Res 1981;9(6):434-47

Hodges HM, Green SE, Crewes H, et al: Effects of chronic chlordiazepoxide treatment on novel and familiar food preference in rats. Psychopharmacology (Berlin) 1981;75(3):311-4

Hodges HM, Green SE: Evidence of a role for GABA in benzodiazepine effects on food preference in rats. Psychopharmacology (Berlin) 1981;75(3):305-10

Hoefke W, Jennewein HM: Mechanisms of antihypertensive action of clonidine in relation to its psychotropic effects. Prog Clin Biol Res 1981;71:75-97

Hoffman DJ, Eastin WC Jr: Effects of malathion, diazinon, and parathion on mallard embryo development and cholinesterase activity. Environ Res 1981 Dec;26(2):472-85

Hogan S, Himms-Hagen J: Abnormal brown adipose tissue in genetically obese mice (ob/ob): effect of thyroxine. Am J Physiol 1981 Dec;241(6):E436-43

Holaday JW, Tortella FC, Belenky GL: Electroconvulsive shock results in a functional activation of endorphin systems. Mod Probl Pharmacopsychiatry 1981;17:142-57

Holdaas H, Langaard O, Eide I, et al: Conditions for enhancement of renin release by isoproterenol, dopamine, and glucagon. Am J Physiol 1982 Mar;242(3):F267-73

Hollinger JL, Hommes OR, van de Wiel TJ, et al: In vitro studies of 5, 10-methylenetetrahydrofolate reductase: inhibition by folate derivatives, folate antagonists, and monoamine derivatives. J Neurochem 1982 Mar;38(3):638-42

Hollister LE: Dependence on benzodiazepines. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):70-82

Hollister LE: Plasma concentrations of tricyclic antidepressants in clinical practice. J Clin Psychiatry 1982 Feb;43(2):66-9

Höllt V: Effects of neuroleptic drugs on endogenous opioid peptides in the rat. Mod Probl Pharmacopsychiatry 1981;17:1-18

Höllt V, Bergmann M: Effects of acute and chronic haloperidol treatment on the concentrations of immunoreactive beta-endorphin in plasma, pituitary and brain of rats. Neuropharmacology 1982 Feb;21(2):147-54

Holmgren E, Crawford IP: Regulation of tryptophan genes in Rhizobium leguminosarum. J Bacteriol 1982 Mar;149(3):1135-7

Holmgren I: Synaptic organization of the dopaminergic neurons in the retina of the cynomolgus monkey. Invest Ophthalmol Vis Sci 1982 Jan;

22(1):8-24

Honegger A, Hughes GJ, Wilson KJ: Chemical modification of peptides by hydrazine. Biochem J 1981 Oct 1;199(1):53-9

Hook VY, Eiden LE, Brownstein MJ: A carboxypeptidase processing enzyme for enkephalin precursors. Nature 1982 Jan 28;295(5847):341-2

Hopkins CR, Semoff S, Gregory H: Regulation of gonadotropin secretion in the anterior pituitary. Philos Trans R Soc Lond [Biol] 1981 Dec 18;296(1080):73-81

Hopkinson G: A neurochemical theory of appetite and weight changes in depressive states. Acta Psychiatr Scand 1981 Sep;64(3):217-25

Horak H, Turner AR, Yau O: Comparison of colony stimulating activities secreted into mouse lung conditioned medium in the presence and absence of lithium chloride. Exp Hematol 1982 Jan;10(1):123-9

Horsthemke B, Bauer K: Chymotryptic-like hydrolysis of luliberin (LH-RF) by an adenohypophyseal enzyme of high molecular weight. Biochem Biophys Res Commun 1981 Dec 31;103(4):1322-8

Horwitz SB, Chia GH, Harracksingh C, et al: Trifluoperazine inhibits phagocytosis in a macrophagelike cultured cell line. J Cell Biol 1981 Dec;91(3 Pt 1):798-802

Hosek K, Bacíková B, Vinař O: Patterns of psychotropic drug prescriptions in two psychiatric hospitals and two out-patient clinics. Act Nerv Super (Praha) 1981;23(4):261-3

Hougardy G: Depression. Treatment. Rev Med Liege 1982 Jan 1; 37(1):14-6 (Fre)

Houslay MD, Dipple I, Gordon LM: Phenobarbital selectively modulates the glucagon-stimulated activity of adenylate cyclase by depressing the lipid phase separation occurring in the outer half of the bilayer of liver plasma membranes. Biochem J 1981 Sep 1;197(3):675-81

Huang YH, Maas JW: D-Amphetamine at low doses suppresses noradrenergic functions. Eur J Pharmacol 1981 Nov 5;75(4):187-95

Huber CT, Duckworth WC, Solomon SS: The reversible inhibition by carbonyl cyanide m-chlorophenyl hydrazone of epinephrine-stimulated lipolysis in perifused isolated fat cells. Biochim Biophys Acta 1981 Dec 23;666(3):462-7

Hue B, Pelhate M, Chanelet J: Effets du piribédil sur la transmission synaptique dans le système nerveux central d'un insecte, la blatte (Periplanet a americana L.). J Pharmacol 1981 Nov-Dec;12(4):455-63 (Eng. Abstr.) (Fre)

Huestis WH, Nelson MJ, Ferrell JE Jr: Calmodulin-dependent spectrin kinase activity in human erythrocytes. Prog Clin Biol Res 1981; 56:137-55

Huidobro-Toro JP, Miranda H: Excitability of beta-endorphin, morphine and catecholamines of the vas deferens of the rat at different stages of development. Eur J Pharmacol 1981 Nov 19;76(1):115-8

Hull DS, Riley MV, Csukas S, et al: Corneal endothelial glutathione after photodynamic change. Invest Ophthalmol Vis Sci 1982 Mar;22(3):405-8

Hum WT, Barta-Bartova A, Birmingham MK: Steroidogenic and glycolytic responses to nucleotides, nucleosides and steroids in rodent adrenal glands: opposing, species-dependent effects of cyclic GMP. J Endocrinol 1981 Dec;91(3):447-56

Hung F, Chan MY: The effect of long-term chlorpromazine and desipramine treatment on adrenal corticosterone, cyclic AMP, and cholesterol distribution in rats. Clin Exp Pharmacol Physiol 1981 Dec; 8(6):567-74

Hunt TP, Fisher JW, Livingston JM, et al: Temperature effects on hydraziine toxicity to bluegills. Bull Environ Contam Toxicol 1981 Nov; 27(5):588-95

Hunzicker-Dunn M: Epinephrine-sensitive adenylyl cyclase activity in rabbit ovarian tissues. Endocrinology 1982 Jan;110(1):233-40

Hussain S: THC effects on fructose utilization and sperm motility [letter] Fertil Steril 1982 Mar;37(3):448

Hyndman AG, Adler R: GABA uptake and release in purified neuronal and nonneuronal cultures from chick embryo retina. Brain Res 1982 Feb;255(2):167-80

Hyttel J: Flupentixol and dopamine receptor selectivity [letter] Psychopharmacology (Berlin) 1981;75(2):217

I

Iacono WG, Peloquin LJ, Lumry AE, et al: Eye tracking in patients with unipolar and bipolar affective disorders in remission. J Abnorm Psychol 1982 Feb;91(1):35-44

Iasenchak SA, Len'o EIu, Pashchenko AE: Vozrastnye izmeneniia funktsional'nogo sostoianiia shchitovidnoĭ zhelezy i tkanevogo obmena ee gormonov. Fiziol Zh 1982 Jan-Feb;28(1):25-9 (Rus)

Iasnetsov VV, Pravdivtsev VA, Titov MI, et al: Sravnitel'noe deĭstvie met-énkefalina i gamma-éndorfina na reaktsii neĭronov dorsomedial'nogo gipotalamusa krolikov pri élektrokozhnoĭ i akupunkturnoĭ stimuliatsii. Dokl Akad Nauk SSSR 1981;260(6):1502-6 (Rus)

Idé C: Degeneration of mouse digital corpuscles. Am J Anat 1982 Jan; 163(1):59-72

Idé C: Regeneration of mouse digital corpuscles. Am J Anat 1982 Jan; 163(1):73-85

Idoipe Tomás C, Idoipe Tomás A, Sanz Sánchez F: Unión ligando-receptor dopaminérgico en vejiga de cobayo. Arch Farmacol Toxicol 1981 Apr; 7(1):123-4 (Spa)

Igwe OJ, Blake JW: Gas/liquid chromatographic analysis of pemoline in biological fluids using electron capture detection. J Chromatogr Sci 1981 Dec;19(12):617-24

Ikeno T, Hashimoto S, Kuzuya H: Amylase released from the parotid gland by pilocarpine elevates the enzyme activity in the submandibular and sublingual glands of rats. Experientia 1982 Feb 15,38(2):251-2

Imai K, Nagatsu T, Yajima T, et al: Developmental changes in the activities of prolinase and prolidase in rat salivary glands, and the effect of thyroxine administration. Mol Cell Biochem 1982 Jan 16;42(1):31-6

Imandt L, Tijhuis D, Wessels H, et al: Lithium stimulates thromboxane B2 formation in human platelets. Prostaglandins Med 1981 Nov; 7(5):421-9

Ingbar SH: The effects of aging on thyroid hormone economy in man. Prog Clin Biol Res 1981;74:135-45 (42 ref.)

Insel TR, Murphy DL: The psychopharmacological treatment of obsessive-compulsive disorder: a review. J Clin Psychopharmacol 1981 Sep;1(5):304-11 (68 ref.)

Isaacs PE, Whitehead JS, Kim YS: Muscarinic acetylcholine receptors of the small intestine and pancreas of the rat: distribution and the effect of vagotomy. Clin Sci 1982 Feb;62(2):203-7

Isambert MF, Henry JP: Effect of diethylpyrocarbonate on pH-driven monoamine uptake by chromaffin granule ghosts. FEBS Lett 1981 Dec 21;136(1):13-8

Ishihara Y, Sugiyama Y, Kitamura S, et al: [Effects of cigarette smoking on pulmonary functions and on plasma levels of serotonin, histamine and serum angiotensin I converting enzyme activity (author's transl)] Nippon Kyobu Shikkan Gakkai Zasshi 1981 Oct;19(10):721-7 (Eng. Abstr.) (Jpn)

Ishikawa K, Ott T, McGaugh JL: Evidence for dopamine as a transmitter in dorsal hippocampus. Brain Res 1982 Jan 28;232(1):222-6

Israël M, Lesbats B: Continuous determination by a chemiluminescent method of acetylcholine release and compartmentation in Torpedo electric organ synaptosomes. J Neurochem 1981 Dec;37(6):1475-83

Ito J, Matsuoka I, Sasa M, et al: Electrophysiologic evidence for involvement of acetylcholine as a neurotransmitter in the lateral vestibular nucleus. Otolaryngol Head Neck Surg 1981 Nov-Dec; 89(6):1025-9

Itoh S, Katsuura G: Suppressive action of cholecystokinin octapeptide on the behavioral effects of L-DOPA in the rat. Eur J Pharmacol 1981 Nov 5;75(4):313-6

Iuvone PM, Marshburn PB: Regulation of tyrosine hydroxylase activity in retinal cell suspensions: effects of potassium and 8-bromo cyclic AMP. Life Sci 1982 Jan 4;30(1):85-91

Ivančová J, Dlabač V, Stika L: Consumption of diazepam, nitrazepam and barbiturates in 5 large hospitals in Prague by defined daily doses per bed/day. Act Nerv Super (Praha) 1981;23(4):267-9

Ivanov V, Popov G: Des résultats comparatifs du traitement de l'anxiété chez le syndrome dépressif aux Tolvon, Vivalan et Alival. Agressologie 1981 Nov;22(D):29-30 (Fre)

Iwata H, Yamagami S, Mizuo H, et al: Cysteine sulfinic acid in the central nervous system: uptake and release of cysteine sulfinic acid by a rat brain preparation. J Neurochem 1982 May;38(5):1268-74

Izquierdo JM, Sotorrío P, Quirós A: Enzyme immunoassay of thyroxin with a centrifugal analyzer. Clin Chem 1982 Jan;28(1):123-5

J

Jack RA: Unintentional haloperidol abuse [letter] Am J Psychiatry 1982 Feb;139(2):258

Jackowski MM, Johnson RA, Exton JH: Regulation of adrenergic stimulation of hepatic adenylate cyclase by divalent cations. Biochim Biophys Acta 1982 Jan 12;714(1):74-83

Jacobsen NO, Olesen OV, Thomsen K, et al: Early changes in renal distal convoluted tubules and collecting ducts of lithium-treated rats: light microscopy, enzyme histochemistry, and 3H-thymidine autoradiography. Lab Invest 1982 Mar;46(3):298-305

Jaffé EH, Cuello AC: Neuronal and glial release of [3H]GABA from the rat olfactory bulb. J Neurochem 1981 Dec;37(6):1457-66

Jancsár SM, Leonard BE: The effects of antidepressant drugs on conditioned taste aversion learning of the olfactory bulbectomized rat. Neuropharmacology 1981 Dec;20(12B):1341-5

Janicki P, Lypko A, Szczudlik A, et al: Substance P levels in the rat forebrain after apomorphine and haloperidol treatment. Pol J Pharmacol Pharm 1981;33(5):499-502

Janicki P, Rewerski W: Farmakologia kliniczna benzodiazepin (BDA). Pol Tyg Lek 1981 Aug 24;36(34):1313-6 (Pol)

Jansson JC, Albertsson-Wikland K, Edén S, et al: Circumstantial evidence for a role of the secretory pattern of growth hormone in control of body growth. Acta Endocrinol (Copenh) 1982 Jan;99(1):24-30

Järbe TU, Swedberg MD, Mechoulam R: A repeated test procedure to assess onset and duration of the cue properties of (-) delta 9-THC, (-) delta 8-THC-DMH and (+) delta 8-THC. Psychopharmacology (Berlin) 1981;75(2):152-7

AUTHOR SECTION

Jatlow PI, Miller R, Swigar M: Measurement of haloperidol in human plasma using reversed-phase high-performance liquid chromatography. J Chromatogr 1982 Jan 8;227(1):233-8

Jaup BH, Dotevall G: The effect of pirenzepine and L-hyoscyamine on gastric emptying and salivary secretion in healthy volunteers. Scand J Gastroenterol 1981;16(6):769-73

Javaid JI, Dekirmenjian H, Davis JM: GLC analysis of trifluoperazine in human plasma. J Pharm Sci 1982 Jan;71(1):63-6

Jędrzejewska A, Staff-Zielińska E, Ostrowski J: Wpływ katecholamin na obraz morfologiczny obwodowego układu wegetatywnego przewodu pokarmowego szczura—ocena w mikroskopie świetlnym. Patol Pol 1981;32(2):233-42 (Eng. Abstr.) **(Pol)**

Jefferson JW: A clarification of 'some hazards of lithium use' [letter] J Clin Psychopharmacol 1981 Nov;1(6):409

Jenden DJ, Jope RS, Fraser SL: A mechanism for the accumulation of choline in erythrocytes during treatment with lithium. Commun Psychopharmacol 1980;4(5):339-44

Jenner FA: Advances in antidepressant treatment? Practitioner 1981 Oct; 225(1360):1378-85

Jenner P, Marsden CD: Substituted benzamide drugs as selective neuroleptic agents. Neuropharmacology 1981 Dec;20(12B):1285-93

Jenner P, Rupniak NM, Hall MD, et al: Hypophysectomy does not prevent development of striatal dopamine receptor supersensitivity induced by repeated neuroleptic treatment. Eur J Pharmacol 1981 Nov 19;76(1):31-6

Jessell TM: Fifty years of substance P [news] Nature 1982 Feb 18; 295(5850):551-3

Jeste DV, Doongaji DR, Panjwani D, et al: Cross-cultural study of a biochemical abnormality in paranoid schizophrenia. Psychiatry Res 1981 Dec;5(3):341-52

Jick H, Dinan BJ, Hunter JR: Triamterene and renal stones. J Urol 1982 Feb;127(2):224-5

Jimerson DC, van Kammen DP, Post RM, et al: Diazepam in schizophrenia: a preliminary double-blind trial. Am J Psychiatry 1982 Apr;139(4):489-91

Jin HM: [Clinical observation on 81 cases of schizophrenia treated with domestic penfluridol (author's transl)] Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1981 Aug;14(3):186-8 **(Chi)**

Jochemsen R, Breimer DD: Assay of flunitrazepam, temazepam and desalkylflurazepam in plasma by capillary gas chromatography with electron-capture detection. J Chromatogr 1982 Jan 8;227(1):199-206

Jochemsen R, van der Graaff M, Boeijinga JK, et al: Influence of sex, menstrual cycle and oral contraception on the disposition of nitrazepam. Br J Clin Pharmacol 1982 Mar;13(3):319-24

Johanson CE, Uhlenhuth EH: Drug preferences in humans. Fed Proc 1982 Feb;41(2):228-33

Johns MA, Azmitia EC, Krieger DT: Specific in vitro uptake of serotonin by cells in the anterior pituitary of the rat. Endocrinology 1982 Mar; 110(3):754-60

Johnson KM, Dewey WL, Bloom AS: Adrenalectomy reverses the effects of delta-9-THC on mouse brain 5-hydroxytryptamine turnover. Pharmacology 1981;23(4):223-9

Johnson PA, Van Tienhoven A, Friedlander J: Role of the dopaminergic system in luteinizing hormone release and ovulation in the hen. Poult Sci 1981 Nov;60(11):2551-6

Johnson SM, Katayama Y, Morita K, et al: Mediators of slow synaptic potentials in the myenteric plexus of the guinea-pig ileum. J Physiol (Lond) 1981 Nov;320:175-86

Johnson SW, Riker WK: Phenytoin antagonism of electrically induced maximal seizures in frogs and mice and effects on central nervous system levels of adenosine 3',5'-monophosphate and guanosine 3',5'-monophosphate. J Pharmacol Exp Ther 1982 Apr;221(1):139-45

Jones AB, Elsohly MA, Bedford JA, et al: Determination of cannabidiol in plasma by electron-capture gas chromatography. J Chromatogr 1981 Nov 13;226(1):99-105

Jones HP, Ghai G, Petrone WF, et al: Calmodulin-dependent stimulation of the NADPH oxidase of human neutrophils. Biochim Biophys Acta 1982 Jan 12;714(1):152-6

Jones RS: Noradrenaline-octopamine interactions on cortical neurones in the rat. Eur J Pharmacol 1982 Jan;77(2-3):159-62

Jope RS: Effects of phosphatidylcholine administration to rats on choline in blood and choline and acetylcholine in brain. J Pharmacol Exp Ther 1982 Feb;220(2):322-8

Jordan D, Spyer KM: Effects of acetylcholine on respiratory neurones in the nucleus ambiguus-retroambigualis complex of the cat. J Physiol (Lond) 1981 Nov;320:103-11

Joseph MH, Kennett GA: In vivo voltammetry in the rat hippocampus as in index of drug effects on extraneuronal 5-HT. Neuropharmacology 1981 Dec;20(12B):1361-4

Josephson I, Sperelakis N: On the ionic mechanism underlying adrenergic-cholinergic antagonism in ventricular muscle. J Gen Physiol 1982 Jan;79(1):69-86

Joyce DA, Beilin LJ, Vandongen R, et al: Plasma free and sulfate conjugated catecholamine levels during acute physiological stimulation in man. Life Sci 1982 Feb 1;30(5):447-54

Jung A, Mayer GP, Hurst JG, et al: Parathyroid gland response to epinephrine: a rate-sensitivity mechanism. Am J Physiol 1982 Jan; 242(1):R151-6

Jungmann E, Althoff PH, Schwedes U, et al: Uber die Behandlung idiopathischer Odeme mit Bromocriptin (author's transl)] Klin Wochenschr 1981 Dec 15;59(24):1353-5 (Eng. Abstr.) **(Ger)**

Jurkowlaniec E, Cytawa J: An attempt to use central dopaminergic stimulation as a reinforcement for T-maze learning in rats. Acta Neurobiol Exp (Warsz) 1981;41(4):357-62

Justafre JC, Gaillard JM: Diminution du sommeil paradoxal chez le rat sous antidépresseur tricyclique: rôle de l'inhibition collatérale. Rev Electroencephalogr Neurophysiol Clin 1981 Nov;11(2):228-35 (Eng. Abstr.) **(Fre)**

Jutisz M, Khar A: Pituitary cell cultures as a tool for the studies on the GnRH-induced release and biosynthesis of gonadotropins. Mater Med Pol 1980 Jan-Jun;12(1-2):53-62

K

Kabes J, Dostal T, Balon R: Clinical trial with clobazam. Agressologie 1981 Oct;22(C):41-2

Kabes J, Dostal T, Balon R: Do have antidepressants of the second generation anxiolytic properties? Agressologie 1981 Nov;22(E):11-3

Kachur JF, Miller RJ, Field M, et al: Neurohumoral control of ileal electrolyte transport. II. Neurotensin and substance P. J Pharmacol Exp Ther 1982 Mar;220(3):456-63

Kadar D, Tang BK, Conn AW: The fate of phenobarbitone in children in hypothermia and at normal body temperature. Can Anaesth Soc J 1982 Jan;29(1):16-23

Kadlecová B: Terapie mentální anorexie se zaměřením na depresivní projevy. Cesk Pediatr 1981 Nov;36(11):666-7 **(Cze)**

Kafka MS, Wirz-Justice A, Naber D, et al: Effect of lithium on circadian neurotransmitter receptor rhythms. Neuropsychobiology 1982 Jan-Feb; 8(1):41-50

Kaibo M, Kubo T, Misu Y: Comparative studies of (--)-, (+/-)-propranolol, atenolol, guanethidine, bretylium and tetracaine on adrenergic transmission. Br J Pharmacol 1981 Oct;74(2):365-70

Kajiyama H, Ohara K, Nomura Y, et al: The increase of cardiac beta 1-subtype of beta-adrenergic receptors in adult rats following neonatal 6-hydroxydopa treatment. Eur J Pharmacol 1982 Jan 8;77(1):75-7

Kalabukhova TN, Okulova ON: Issledovanie izmeneniia svoistv belkovogo i nukleoinovogo komponentov iskusstvennogo nukleoproteida pod deistviem gamma-i UF-izlucheniia. Radiobiologiia 1981 Nov-Dec; 21(6):912-5 (Eng. Abstr.) **(Rus)**

Kalninia IE, Baumanas EA, Kalrane ChB, et al: Modifitsirovanie aktivnosti mitokhondrial'nykh monoaminoksidaz mozga nekotorymi proizvodnymi gidrazina. Vopr Med Khim 1981 Nov-Dec;27(6):773-9 (Eng. Abstr.) **(Rus)**

Kalokerinos A, Dettman G: On your metal? Amazing zinc! Australas Nurses J 1981 Oct;10(10):22

Kalra PS, Kalra SP: Differential effects of low serum levels of estradiol-17 beta on hypothalamic LHRH levels and LH secretion in castrated male rats. Neuroendocrinology 1981 Dec;33(6):340-6

Kalvach Z, Hálková E, Bastecký J: Further clinical experience with oxyprothepin-decanoate. Act Nerv Super (Praha) 1981;23(4):271-2

Kamilov FKh, Davletov EG, Gil'manov AZh: Izmeneniia soderzhaniia nekotorykh gormonov v syvorotke krovi nepolovozrelykh krysiat posle termicheskogo ozhoga. Vopr Med Khim 1982 Jan-Feb;28(1):56-9 (Eng. Abstr.) **(Rus)**

Kamoi K: [Effects of baroregulation on osmoregulation of arginine vasopressin in rats (author's transl)] Nippon Naibunpi Gakkai Zasshi 1981 Oct 20;57(10):1489-95 (Eng. Abstr.) **(Jpn)**

Kamp CW, Morgan WW: Benzodiazepines suppress the light response of retinal dopaminergic neurons in vivo. Eur J Pharmacol 1982 Feb 5; 77(4):343-6

Kanaho Y, Sato T, Fujii T: The affinity of various phenothiazine drugs for membranes of intact human erythrocytes and their membrane-transforming activity. Mol Pharmacol 1981 Nov;20(3):704-8

Kanamori H, Morimoto K, Kinae N, et al: [Mutagenicity of the reaction products of L-ascorbic acid and L-tryptophan (author's transl)] Yakugaku Zasshi 1981 Jul;101(7):596-604 (Eng. Abstr.) **(Jpn)**

Kane JM, Rifkin A, Quitkin F, et al: Fluphenazine vs placebo in patients with remitted, acute first-episode schizophrenia. Arch Gen Psychiatry 1982 Jan;39(1):70-3

Kaneko S, Hill RG: [The effects of phenobarbitone on the inhibitory action of GABA (author's transl)] No To Shinkei 1982 Jan;34(1):77-84 (Eng. Abstr.) **(Jpn)**

Kaneto H, Nagaoka J: Further studies on the determinant role of brain level of pentobarbital for the development of acute hypnotic tolerance. J Pharmacobiodyn 1981 Sep;4(9):700-5

Kanje M, Kjellstrand P, Fex K, et al: Neurotransmitter metabolizing enzymes and plasma butyrylcholinesterase in mice exposed to trichloroethylene. Acta Pharmacol Toxicol (Copenh) 1981 Sep; 49(3):205-9

Kanter SL, Hollister LE, Williams M: Extraction of glucuronide metabolites of delta 9-tetrahydrocannabinol by diethyl ether. J Chromatogr 1982 Jan 1;234(1):255–60

Kaplan DJ, Hurley LH: Anthramycin binding to deoxyribonucleic acid–mitomycin C complexes. Evidence for drug–induced deoxyribonucleic acid conformational change and cooperativity in mitomycin C binding. Biochemistry 1981 Dec 22;20(26):7572–80

Karlsson KE: Two–phase derivatization of amitriptyline and structurally related tertiary amines for gas chromatography with electron–capture detection. J Chromatogr 1981 Dec 18;219(3):373–8

Kasagi K, Konishi J, Kousaka T, et al: [Radioimmunoassay of free thyroxine with microencapsulated anti–T4 specific antibody (author's transl)] Kaku Igaku 1981 Aug;18(7):973–83 (Jpn)

Kasschau MR, Mansour TE: Serotonin–activated adenylate cyclase during early development of Schistosoma mansoni. Nature 1982 Mar; 296(5852):66–8

Kastin AJ, Honour LC, Coy DH: Kyotorphins affect aversive pecking in chicks. Physiol Behav 1981 Dec;27(6):1073–6

Kato K, Niibe T, Hosoya N, et al: [The effect of bromocriptine induced estradiol–17 beta in amenorrhea patients with normoprolactinemia and hyperprolactinemia (author's transl)] Horumon To Rinsho 1981 Aug; 29(8):931–5 (Jpn)

Kato T, Yamaguchi T, Togari A, et al: Ontogenesis of monoamine–synthesizing enzyme activities and biopterin levels in rat brain or salivary glands, and the effects of thyroxine administration. J Neurochem 1982 Apr;38(4):896–901

Katoh N, Helfman DM, Wrenn RW, et al: Differential regulation of calcium–dependent and calcium–independent cyclic nucleotide phosphodiesterases from heart by palmitoylcarnitine and palmitoyl coenzyme A. Biochim Biophys Acta 1982 Jan 12;714(1):129–35

Katz IR: Oxygen dependence of dopamine–beta–hydoxylase activity and lactate metabolism in synaptosomes from rat brain. Brain Res 1982 Jan 14;231(2):399–409

Katz IR: Monoamine oxidase–catalyzed metabolism of 3,4–dihydroxyphenylethylamine in the dopaminergic synaptosomes from rat corpus striatum. J Neurochem 1982 Mar;38(3):859–62

Katz Z, Borenstein R, Lancet M: Combined bromocryptine and hMG treatment in hyperprolactinemic infertility. Int J Fertil 1981;26(4):290–2

Kaufman JM, Elewaut A, Vermeulen A: Effect of domperidone on prolactin (PRL)and thyrotrophin (TSH) secretion. Arch Int Pharmacodyn Ther 1981 Dec;254(2):293–303

Kavaliers M: Period lengthening and disruption of socially facilitated circadian activity rhythms of goldfish by lithium. Physiol Behav 1981 Oct;27(4):625–8

Kawai K, Orci L, Unger RH: High somatostatin uptake by the isolated perfused dog pancreas consistent with 'insulo–acinar' axis. Endocrinology 1982 Feb;110(2):660–2

Keane PE, Menager J, Strolin Benedetti M: The effect of monoamine oxidase A and B inhibitors on rat serum prolactin. Neuropharmacology 1981 Dec;20(12A):1157–62

Keane PE, Strolin Benedetti M, Dow J: The effect of niaprazine on the turnover of 5–hydroxytryptamine in the rat brain. Neuropharmacology 1982 Feb;21(2):163–9

Keenan L, Koopowitz H: Physiology and in situ identification of putative aminergic neurotransmitters in the nervous system of Gyrocotyle fimbriata, a parasitic flatworm. J Neurobiol 1982 Jan;13(1):9–21

Keitner GI: Phenelzine treatment without switch to mania [letter] Am J Psychiatry 1982 Mar;139(3):386

Kellar KJ, Cascio CS, Bergstrom DA, et al: Electroconvulsive shock and reserpine: effects on beta–adrenergic receptors in rat brain. J Neurochem 1981 Oct;37(4):830–6

Kendler KS, Davis KL: The genetics and biochemistry of paranoid schizophrenia and other paranoid psychoses. Schizophr Bull 1981; 7(4):689–709 (86 ref.)

Kerdelhué B, Bethea CL, Ling N, et al: Beta–endorphin concentrations in serum, hypothalamus and central gray of hypophysectomized and mediobasal hypothalamus lesioned rats. Brain Res 1982 Jan 7; 231(1):85–91

Kerr-Wilson RH, MacKenzie L, Fraser HM: Effects of chronic LHRH agonist treatment on the endometrium and ovaries of the stumptailed macaque. Contraception 1981 Dec;24(6):647–55

Kersten L, Bräunlich H: Der Einfluss von Diuretika auf die Verteilung und renale Ausscheidung von Lithium bei Ratten verschiedenen Alters. Acta Biol Med Ger 1981;40(6):837–48 (Eng. Abstr.) (Ger)

Keserü P, Varsányi E, Paál T: Gyógyszerkészítmények in vitrol biofarmáciai ellenörzése. 2. Különbözö Kioldódásvizsgáló készülékek összehasonlító vizsgálata Aparkazin (dietazinium–klorid) tartalmú drazsékkal. Acta Pharm Hung 1981 Nov;51(6):264–9 (Eng. Abstr.) (Hun)

Kesler DJ, Weston PG, Pimentel CA, et al: Diminution of the in vitro response to luteinizing hormone by corpora lutea induced by gonadotropin releasing hormone treatment of postpartum suckled beef cows. J Anim Sci 1981 Sep;53(3):749–54

Kessler JA, Black IB: Regulation of substance P in adult rat sympathetic ganglia. Brain Res 1982 Feb 18;234(1):182–7

Keyes SR, Rudnick G: Coupling of transmembrane proton gradients to platelet serotonin transport. J Biol Chem 1982 Feb 10;257(3):1172–6

Khandelwal JK, Szilagyi PI, Barker LA, et al: Simultaneous measurement of acetylcholine and choline in brain by pyrolysis–gas chromatography–mass spectrometry. Eur J Pharmacol 1981 Dec 3; 76(2–3):145–56

Khil'ko AS, Kamenev BA: Morfologicheskie izmeneniia v krovetvornykh organakh krys pod vliianiem adrenalina. Fiziol Zh 1982 Jan–Feb; 28(1):40–5 (Eng. Abstr.) (Rus)

Kigasawa K, Maruyama K, Tanaka M, et al: [Biopharmaceutical studies of drugs. V. Dissolution properties and bioavailability of ground mixtures of poorly water soluble drugs and soluble proteins (author's transl)] Yakugaku Zasshi 1981 Aug;101(8):733–9 (Eng. Abstr.) (Jpn)

Kilpatrick DL, Jones BN, Kojima K, et al: Identification of the octapeptide [Met]enkephalin –Arg6–Gly7–Leu8 in extracts of bovine adrenal medulla. Biochem Biophys Res Commun 1981 Nov 30;103(2):698–705

Kilpatrick IC, Starr MS, James TA, et al: Evidence for the involvement of nigrothalamic GABA neurons in circling behaviour in the rat. Adv Biochem Psychopharmacol 1981;30:205–24

Kimura T, Share L, Wang BC, et al: Central effects of dopamine and bromocriptine on vasopressin release and blood pressure. Neuroendocrinology 1981 Dec;33(6):347–51

Kimura T, Ohta M, Kawamura J: [On the National Institute of Hygienic Sciences Standard (Japanese Pharmacopoeia Standard) 'Epinephrine Bitartrate Reference Standard (Control 781)' and 'Norepinephrine Bitartrate Reference Standard (Control 791)' (author's transl)] Eisei Shikenjo Hokoku 1981;99:118–21 (Eng. Abstr.) (Jpn)

King DL, Bonicamp JM, Jones DW: Novel thin–layer chromatographic visualization reagent for phencyclidine [letter] Clin Chem 1982 Jan; 28(1):247

King JA, Millar RP: Decapeptide luteinizing hormone releasing hormone in ovine pineal gland. J Endocrinol 1981 Dec;91(3):405–14

King MG, Geffard MR, Chavreau J, et al: Des–tyr–gamma–endorphin (DT gamma E) and pineal levels of melatonin and arginine vasopressin (AVP). Eur J Pharmacol 1981 Dec 3;76(2–3):271–4

King R, Raese JD, Barchas JD: Catastrophe theory of dopaminergic transmission: a revised dopamine hypothesis of schizophrenia. J Theor Biol 1981 Oct 21;92(4):373–400

Kinsel JF, Melnik EI, Lindenbaum S, et al: The effect of amine structure on complexation with lasalocid in model membrane systems. I. Identification of charged complexes in lipid bilayer membranes. Biochim Biophys Acta 1982 Jan 22;684(2):233–40

Kirchhoff J, Hornung E, Ghraf R, et al: Interactions of catecholestrogens with cytoplasmic and nuclear estrogen receptors in rat pituitary gland and hypothalamus. J Neurochem 1981 Dec;37(6):1540–7

Kiss A, Culman J, Kvetňanský R, et al: Distribution of catecholamines and serotonin in 17 portions of rat ventromedial nucleus and effect of acute immobilization stress. Endocrinol Exp (Bratisl) 1981 Dec; 15(4):219–28

Kiss L, Kóródi I, Nánási P: Study on the role of tyrosine side–chains at the active centre of emulsin beta–D–glucosidase. Biochim Biophys Acta 1981 Dec 15;662(2):308–11

Klauschenz E, Bienert M, Egler H, et al: Tritium labeling of gonadotropin releasing hormone in its proline and histidine residues. Peptides (Fayetteville) 1981 Winter;2(4):445–52

Klein HE, Broucek B, Greil W: Lithium withdrawal triggers psychotic states [letter] Br J Psychiatry 1981 Sep;139:255–6

Kleinman I, Ananth J: Tricyclic continuation and maintenance therapy in unipolar depression. Psychosomatics 1981 Dec;22(12):1031–6

Kleinrok A, Tomaszewski A, Billewicz–Stankiewicz J: The effects of intracerebroventricularly applied kainic acid on acetylcholine content and release in rat brain cortex and striatum. Pol J Pharmacol Pharm 1981;33(4):453–8

Kleinrok Z, Turski L: Biochemical consequences of kainic acid injection into the lateral brain ventricle in rat. Acta Biochim Pol 1981; 28(2):111–22

Kleinrok Z, Zarkowski AM: Central neurotropic activity of homovanillic acid. Acta Physiol Pol 1981 Sep–Oct;32(5):477–85

Klemm N: A modified glyoxylic acid–formaldehyde technique for histofluorescence of catecholamine–containing neurons in cryostat sections of the insect brain. J Histochem Cytochem 1982 Apr; 30(4):398–400

Kleshchinov VN, Kolomeets NS: O funktsional'noi roli interkhromatinovykh granul iadra. Biull Eksp Biol Med 1981 Oct; 91(10):504–5 (Eng. Abstr.) (Rus)

Kletzky OA, Davajan V, Mishell DR Jr: The effect of gonadotropin–releasing hormone on ovarian estradiol secretion. Am J Obstet Gynecol 1982 Feb 15;142(4):427–31

Kline NS: A controlled comparison of trimipramine and amitriptyline. J Clin Psychiatry 1981 Mar;43(3):100–4

Klinger W: Liver damage in rats by allylisopropylacetamide (AIA), an inducer of delta–aminolevulinic acid synthetase (ALAS). Acta Pharmacol Toxicol (Copenh) 1981 May;48(5):404–8

Klinman JP, Krueger M: Dopamine beta–hydroxylase: activity and inhibition in the presence of beta–substituted phenethylamines. Biochemistry 1982 Jan 5;21(1):67–75

Knapp S, Mandell AJ, Russo PV, et al: Strain differences in kinetic and thermal stability of two mouse brain tryptophan hydroxylase activities.

AUTHOR SECTION

Brain Res 1981 Dec 28;230(1-2):317-36

Knappenberg M, Michel A, Scarso A, et al: The conformational properties of somatostatin. IV. The conformers contributing to the conformation equilibrium of somatostatin in aqueous solution as found by semi-empirical energy calculations and high-resolution NMR experiments. Biochim Biophys Acta 1982 Jan 18;700(2):229-46

Knecht M, Amsterdam A, Catt KJ: Inhibition of granulosa cell differentiation by gonadotropin-releasing hormone. Endocrinology 1982 Mar;110(3):865-72

Knehans AW, Romsos DR: Reduced norepinephrine turnover in brown adipose tissue of ob/ob mice. Am J Physiol 1982 Apr;242(4):E253-61

Knesevich JW: Successful treatment of obsessive-compulsive disorder with clonidine hydrochloride. Am J Psychiatry 1982 Mar;139(3):364-5

Knodell RG, Allen RC, Kyner WT: Effects of ethinyl estradiol on pharmacokinetics of meperidine and pentobarbital in the rat. J Pharmacol Exp Ther 1982 Apr;221(1):1-6

Kobinger W, Pichler L: alpha 2-Adrenoceptor agonistic effect of B-HT 920 in isolated perfused hindquarters of rats. Eur J Pharmacol 1981 Nov 19;76(1):101-5

Kochman K, Kerdelhué B, Ostrowska A, et al: Biosynthesis, in vivo, of gonadotropin-releasing hormone in the hypothalamus of normal and ovariectomized female rats. Mol Cell Endocrinol 1982 Feb; 25(2):193-202

Kochman K, Kerdelhué B: Degradation of luteinizing hormone releasing hormone LH-RH by the hypothalamic and pituitary tissue in the presence of its analogs and TRH. Mater Med Pol 1980 Jan-Jun; 12(1-2):114-8

Kochman K: Gromadzenie hormonów w neuronach podwzgórza. Acta Physiol Pol 1981;32(5 Suppl 23):79-85 (37 ref.) (Pol)

Kohno Y, Tanaka M, Nakagawa R, et al: Developmental difference in noradrenaline and 3-methoxy-4-hydroxyphenylethyleneglycol sulfate (MHPG-SO4) levels in rat whole brain. Kurume Med J 1981;28(1):95-8

Kolter TR, Pols-Valkhof N, Schuiling GA: Adaptation of the pituitary gland to prolonged LRH stimulation. Experientia 1981 Dec 15; 37(12):1349-51

Kolter TR, Pols-Valkhof N, Schuiling GA: Long-lasting desensitizing effect of short-term LRH exposure on the pituitary responsiveness to LRH in the ovariectomized rat. Acta Endocrinol (Copenh) 1982 Feb; 99(2):200-5

Kolter TR, Pols-Valkhof N, Schuiling GA: Kinetics of LRH-induced LH-release in vivo: influence of LRH pre-treatment. Acta Endocrinol (Copenh) 1982 Feb;99(2):195-9

Kolter TR, Pols-Valkhof N, Schuiling GA: Short-term kinetics of LRH-induced LH-release in the long-term ovariectomized rat. Acta Endocrinol (Copenh) 1982 Feb;99(2):187-94

Kolter TR, van der Gugten AA, Pols-Valkhof N, et al: Pattern of prolactin secretion and pituitary responsiveness to LRH in pseudopregnant rats maintained in constant light. Acta Endocrinol (Copenh) 1982 Jan; 99(1):31-8

Kojima H, Suetake K, Yokoo H, et al: Dopamine-containing cells in rabbit nodose ganglia. Experientia 1981 Dec 15;37(12):1332-3

Kojima M, Kado Y, Ishida R: [Effects of afloqualone, a centrally acting muscle relaxant, on the sleep-wakefulness cycle in cats with chronically implanted electrodes (author's transl)] Nippon Yakurigaku Zasshi 1981 Nov;78(5):471-82 (Eng. Abstr.) (Jpn)

Koketsu K: Electropharmacological actions of catecholamine in sympathetic ganglia. Multiple modes of actions to modulate the nicotinic transmission. Jpn J Pharmacol 1981;31 Suppl:27P-28P

Kokkinidis L, Anisman H: Amphetamine psychosis and schizophrenia: a dual model. Neurosci Biobehav Rev 1981 Winter;5(4):449-61 (173 ref.)

Kolomazník M, Suva J, Svejnohová D, et al: Lithium levels in the ejaculate, spermiogram and adjuvant psychopharmacological therapy. Act Nerv Super (Praha) 1981;23(4):275-6

Komiya E, Sato H, Yamada R: [Studies on catecholamine secretion from adrenal medulla—acetylcholine stimulation (author's transl)] Horumon To Rinsho 1981 Aug;29(8):915-8 (Jpn)

Kondo K, Ebihara A, Suzuki H, et al: Role of dopamine in the regulation of blood pressure and the renin—angiotensin—aldosterone system in conscious rats. Clin Sci [Suppl] 1981 Dec;61(7):235s-237s

Kononenko VIa, Rachitskaia IV: Izofermentnye spektry laktatdegidrogenazy v nekotorykh otdelakh golovnogo mozga krys i vliianie na nikh tireoidina. Ukr Biokhim Zh 1982;54(1):26-30 (Eng. Abstr.) (Rus)

Kononenko VIa, Mishunina TM: Bliianie gidrokortizona na solderzhanie gamma-aminomaslianoĭ kisloty i glutamatedkarboksilaznuiu aktivnost' v otedelakh golovnogo mozga krys. Ukr Biokhim Zh 1982;54(1):31-5 (Eng. Abstr.) (Rus)

Konturek SJ, Jaworek J, Cieszkowski M, et al: Effect of thyrotropin-releasing hormone on gastro-intestinal secretions in dogs. Life Sci 1981 Nov 30;29(22):2289-98

Koop H, Schwab E, Arnold R, et al: Effect of food deprivation on rat gastric somatostatin and gastrin release. Gastroenterology 1982 May; 82(5 Pt 1):871-6

Kopytova FV, Mednikova YuS, Rusinova EV: Analog of a conditioned reflex of sensomotor cortical units following microinjection of acetylcholine. Neurosci Behav Physiol 1981 May-Jun;11(3):213-20

Korf J, van der Heyden JA, Venema K, et al: Distribution and release of GABA in the basal ganglia. Adv Biochem Psychopharmacol 1981; 30:105-17

Koritz SB: The effect of the administration of the adrenocorticotrophic hormone to rats on in vivo steroidogenesis and on the reduction cytochrome P-450 in adrenal mitochondria. Biochim Biophys Acta 1982 Feb 2;714(2):382-5

Korneev AIa, Lideman RR: Fiziko-khimicheskaia geterogennost' GAMK-retseptorov i vyiavlenie razlichiĭ v strukturnoĭ sviazi s benzodiazepinovymi retseptorami. Zh Nevropatol Psikhiatr 1981; 81(11):1661-2 (Eng. Abstr.) (Rus)

Korneev AIa, Mukhin AG, Faktor MI: Molekuliarnye mekhanizmy farmakologicheskogo deĭstviia benzodiazepinov. Vestn Akad Med Nauk SSSR 1982;(1):20-8 (Eng. Abstr.) (Rus)

Korotkov KO, Zhulin VV, Kruglikov RI: Sviazyvanie 3H-diazepama sinapticheskimi membranami kory bol'shikh polushariĭ golovnogo mozga krys pri vyrabotke uslovnogo refleksa. Biull Eksp Biol Med 1981 Dec;92(12):695-6 (Eng. Abstr.) (Rus)

Kosík S, Takáč M, Ponist J, et al: Účinky heparínu na rádioanalyticky stanovované ukazovatele štítnej žl'azy. Vnitr Lek 1982 Feb;28(2):122-8 (Eng. Abstr.) (Slo)

Koss MC: A quantitative assessment of CNS sympatho-inhibition produced by psychotropic drugs. Neuropharmacology 1982 Jan; 21(1):73-9

Köster G, Breuer H, Schneider HT: Effect of 2-substituted oestrogens in vivo on the metabolism of noradrenaline in rat brain. Acta Endocrinol (Copenh) 1982 Jan;99(1):1-8

Kostin GM, Kol'tsov EV, Luzhnikov EA, et al: Gemoreologicheskoe obosnovanie transfuzionnoĭ terapii pri ostrykh ekzogennykh intoksikatsiiakh. Probl Gematol Pereliv Krovi 1981 Oct;26(10):37-41 (Eng. Abstr.) (Rus)

Kotagal N, Patke C, Landt M, et al: Regulation of pancreatic islet-cell plasma membrane Ca2+ + Mg2+-ATPase by calmodulin. FEBS Lett 1982 Jan 25;137(2):249-52

Koumjian K: The use of valium as a form of social control. Soc Sci Med [E] 1981 Aug;15(3):245-9

Koup JR, Gibaldi M, Godolphin W: Single point estimation of phenytoin dosing: a reappraisal. Res Commun Chem Pathol Pharmacol 1981 Nov; 34(2):231-9

Koupilová M, Hrdina V, Fusek J: Exploitation of the antagonistic properties of some drugs against poisoning with psychochemicals. Act Nerv Super (Praha) 1981;23(4):292-3

Kovacs P, Takácsi Nagy G: Az izotonizálás vizsgálata ozmometriás módszerrel. Acta Pharm Hung 1982 Jan;52(1):22-32 (Eng. Abstr.) (Hun)

Kozhechkin SN, Ruchinskaia TIu, Sanadiradze GS, et al: Depoliarizatsiia pervichnykh afferentov, vyzvannaia gamma-aminomaslianoĭ kislotoĭ, vvedennoĭ v tsentral'nyĭ kanal spinnogo mozga koshki. Biull Eksp Biol Med 1981 Dec;92(12):703-5 (Eng. Abstr.) (Rus)

Krall JF, Connelly M, Tuck ML: In vitro desensitization of human lymphocytes by epinephrine. Biochem Pharmacol 1982 Jan 1; 31(1):117-9

Kramer KJ, Rupley JA: Interaction of thyroxine with lysozyme. Physiol Chem Phys 1981;13(4):313-7

Krantis A, Kerr DI: The effect of GABA antagonism on propulsive activity of the guinea-pig large intestine. Eur J Pharmacol 1981 Nov 19;76(1):111-4

Krantis A, Kerr DI: Gaba induced excitatory responses in the guinea-pig small intestine are antagonized by bicuculline, picrotoxinin and chloride ion blockers. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov; 317(3):257-61

Krebs-Roubicek E, Koehl J, Poeldinger W: Treatment of anxious depression with intravenous infusions of a combination of drugs. Agressologie 1981 Nov;22(D):25-6

Krieg RJ Jr, Johnson JH: Differential time- and dose-dependent effects in the haloperidol blockade of luteinizing hormone release and ovulation. Neuroendocrinology 1981 Dec;33(6):372-5

Krishnamurty VS: Dual influence of hydralazine on constrictor response to noradrenaline in isolated arterial smooth muscle. Can J Physiol Pharmacol 1981 Nov;59(11):1159-69

Kristiansen JE, Blom J: Effect of chlorpromazine on the ultrastructure of Staphylococcus aureus. Acta Pathol Microbiol Scand [B] 1981 Dec; 89(6):399-405

Kriuchkova VI: Vliianie urovnia kholinergicheskikh protsessov v organizme na legochnyĭ surfaktant. Fiziol Zh SSSR 1981 Nov; 67(11):1643-6 (Rus)

Krivosheev OG, Isachenkov VA, Nabatchikova NA, et al: Immunoreaktivnyĭ liuteniziruiushchiĭ gormon v TsNS i perifericheskikh tkaniakh gipofizektomirovannykh krys. Probl Endokrinol (Mosk) 1982 Jan-Feb;28(1):58-64 (Rus)

Krnjevic K, Reiffenstein RJ, Ropert N: Disinhibitory action of acetylcholine in the rat's hippocampus: extracellular observations. Neuroscience 1981;6(12):2465-74

Kromann N, Christiansen J, Flachs H, et al: Differences in single dose phenytoin kinetics between Greenland Eskimos and Danes.

AUTHOR SECTION

Ther Drug Monit 1981;3(3):239–45

Krstic MK, Djurkovic D: Comparison of the cardiovascular responses to intracerebroventricular administration of tryptamine, 5–hydroxytryptamine, tryptophan and 5–hydroxytryptophan in rats. Arch Int Physiol Biochim 1981 Nov;89(4):385–91

Krstulovic AM, Bertani–Dziedzic L, Bautista–Cerqueira S, et al: Simultaneous determination of 4–hydroxy–3–methoxyphenylacetic (homovanillic) acid and other monoamine metabolites in human lumbar cerebrospinal fluid: an improved high–performance liquid chromatographic study with electrochemical detection. J Chromatogr 1982 Feb 12;227(2):379–89

Kruglikov RI, Gol'dberg MV, Maizelis MYa, et al: Effects of metenkephalin on the formation and fixation of defensive temporal associations and on the incorporation of C14–leucine in brain proteins of the rat. Biol Bull Acad Sci USSR 1980 Sep–Oct;7(5):432–4

Krulich L, Mayfield MA, Steele MK, et al: Differential effects of pharmacological manipulations of central alpha 1– and alpha 2–adrenergic receptors on the secretion of thyrotropin and growth hormone in male rats. Endocrinology 1982 Mar;110(3):796–804

Krut'ko BT: Issledovanie katekholaminovoĭ reguliatsii ATF–aznoĭ aktivnosti pecheni i pochek mysheĭ. Probl Endokrinol (Mosk) 1982 Jan–Feb;28(1):73–8 (Eng. Abstr.) **(Rus)**

Kryzhanovskiĭ GN, Polgar AA, Zinkevich VA, et al: Vliianie stolbniachnogo toksina na mekhanizmy reguliatsii ionami kal'tsiia sekretsii peredatchika v nervno–myshechnom soedinenii. Biull Eksp Biol Med 1981 Dec;92(12):648–51 (Eng. Abstr.) **(Rus)**

Kubo T, Misu Y: Cardiovascular response to microinjection of physostigmine and choline into the dorsal medullary site of the rat. Neuropharmacology 1981 Nov;20(11):1091–5

Kudriavtseva NN, Iakimenko MA: Vliianie serotonina na sokratitel'nyĭ termogenez. Fiziol Zh SSSR 1981 Dec;67(12):1862–5 (Eng. Abstr.) **(Rus)**

Kuhn W, Neuser D, Przuntek H: [3H]Diazepam displacing activity in human cerebrospinal fluid. J Neurochem 1981 Oct;37(4):1045–7

Kulig BM: Some behavioral effects of antiepileptic drugs during acute and prolonged treatment in the rat. Acta Neurol Scand [Suppl] 1981; 89:59–67

Kulik FA, Wilbur R: Case report of painful ejaculation as a side effect of amoxapine. Am J Psychiatry 1982 Feb;139(2):234–5

Kulikov AV: Bystryĭ neizotopnyĭ metod opredeleniia aktivnosti triptofangidroksilazy v golovnum mozge. Vopr Med Khim 1982 Jan–Feb;28(1):135–9 **(Rus)**

Kumar MS, Chen CL, Besch EL, et al: Altered hypothalamic dopamine depletion rate and LHRH content in noncyclic hamsters. Brain Res Bull 1982 Jan;8(1):33–6

Kumar P, Agarwal JC, Nath C, et al: Substituted dopamine quinazolones as potent antiparkinsonian agents. Pharmazie 1981 Nov;36(11):780

Kuo CH, Rush GF, Hook JB: Renal cortical accumulation of phenobarbital in rats and rabbits: lack of correlation with induction of renal microsomal monooxygenases. J Pharmacol Exp Ther 1982 Mar;220(3):547–51

Küpfer U, Stämpfli H: Einfluss eines im Puerperium verabreichten GnRH–Analoges (Hoe 766) auf die Fruchtbarkeit von Milchkühen. Schweiz Arch Tierheilkd 1981;123(7):355–62 (Eng. Abstr.) **(Ger)**

Kuribara H, Tadokoro S: Enhancement of the avoidance–suppressing effects of neuroleptic agents after repeated administration: changes in the discriminated avoidance response in rats. Psychopharmacology (Berlin) 1981;75(2):148–51

Kuriyama K, Ida S, Nishimura C: Differential effects of light and dark adaptations on function and metabolism of retinal taurine and gamma–aminobutyric acid (GABA). Adv Exp Med Biol 1981; 139:221–38

Kurose M, Saeki K: Histamine release induced by neurotensin from rat peritoneal mast cells. Eur J Pharmacol 1981 Dec 3;76(2–3):129–36

Kvetnanskiĭ R, Belova TI, Oprshalova Z, et al: Izmeneniia urovnia katekholaminov v adrenalinsinteziruiushchikh strukturakh prodolgovatogo mozga krys, razlichnym obrazom reagiruiushchikh na dlitel'nuiu odnorazovuiu immobilizatsiiu. Probl Endokrinol (Mosk) 1981; 27(6):58–63 (Eng. Abstr.) **(Rus)**

Kvetnianski R, Tigranian RA: Soderzhanie katekholaminov v krovi u krys posle poleta na biosputnike 'Kosmos–936'. Kosm Biol Aviakosm Med 1982 Jan–Feb;16(1):80–3 (Eng. Abstr.) **(Rus)**

L

Labrie F, Séguin C, Bélanger A, et al: Contraception with LHRH agonists, a new physiological approach. Reproduccion 1981 Oct–Dec;5(4):229–41 (48 ref.)

Labrie F, Bélanger A, Kelly PA, et al: Antifertility effects of luteinizing hormone–releasing hormone (LHRH) agonists. Prog Clin Biol Res 1981; 74:273–91 (70 ref.)

Lackoff A, Jackson IM: Calcium dependency of potassium–stimulated thyrotropin–releasing hormone secretion from rat neurohypophysis in vitro. Neurosci Lett 1981 Dec 11;27(2):177–81

Lackovic Z, Relja M, Neff NH: Catabolism of endogenous dopamine in peripheral tissues: is there an independent role for dopamine in peripheral neurotransmission? J Neurochem 1982 May;38(5):1453–8

Lai JC, Leung TK, Guest JF, et al: The effects of chronic manganese chloride treatment expressed as age–dependent, transient changes in rat brain synaptosomal uptake of amines. J Neurochem 1982 Mar; 38(3):844–7

Lai JC, Lim L, Davison AN: Differences in the inhibitory effect of Cd2+, Mn2+ and Al3+ on the uptake of dopamine by synaptosomes from forebrain and from striatum of the rat. Biochem Pharmacol 1981 Nov 15;30(22):3123–5

Lambert PA, Chabannes JP: Thérapeutiques biologiques dans la schizophrénie. Soins Psychiatr 1981 Dec;(14):19–22 **(Fre)**

Landt M, McDaniel ML, Bry CG, et al: Calmodulin–activated protein kinase activity in rat pancreatic islet cell membranes. Arch Biochem Biophys 1982 Jan;213(1):148–54

Lane AN, Kirschner K: The mechanism of tryptophan binding to tryptophan synthase from Escherichia coli. Eur J Biochem 1981 Nov; 120(2):379–87

Lange H: EEG spectral analysis in vital depression: ultradian cycles. Biol Psychiatry 1982 Jan;17(1):3–21

Langeloh A, Jurkiewicz A: Analysis of the effects of dopamine and noradrenaline in relation to the proposed postsynaptic dopamine receptor in rat vas deferens. Naunyn Schmiedebergs Arch Pharmacol 1982 Feb;318(3):202–9

Langer SZ, Zarifian E, Briley M, et al: High–affinity 3H–imipramine binding: a new biological marker in depression. Pharmacopsychiatria 1982 Jan;15(1):4–10 (57 ref.)

Larkin AR: What's a medication group? J Psychosoc Nur Ment Health Serv 1982 Feb;20(2):35–7

Larsson OM, Thorbek P, Krogsgaard–Larsen P, et al: Effect of homo–beta–proline and other heterocyclic GABA analogues on GABA uptake in neurons and astroglial cells and on GABA receptor binding. J Neurochem 1981 Dec;37(6):1509–16

Lascelles PT: Drug assays in neuropsychiatry. Psychol Med 1981 Nov; 11(4):661–7 (39 ref.)

Lassalles JP, Hyver C, Thellier M: Oscillation of the electrical potential of the frog skin under the effect of Li+: theoretical formulation. Biophys Chem 1981 Sep;14(1):65–80

Lata A, Satsangi RK, Srivastava VK, et al: Monoamine oxidase inhibitory and CNS activities of some quinazolinones. Arzneimittelforsch 1982; 32(1):24–7

Lathrop DA, Valle–Aguilera JR, Millard RW, et al: Comparative electrophysiologic and coronary hemodynamic effects of diltiazem, nisoldipine and verapamil on myocardial tissue. Am J Cardiol 1982 Feb 18;49(3):613–20

Lau YS, Gnegy ME: Chronic haloperidol treatment increased calcium–dependent phosphorylation in rat striatum. Life Sci 1982 Jan 4;30(1):21–8

Laurian S, Le PK, Baumann P, et al: Relationship between plasma–levels of chlorpromazine and effects on EEG and evoked potentials in healthy volunteers. Pharmacopsychiatria 1981 Nov;14(6):199–204

Lauritsen BJ, Mellerup ET, Plenge P, et al: Serum lithium concentrations around the clock with different treatment regimens and the diurnal variation of the renal lithium clearance. Acta Psychiatr Scand 1981 Oct;64(4):314–9

Laux G: Medikamentöse Therapie von Angst–Zuständen. Krankenpfl J 1982 Feb 15;20(2):22–4 **(Ger)**

Laverriere JN, Gourdji D, Picart R, et al: Thyroliberin is rapidly transferred to the nucleus of GH3 pituitary cells at both 4 degree C and 37 degree C. Biochem Biophys Res Commun 1981 Dec 15; 103(3):833–40

Lavoie PA: On the mechanism of the inhibition of fast axonal transport caused by exposure of frog spinal ganglia to the sodium–deficient medium. Neurosci Lett 1981 Dec 11;27(2):131–4

Lawless L, DeMonaco HJ: Acute carbamazepine toxicity resulting from overdose [letter] Neurology (NY) 1982 Mar;32(3):328–9

Le Fur G, Phan T, Canton T, et al: Evidence for a coupling between dopaminergic receptors and phospholipid methylation in mouse B lymphocytes. Life Sci 1981 Dec 28;29(26):2737–49

Le Goues G: Les dépressions du troisième âge. Soins Psychiatr 1982 Jan; (15):19–23 **(Fre)**

Leander JD: Antagonism by methysergide of the effects of L–5–hydroxytryptophan and quipazine on schedule–controlled responding. Neuropharmacology 1981 Dec;20(12A):1141–3

Leary PM: DOes the child with a learning disability have a biochemical defect? S Afr Med J 1982 Jan 2;61(1):14–6

Lechin F, van der Dijs B: Intestinal pharmacomanometry and glucose tolerance: two kinds of dopaminergic mechanisms in the human. Acta Gastroenterol Latinoam 1981;11(2):247–59 (116 ref.)

Lecomte P, Wang NG, Sundaram K, et al: The antiandrogenic action of gonadotropin–releasing hormone and its agonists on the mouse kidney. Endocrinology 1982 Jan;110(1):1–6

Lederman RP, Lederman E, Work BA Jr, et al: The relationship of maternal prenatal development to progress in labor and fetal–newborn health. Birth Defects 1981;17(6):5–28

Lee ML: Glucagon in anaphylaxis [letter] J Allergy Clin Immunol 1982

AUTHOR SECTION

Mar;69(3):331-2

Leelavathi DE, Misra CH, Shelat H, et al: Effects of acute and chronic administration of phencyclidine on dopaminergic receptors in rat striatum. Commun Psychopharmacol 1980;4(5):417-24

Lefevre B, Kralem Z, Epstein Y, et al: Inhibin-like activity and steroid content in human follicular fluid during the periovulatory period. Int J Fertil 1981;26(4):295-6

Lehmann J, Langer SZ: Phenoxybenzamine blocks dopamine autoreceptors irreversible: implications for multiple dopamine receptor hypotheses. Eur J Pharmacol 1981 Nov 5;75(4):247-54

Lehmann M, Keul J, Huber G, et al: Plasma catecholamines in trained and untrained volunteers during graduated exercise. Int J Sports Med 1981 Aug;2(3):143-7

Lehmann M, Keul J, Hesse A: Zur aeroben und anaeroben Kapazität sowie Catecholaminexkretion von Kindern und Jugendlichen während langdauernder submaximaler Körperarbeit. Eur J Applied Physiol 1982; 48(1):135-45 (Eng. Abstr.) (Ger)

Lehmann WD, Theobald N, Heinrich HC: Assay for plasma free phenylalanine and tyrosine by high-pressure liquid chromatography and field desorption mass spectrometry and its application to an in vivo study of the phenylalanine hydroxylating system in man. Biomed Mass Spectrom 1981 Dec;8(12):598-605

Leighton HJ: Quantitative assessment of the pre- and postsynaptic alpha adrenoceptor antagonist potency of amitriptyline. J Pharmacol Exp Ther 1982 Feb;220(2):299-304

Lemay A, Faure N, Labrie F: Sensitivity of pituitary and corpus luteum responses to single intranasal administration of (D-ser[TBU]6-des-gly-NH2(10)) luteinizing hormone-releasing hormone ethylamide (Buserelin) in normal women. Fertil Steril 1982 Feb;37(2):193-200

Lemperiere T, Feline A, Ades J, et al: Etude ouverte de la mainsérine. Encephale 1981;7(4 Suppl):445-54 (Eng. Abstr.) (Fre)

Lempérière T, Quetin AM, Ferrand I, et al: Que dire à la famille d'un malade déprimé? Rev Infirm 1981 Oct;31(15):57-60 (Fre)

Lénárd L, Hahn Z: Amygdalar noradrenergic and dopaminergic mechanisms in the regulation of hunger and thirst-motivated behavior. Brain Res 1982 Feb 4;233(1):115-32

Leppäluoto J, Suhonen AS: High pressure liquid chromatography purification of human urinary samples for thyrotropin-releasing hormone radioimmunoassay. J Clin Endocrinol Metab 1982 May; 54(5):914-8

Lerer B, Ebstein RP, Belmaker RH: Subsensitivity of human beta-adrenergic adenylate cyclase after salbutamol treatment of depression. Psychopharmacology (Berlin) 1981;75(2):169-72

Lerner MH, Rosengarten H, Friedhoff AJ: Solubilization and characterization of 3H-spiroperidol binding sites of calf caudate. Life Sci 1981 Dec 7;29(23):2367-74

Leroux P, Tonon MC, Jegou S, et al: In vitro study of frog (Rana ridibunda Pallas) neurointermediate lobe secretion by use of a simplified perifusion system. I. Effect of TRH analogs upon alpha-MSH release. Gen Comp Endocrinol 1982 Jan;46(1):13-23

Leshem M: Ontogeny of fenfluramine and amphetamine anorexia compared in rat pups. Pharmacol Biochem Behav 1981 Dec; 15(6):859-63

Lesiecka M, Cytawa J: The effect of intrahypothalamic serotonin reinforcement on directional preference in rats. Acta Neurobiol Exp (Warsz) 1981;41(5):439-46

Leung PC, Whitmoyer DI, Sawyer CH: Electrophysiologic correlates of steroid modulation of luteinizing hormone release. Am J Physiol 1982 Mar;242(3):E164-70

Levison PK: An analysis of commonalities in substance abuse and habitual behavior. Natl Inst Drug Abuse Res Monogr Ser 1981 Jul;(37):27-41

Levitt B, Westfall DP: Factors influencing the release of purines and norepinephrine in the rabbit portal vein. Blood Vessels 1982 Jan-Feb; 19(1):30-40

Lew EO, Richardson JS: Neurochemical and behavioural correlates of the interaction between amphetamine and delta 9-tetrahydrocannabinol in the rat. Drug Alcohol Depend 1981 Sep;8(2):93-101

Lew GM: Age differences in blood pressure and norepinephrine concentration in normotensive rats after higher doses of estrogen. Gen Pharmacol 1982;13(1):75-8

Lewis MH, Baker AL, Ipp E, et al: Effect of somatostatin on determinants of bile flow in unanesthetized dogs. Ann Surg 1982 Jan;195(1):97-103

Lewis MJ: Age-related decline in brain stimulation reward: rejuvenation by amphetamine. Exp Aging Res 1981 Fall;7(3):225-34

Lewis MJ, Groom GV, Barber R, et al: The effects of propranolol and acebutolol on the overnight plasma levels of anterior pituitary and related hormones. Br J Clin Pharmacol 1981 Nov;12(5):737-42

Libe ML, Bogdanova ED, Rozenberg AE, et al: Sviazyvanie 3H-serotonina, 3H-diazepama i perekisnoe okislenie lipidov v membranakh mozga. Biull Eksp Biol Med 1981 Nov;92(11):552-4 (Eng. Abstr.) (Rus)

Lidov HG, Molliver ME: The structure of cerebral cortex in the rat following prenatal administration of 6-hydroxydopamine. Brain Res 1982 Jan;255(1):81-108

Liebman JM, Neale R, Norelka L, et al: Differential reversal of various dopamine antagonists by anticholinergics in Sidman avoidance: possible relationship to adrenergic blockade. Psychopharmacology (Berlin) 1981; 75(3):248-53

Lien EL, Garsky VM: Route of administration as a factor in the selectivity of hormone suppression of a somatostatin analog in rats. Horm Metab Res 1981 Dec;13(12):675-8

Liesi P, Paetau A, Rechardt L, et al: Glial uptake of monoamines in primary cultures of rat median raphe nucleus and cerebellum. A combined monoamine fluorescence and glial fibrillary acidic protein immunofluorescence study. Histochemistry 1981;73(2):239-50

Lightman SL, Iversen LL, Forsling ML: Dopamine and [D-ALA2, D-Leu5]enkephalin inhibit the electrically stimulated neurohypophyseal release of vasopressin in vitro: evidence for calcium-dependent opiate action. J Neurosci 1982 Jan;2(1):78-81

Lindberg M, Johannesson A, Forslind B: The effect of occlusive treatment on human skin: an electron microscopic study on epidermal morphology as affected by occlusion and dansyl chloride. Acta Derm Venereol (Stockh) 1982;62(1):1-5

Linden M, Schüssler G, Müller-Oerlinghausen B: Clinical trial of a test stick to control patient compliance under nomifensine treatment. Br J Psychiatry 1982 Jan;140:50-4

Lindsay WR: The effects of labeling: blind and nonblind ratings of social skills in schizophrenic and nonschizophrenic control subjects. Am J Psychiatry 1982 Feb;139(2):216-9

Lindström P, Sehlin J, Täljedal IB: Uptake mechanisms of 5-HT in pancreatic beta-cells. Ups J Med Sci 1981;86(2):143-8

Linnoila M, Rosenblatt JE, Jeste D, et al: Disparate serum thioridazine concentrations: liquid chromatography versus radioreceptor assay. Acta Pharmacol Toxicol (Copenh) 1982 Jan;50(1):25-9

Liotta AS, Houghten R, Krieger DT: Identification of a beta-endorphin-like peptide in cultured human placental cells. Nature 1982 Feb 18;295(5850):593-5

Lippmann S: Lithium's effects on the kidney. Postgrad Med 1982 Mar; 71(3):99-104, 107-8

Lippo de Becemberg I, Herrera V, Perez Ayuso E, et al: Effects of cholinergic agents on rat liver plasma membrane guanylate cyclase. FEBS Lett 1982 Jan 25;137(2):303-6

Lipshits RU, Zviagintseva TV: Vysvobozhdenie serotonina i gistamina pri éksperimental'noĭ kozhnoĭ rane. Fiziol Zh 1982 Jan-Feb;28(1):107-9 (Rus)

Liston DR, Franz DN, Gibb JW: Biochemical evidence for alteration of neostriatal dopaminergic function by 5,7-dihydroxytryptamine. J Neurochem 1982 May;38(5):1329-35

Lloyd HG, Perkins MN, Stone TW: Ethylenediamine as a specific releasing agent of gamma-aminobutyric acid in rat striatal slices. J Neurochem 1982 Apr;38(4):1168-9

Lloyd KG, Arbilla S, Beaumont K, et al: gamma-Aminobutyric acid (GABA) receptor stimulation. II. Specificity of progabide (SL 76002) and SL 75102 for the GABA receptor. J Pharmacol Exp Ther 1982 Mar;220(3):672-7

Lodge D, Anis NA: Effects of phencyclidine on excitatory amino acid activation of spinal interneurones in the cat. Eur J Pharmacol 1982 Jan;77(2-3):203-4

Loew DM, Weil C: Hydergine in senile mental impairment. Gerontology 1982 Jan-Feb;28(1):54-74 (76 ref.)

Loga S, Curry S, Lader M: Interaction of chlorpromazine and nortriptyline in patients with schizophrenia. Clin Pharmacokinet 1981 Nov-Dec; 6(6):454-62

Logan WJ, Harik SI: Specific uptake of norepinephrine and dopamine by homogenates of rat cerebral cortex after locus ceruleus lesion. J Neurosci 1982 Mar;2(3):394-8

Login IS, Cronin MJ, MacLeod RM: Neuroleptic malignant syndrome caused by dopamine depleting drugs [letter] Neurology (NY) 1982 Feb; 32(2):218-9

Loh YP, Gritsch HA: Evidence for intragranular processing of pro-opiocortin in the mouse pituitary intermediate lobe. Eur J Cell Biol 1981 Dec;26(1):177-83

Lombrail P, Feuilhade F, Hervé P, et al: Agranulocytose au cours d'un traitement par la miansérine. Therapie 1981 Sep-Oct;36(5):593-4(Fre)

Long RA, Weppelman RM, Taylor JE, et al: Purification and characterization of avian dopamine beta-hydroxylase. Biochemistry 1981 Dec 22;20(26):7423-31

Longas MO, Meyer K: Sequential hydrolysis of hyaluronate by beta-glucuronidase and beta-N-acetylhexosaminidase. Biochem J 1981 Aug 1;197(2):275-82

Longobardi M, Bondavalli F, Schenone P, et al: Synthesis and pharmacological activity of derivatives of exo-trimethylenenorbornane, IV. Farmaco [Sci] 1982 Jan;37(1):48-54

Lôo H: Implications thérapeutiques de la caractérisation biochimique des dépressions. Encephale 1981;7(4 Suppl):429-40 (62 ref.) (Eng. Abstr.) (Fre)

Lorén I, Björklund A, Falck B, et al: The aluminum-formaldehyde (ALFA) histofluorescence method for improved visualization of catecholamines and indoleamines. I. A detailed account of the methodology for central nervous tissue using paraffin, cryostat or Vibratome sections. J Neurosci Methods 1980 Jun;2(3):277-300

Löscher W, Böhme G, Schäfer H, et al: Effect of metabolites of valproic acid on the metabolism of GABA in brain and brain nerve endings. Neuropharmacology 1981 Dec;20(12A):1187-92

Löscher W, Frey HH: Transport of GABA at the blood-CSF interface. J Neurochem 1982 Apr;38(4):1072-9

Löscher W, Frey HH: Pharmacokinetics of diazepam in the dog. Arch Int Pharmacodyn Ther 1981 Dec;254(2):180-95

Löw M, Kisfaludy L, Hajós G, et al: Conformation-activity relationships of corticotropin segments. Acta Biochim Biophys Acad Sci Hung 1981; 16(1-2):105-8

Lu KH, Simpkins JW, Chen HT, et al: Patterns of pituitary LH release during sustained stimulation by synthetic LED in cycling female rats. Mater Med Pol 1980 Jan-Jun;12(1-2):63-9

Lyskowski J, Nasrallah HA: Slowed release lithium: a review and a comparative study. J Clin Psychopharmacol 1981 Nov;1(6):406-8

M

McCafferty JP, Roesler JM, Pendleton RG: Studies on the mechanisms involved in the cardiovascular response of the rat to hemorrhage. Arch Int Pharmacodyn Ther 1981 Nov;254(1):58-69

McCandless M, Nishiyama A, Petersen OH, et al: Mouse pancreatic acinar cells: voltage-clamp study of acetylcholine-evoked membrane current. J Physiol (Lond) 1981 Sep;318:57-71

McCann SM, Vijayan E, Samson WK, et al: Role of brain peptides in the control of pituitary hormone release. Mater Med Pol 1980 Jan-Jun; 12(1-2):47-52

McComb DJ, Horvath E, Kovacs K, et al: Enhanced responsiveness of lactotrophs in ectopic pituitaries to bromocryptine and estrone acetate. Acta Anat (Basel) 1981 Jun;110(2):113-20

McCredie E, Goddard C, Vinson GP, et al: Subcellular compartmentation of steroidogenesis in the zona fasciculata/reticularis of the rat adrenal cortex. J Steroid Biochem 1981 Dec;14(12):1269-77

McCulloch J, Kelly PA: Alterations in local cerebral glucose utilisation in specific thalamic nuclei following apomorphine. J Cereb Blood Flow Metab 1981;1(1):133-6

McCurdy HH, Lewellen LJ, Cagle JC, et al: A rapid procedure for the screening and quantitation of barbiturates, diazepam, desmethyldiazepam and methaqualone. J Anal Toxicol 1981 Sep-Oct; 5(5):253-7

MacDonald VW, Charache S: Drug-induced oxidation and precipitation of hemoglobins A, S and C. Biochim Biophys Acta 1982 Feb 4; 701(1):39-44

McEachron DL, Kripke DF, Hawkins R, et al: Lithium delays biochemical circadian rhythms in rats. Neuropsychobiology 1982 Jan-Feb;8(1):12-29

McElnay JC, Temple DJ: The use of buccal partitioning as a model to examine the effects of aluminium hydroxide gel on the absorption of propranolol. Br J Clin Pharmacol 1982 Mar;13(3):399-403

McEvoy JP, Libiger J, Wilson WH, et al: Viloxazine HCl in the treatment of endogenous depression: a standard (imipramine) controlled clinical study. J Clin Psychiatry 1981 Mar;43(3):111-2

McGregor GP, Woodhams PL, O'Shaughnessy DJ, et al: Developmental changes in bombesin, substance P, somatostatin and vasoactive intestinal polypeptide in the rat brain. Neurosci Lett 1982 Jan 22;28(1):21-7

McGuirk SM, Muir WW, Sams RA: Pharmacokinetic analysis of intravenously and orally administered quinidine in cows. Am J Vet Res 1981 Sep;42(9):1482-7

Machaňová L, Bartos S: Effect of epinephrine on glucose metabolism in kid liver slices. Physiol Bohemoslov 1981;30(6):573-6

Machen TE, Rutten MJ, Ekblad EB: Histamine, cAMP, and activation of piglet gastric mucosa. Am J Physiol 1982 Feb;242(2):G79-84

McIlwain H: The flow of thought and the flow of substance in the brain. Biol Psychol 1981 Mar-May;12(2-3):147-69

McIntyre IM, Norman TR, Burrows GD, et al: Determination of nomifensine plasma concentrations: a comparison of radioimmunoassay and gas chromatography. Br J Clin Pharmacol 1981 Nov;12(5):691-4

Mackay-Sim A, Lang DG: Rats' responses to blood and body odors of stressed and non-stressed conspecifics. Physiol Behav 1981 Sep; 27(3):503-10

MacKenzie DS: In vivo thyroxine release in day-old cockerels in response to acute stimulation by mammalian and avian pituitary hormones. Poult Sci 1981 Sep;60(9):2136-43

Mackenzie IC, Bickenbach JR, Rittman BR: Reactivity of epidermal Langerhans cells to a histochemical method for demonstration of beta-glucuronidase. J Invest Dermatol 1982 Mar;78(3):239-42

McMillan DE, Cole-Fullenwider DA, Hardwick WC, et al: Phencyclidine discrimination in the pigeon using color tracking under second-order schedule. J Exp Anal Behav 1982 Jan;37(1):143-7

McMillan DE: Effects of chemicals on delayed matching behavior in pigeons I: acute effects of drugs. Neurotoxicology (Park Forest II) 1981 Nov;2(3):485-98

McMurtry JP, Wexler BC: Hyperprolactinemia and hyperadrenocorticism accompanied by normal blood pressure in Sprague-Dawley rats. Proc Soc Exp Biol Med 1981 Oct;168(1):114-8

McNatty KP, Ball K, Gibb M, et al: Induction of cyclic ovarian activity in seasonally anoestrous ewes with exogenous GnRH. J Reprod Fertil 1982 Jan;64(1):93-6

Macrides F, Davis BJ, Youngs WM, et al: Cholinergic and catecholaminergic afferents to the olfactory bulb in the hamster: a neuroanatomical, biochemical, and histochemical investigation. J Comp Neurol 1981 Dec 10;203(3):495-514

McRoberts JA, Erlinger S, Rindler MJ, et al: Furosemide-sensitive salt transport in the Madin-Darby canine kidney cell line. Evidence for the cotransport of Na+, K+, and Cl-. J Biol Chem 1982 Mar 10; 257(5):2260-6

Madden KS, van der Kloot W: At the frog neuromuscular junction prostaglandin synthase inhibitors depress and PGE partially restores quantal acetylcholine release. Brain Res 1982 Feb 25;234(2):464-8

Madle E, Obe G, Hansen J, et al: Harman and norharman: induction of sister-chromatid exchanges in human peripheral lymphocytes in vitro and interaction with isolated DNA. Mutat Res 1981 Dec;90(4):433-42

Madsen PW, Hare BD, Sangdee C, et al: Contrasting effects of clonidine and 5-hydroxytryptophan on spinal sympathetic pathways. Clin Exp Hypertens 1981;3(6):1151-63

Maggi JC, Angelats J, Scott JP: Gangrene in a neonate following dopamine therapy. J Pediatr 1982 Feb;100(2):323-5

Magleby KL, Pallotta BS: A study of desensitization of acetylcholine receptors using nerve-released transmitter in the frog. J Physiol (Lond) 1981 Jul;316:225-50

Magnussen I, Jensen TS, Rand JH, et al: Plasma accumulation of metabolism of orally administered single dose L-5-hydroxytryptophan in man. Acta Pharmacol Toxicol (Copenh) 1981 Sep;49(3):184-9

Magous R, Bali JP, Moroder L, et al: Effect of Nin-formylation of the tryptophan residue on gastrin (HG-13) binding and on gastric acid secretion. Eur J Pharmacol 1982 Jan 8;77(1):11-6

Maia H Jr, Barbosa IC, Maia H, et al: Mid-cycle contraception with LHRH in women. Reproduccion 1981 Oct-Dec;5(4):251-60

Maickel RP, Tocco DR: The effects of single doses of alkali metal cations on deprivation-induced fluid consumption by rats. Res Commun Chem Pathol Pharmacol 1981 Dec;34(3):493-502

Mailman RB, Lewis MH: Food additives and developmental disorders: the case of erythrosin (FD&C Red 3), or guilty until proven innocent? Appl Res Ment Retard 1981;2(4):297-305

Mais DE, Bosin TR: Structural specificity of the inhibition of serotonin accumulation in rat lung slices. Res Commun Chem Pathol Pharmacol 1981 Nov;34(2):241-50

Maj J: Atypical antidepressant drugs - psychopharmacological profile and mechanism of action. Pharmacopsychiatria 1982 Jan;15(1):26-30

Majocha RE, Pearse RN, Baldessarini RJ, et al: The noradrenergic system in cultured aggregates of fetal rat brain cells: morphology of the aggregates and pharmacological indices of noradrenergic neurons. Brain Res 1981 Dec 28;230(1-2):235-52

Malakhovskaia DB, Sviderskaia GE: Vliiania GAMK na dvigatel'nuiu aktivnost' krys v rannem postnatal'nom periode razvitiia. Zh Vyssh Nerv Deiat 1982 Jan-Feb;32(1):115-21 (Eng. Abstr.) **(Rus)**

Maley B, Elde R: Localization of substance P-like immunoreactivity in cell bodies of the feline dorsal vagal nucleus. Neurosci Lett 1981 Dec 11;27(2):187-91

Malmgren R, Asberg M, Olsson P, et al: Defective serotonin transport mechanism in platelets from endogenously depressed patients. Life Sci 1981 Dec 21;29(25):2649-58

Malnoë A, Cox JA, Stein EA: Ca2+-dependent regulation of calmodulin binding and adenylate cyclase activation in bovine cerebellar membranes. Biochim Biophys Acta 1982 Jan 12;714(1):84-92

Malyshenko NM: Rol' kortikosteroidov v formirovanii reaktsiĭ strakha i agressi. Zh Vyssh Nerv Deiat 1982 Jan-Feb;32(1):144-51 (Eng. Abstr.) **(Rus)**

Manch JN: Mapping of a new pan mutation in Escherichia coli K-12. Can J Microbiol 1981 Nov;27(11):1231-3

Mandell AJ, Russo PV: Short-term regulation of hydroxylase cofactor activity in rat brain. J Neurochem 1981 Dec;37(6):1573-8

Mangini RJ: Cimetidine--benzodiazepine interactions [letter] Am J Hosp Pharm 1982 Feb;39(2):236, 242

Mann DR, Jackson GG, Blank MS: Influence of adrenocorticotropin and adrenalectomy on gonadotropin secretion in immature rats. Neuroendocrinology 1982 Jan;34(1):20-6

Männistö P, Mattila J, Kaakkola S: Possible involvement of nigrostriatal dopamine system in the inhibition of thyrotropin secretion in the rat. Eur J Pharmacol 1981 Dec 17;76(4):403-9

Mansky T, Mestres-Ventura P, Wuttke W: Involvement of GABA in the feedback action of estradiol on gonadotropin and prolactin release: hypothalamic GABA and catecholamine turnover rates. Brain Res 1982 Jan 14;231(2):353-64

Mantelli L, Manzini S, Mugelli A, et al: The influence of some cardiodepressant drugs on the histamine-induced restoration of contractility in potassium-depolarized heart preparations. Arch Int Pharmacodyn Ther 1981 Nov;254(1):99-108

Manukhina EB, Vorontsova EIa, Volina EV, et al: Issledovanie dinamiki soderzhaniia noradrenalina v vorotnoĭ vene pecheni i predserdii krys pri stresse. Biull Eksp Biol Med 1981 Dec;92(12):673-4 (Eng. Abstr.) **(Rus)**

Marangos PJ, Trams E, Clark-Rosenberg RL, et al: Anticonvulsant doses

AUTHOR SECTION

of inosine result in brain levels sufficient to inhibit [3H] diazepam binding. Psychopharmacology (Berlin) 1981;75(2):175–8

Marangos PJ, Crawley JN: Chronic benzodiazepine treatment increases [3H]muscimol binding in mouse brain. Neuropharmacology 1982 Jan; 21(1):81–4

Marani E, Rietveld WJ, Boon ME, et al: Fluorescence–displacement from the median eminence towards the arcuate nucleus at puberty. Histochemistry 1981;73(2):165–9

Marchi M, Hoffman DW, Giacobini E, et al: Development and aging of cholinergic synapses. VI. Mechanisms of acetylcholine biosynthesis in the chick iris. Dev Neurosci 1981;4(6):442–50

Marchi M, Paudice P, Raiteri M: Autoregulation of acetylcholine release in isolated hippocampal nerve endings. Eur J Pharmacol 1981 Jul 17; 73(1):75–9

Mardente S, Bicchi C, Nano GM: GLC–ECD determination of 1–(2–hydroxyethyl)–3–hydroxy–7–chloro–1,3–dihydro–5–(O–fluorophe (SAS 643) in plasma and urine and identification of its main biotransformation products. Ther Drug Monit 1981;3(4):351–6

Margalit R, Shanzer A: A study of Li+–selective permeation through lipid bilayer membranes mediated by a new ionophore (AS701). Biochim Biophys Acta 1981 Dec 7;649(2):441–8

Maroun R, Mattice WL: Solution conformations of the pituitary opioid peptide dynorphin–(1–13). Biochem Biophys Res Commun 1981 Nov 30;103(2):442–6

Marshall I, Phillips DG, Nasmyth PA: Calcium ions, morphine tolerance and noradrenergic transmission in the mouse vas deferens. Eur J Pharmacol 1981 Nov 5;75(4):205–13

Martens GJ, Jenks BG, Van Overbeeke AP: Biosynthesis of pairs of peptides related to melanotropin, corticotropin and endorphin in the pars intermedia of the amphibian pituitary gland. Eur J Biochem 1982 Feb;122(1):1–10

Martensz ND, Herbert J: Drug–induced hyperprolactinaemia and discharges of luteinizing hormone evoked by oestrogen in ovariectomized rhesus monkeys. J Endocrinol 1982 Jan;92(1):111–22

Martin A, Masson JM, Jusseaume P, et al: La déméxiptiline dans le traitement des états mélancoliques (réflexions après trois années d'utilisation). Ann Med Psychol (Paris) 1981 Nov;139(9):1023–35 **(Fre)**

Martin AF, Pagani ED, Solaro RJ: Thyroxine–induced redistribution of isoenzymes of rabbit ventricular myosin. Circ Res 1982 Jan;50(1):117–24

Martin GE, Haubrich DR, Williams M: Pharmacological profiles of the putative dopamine autoreceptor agonists 3–PPP and TL–99. Eur J Pharmacol 1981 Nov 19;76(1):15–23

Martin GE, Bendesky RJ: Further evidence for a GABA–like action on kojic amine. Neurosci Lett 1981 Nov 18;27(1):37–40

Martin JE, McKeel DW Jr, Sattler C: Melatonin directly inhibits rat gonadotroph cells. Endocrinology 1982 Apr;110(4):1079–84

Martin LL, Bouchal RL, Smith DJ: Ketamine inhibits serotonin uptake in vivo. Neuropharmacology 1982 Feb;21(2):113–8

Martin LL, Smith DJ: Ketamine inhibits serotonin synthesis and metabolism in vivo. Neuropharmacology 1982 Feb;21(2):119–25

Martin MR, James ED: Treatment of unstable detrusor (irritable bladder) using fluphenazine and nortriptyline: progress report. Prog Clin Biol Res 1981;78:335–8

Martin RP, Lam SW, McGonigle EJ, et al: GLC determination of bromperidol in tablets. J Pharm Sci 1982 Jan;71(1):112–4

Martin WR, McNicholas LF: Benzodiazepine dependence studies in rodents. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):37–42

Martinez–Aguirre E: Antagonism of ketamine by 4–aminopyridine and physostigmine [letter] Br J Anaesth 1982 Jan;54(1):110

Mastalerz P, Kupczyk–Subotkowska L, Herman ZS, et al: Analgesic activity of enkephalin analogues containing aminophosphonic acid residues at C–terminal position. Naturwissenschaften 1982 Jan; 69(1):46–7

Masuoka T, Masuda Y, Kiryu Y: [Basic and clinical evaluation of the method of free thyroxine levels in serum with radioimmunoassay (author's transl)] Horumon To Rinsho 1981 Aug;29(8):1025–9 **(Jpn)**

Mathew RJ, Ho BT, Davis C, et al: Depression, antidepressants, and plasma DBH. Psychiatry Res 1981 Dec;5(3):331–4

Mathew RJ, Ho BT, Taylor DL, et al: Catecholamine and dopamine–beta–hydroxylase in anxiety. J Psychosom Res 1981; 25(6):499–504

Mathew RJ, Ho BT, Khan MM, et al: True and pseudo cholinesterases in depression. Am J Psychiatry 1982 Jan;139(1):125–7

Matsuda M: [Function of gamma–aminobutyric acid in central nervous system (author's transl)] Seikagaku 1981;53(7):517–22 (24 ref.) **(Jpn)**

Matsumoto RM, Cho AK: Conversion of N–hydroxyamphetamine to phenylacetone oxime by rat liver microsomes. Biochem Pharmacol 1982 Jan 1;31(1):105–8

Matsumoto S: Effects of carotid Body chemoreceptor stimulation by 5–HT on phrenic nerve activity and ventilation in the rabbit. Arch Int Pharmacodyn Ther 1981 Dec;254(2):282–92

Matsuo E, Yamada K: Acid mucopolysaccharide and one of its glomerular degrading enzymes beta–glucuronidase in experimental and human glomerulonephritis. Renal Physiol 1980;3(1–6):97–105

Matsuzaki T, Shiosaka S, Inagaki S, et al: Distribution of neuropeptides in the dorsal pontine tegmental area of the rat. Cell Mol Biol 1981; 27(5):499–508

Matteri RL, Moberg GP: Effect of cortisol or adrenocorticotrophin on release of luteinizing hormone induced by luteinizing hormone releasing hormone in the diary heifer. J Endocrinol 1982 Jan;92(1):141–6

Matthews RW, Lemon MJ: Quantitative autoradiographic study of tryptophane movement in guinea–pig submandibular glands. Arch Oral Biol 1981;26(11):911–4

Mattila J: Studies on the mechanism of the GABAergic inhibition of TSH secretion in male rats. Acta Pharmacol Toxicol (Copenh) 1981 Apr;48(4):320–5

Matuszek M, Ishikawa Y: Effects of 5,7–dihydroxytryptamine and 6–hydroxydopamine on fever response in conscious rats. Pol J Pharmacol Pharm 1981;33(3):305–12

Mawson D, Marks IM, Ramm L: Clomipramine and exposure for chronic obsessive–compulsive rituals: III. Two year follow–up and further findings. Br J Psychiatry 1982 Jan;140:11–8

Mayer DJ, Watkins LR: Role of endorphins in endogenous pain control systems. Mod Probl Pharmacopsychiatry 1981;17:68–96

Mazurek N, Pecht I, Teichberg VI, et al: The role of the N–terminal tetrapeptide in the histamine releasing action of substance P. Neuropharmacology 1981 Nov;20(11):1025–7

Mediavilla A, Pazos A, Flórez J: Acciones respiratorias de la dopamina intracerebroventricular en la rata. Arch Farmacol Toxicol 1981 Apr; 7(1):73–6 **(Spa)**

Meibach RC, Katzman R: Origin, course and termination of dopaminergic substantia nigra neurons projecting to the amygdaloid complex in the cat. Neuroscience 1981;6(11):2159–71

Meiselman HJ: Morphological determinants of red cell deformability. Scand J Clin Lab Invest [Suppl] 1981;41(156):27–34

Mekhova GM, Poskalenko AN: Vliianie novogo antidepressanta tséfedrina na kompensatornuiu gipertrofiiu iaichnika i ingibiruiushchil ee éffekt éstrogena. Farmakol Toksikol 1982 Jan–Feb;45(1):52–4 (Eng. Abstr.) **(Rus)**

Meller E, Friedman E: Lithium dissociates haloperidol–induced behavioral supersensitivity from reduced dopac increase in rat striatum. Eur J Pharmacol 1981 Nov 19;76(1):25–9

Meller E, Friedman E: Differential dose– and time–dependent effects of molindone on dopamine neurons of rat brain: mediation by irreversible inhibition of monoamine oxidase. J Pharmacol Exp Ther 1982 Mar; 220(3):609–15

Mellström B, von Bahr C: Demethylation and hydroxylation of amitriptyline, nortriptyline, and 10–hydroxyamitriptyline in human liver microsomes. Drug Metab Dispos 1981 Nov–Dec;9(6):565–8

Memo M, Pradhan S, Hanbauer I: Cocaine–induced supersensitivity of striatal dopamine receptors: role of endogenous calmodulin. Neuropharmacology 1981 Dec;20(12A):1145–50

Mena EE, Foster AC, Fagg GE, et al: Identification of synapse specific components: synaptic glycoproteins, proteins, and transmitter binding sites. J Neurochem 1981 Dec;37(6):1557–66

Ménard D, Malo C: Lack of effect of cortisone, thyroxine and insulin on the developmental pattern of mouse intestinal glucose–6–phosphatase activity. Experientia 1982 Jan 15;38(1):111–2

Mendlewicz J: Biological factors in affective disorders and their relevance to lithium prophylaxis. Pharmacopsychiatria 1982 Jan;15(1):11–8

Menkes DB, Aghajanian GK: alpha 1–Adrenoceptor–mediated responses in the lateral geniculate nucleus are enhanced by chronic antidepressant treatment. Eur J Pharmacol 1981 Aug 27;74(1):27–35

Merritt JE, Tomlinson S, Brown BL: Phenothiazines inhibit prolactin secretion in vitro. A possible role for calmodulin in stimulus—secretion coupling in the pituitary. FEBS Lett 1981 Nov 30;135(1):107–10

Messer A: Primary monolayer cultures of the rat corpus striatum: morphology and properties related to acetylcholine and gamma–aminobutyrate. Neuroscience 1981;6(12):2677–87

Mesripour M, Clark JB: Tyrosine hydroxylase activity in rat brain synaptosomes: direct measurement using high performance liquid chromatography. J Neurochem 1982 Apr;38(4):1139–43

Mettrick DF, Rahman MS, Podesta RB: Effect of 5–hydroxytryptamine (5–HT; serotonin) on in vitro glucose uptake and glycogen reserves in Hymenolepis diminuta. Mol Biochem Parasitol 1981 Dec; 4(3–4):217–23

Meuer S, Hugli TE, Andreatta RH, et al: Comparative study on biological activities of various anaphylatoxins (C4a, C3a, C5a). Investigations on their ability to induce platelet secretion. Inflammation 1981 Dec; 5(4):263–73

Meuer S, Zanker B, Hadding U, et al: Low zone desensitization: a stimulus–specific control mechanism of cell response. Investigations on anaphylatoxin–induced platelet secretion. J Exp Med 1982 Mar 1; 155(3):698–710

Meurling S, Plantin LO: The concentrations of trace elements in blood from healthy newborn infants. Acta Chir Scand 1981;147(6):481–5

Meyer D, Halfin V: Toxicity secondary to meperidine in patients on monoamine oxidase inhibitors: a case report and critical review. J Clin Psychopharmacol 1981 Sep;1(5):319–21

Meyer J, Portmann P: Fluorometric determination of the D–norpseudoephedrine in the plasma. Plasma levels during the resorption from the free and extended-release form. Pharm Acta Helv 1982;57(1):12-5

Michalodimitrakis M, Parchas S, Coutselinis A: Fatal hydantoin syndrome: congenital malformation of the urinary tract-a case report. Clin Toxicol 1981;18(9):1095-7

Michel G, Vásquez R, Basso L: Seguimiento de pacientes tratados con fenotiazinas de depósito, en Valparaíso, Chile. Bol Of Sanit Panam 1981 Nov;91(5):418-27 (Eng. Abstr.) (Spa)

Milanés MV, Serrano JS: Mecanismo periférico implicado en las interacciones de atropina, anfetamina y reserpina sobre la temperatura corporal de la rata consciente. Arch Farmacol Toxicol 1981 Apr; 7(1):77-8 (Spa)

Millan MJ: Stress and endogenous opioid peptides: a review. Mod Probl Pharmacopsychiatry 1981;17:49-67

Millan MJ, Duka T: Anxiolytic properties of opiates and endogenous opioid peptides and their relationship to the actions of benzodiazepines. Mod Probl Pharmacopsychiatry 1981;17:123-41

Millard WJ, Martin JB Jr, Audet J, et al: Evidence that reduced growth hormone secretion observed in monosodium glutamate-treated rats is the result of a deficiency in growth hormone-releasing factor. Endocrinology 1982 Feb;110(2):540-50

Miller AM, Yunis AA: Reversal of in vitro drug induced myeloid suppression by lithium. Exp Hematol 1981 Aug;9(7):775-80

Miller LH, Kastin AJ, Hayes M, et al: Inverse relationship between onset and duration of EEG effects of six peripherally administered peptides. Pharmacol Biochem Behav 1981 Dec;15(6):845-8

Miller RR, Ayres JA, Calhoun LL, et al: Comparative short-term inhalation toxicity of ethylene glycol monomethyl ether and propylene glycol monomethyl ether in rats and mouse. Toxicol Appl Pharmacol 1981 Dec;61(3):368-77

Milner N: Models of rationality and mental health rights. Int J Law Psychiatry 1981;4(1-2):35-52

Mindel JS, Koenigsberg AM, Kharlamb AB, et al: The effect of echothiophate on the biphasic response of rabbit ocular pressure to dipivefrin. Arch Ophthalmol 1982 Jan;100(1):147-51

Minganti A, Falugi C: An epithelial localization of acetylcholinesterase in the ascidian Ciona intestinalis embryos and larvae. Acta Embryol Morphol Exp 1980 Oct;1(2):143-55

Miranda H, Vergara JF, Rosselot F, et al: Biogenic amines and beta-endorphin responses in the rat vas deferens. Gen Pharmacol 1982; 13(1):45-8

Mirmiran M, Corner M: Neuronal discharge patterns in the occipital cortex of developing rats during active and quiet sleep. Brain Res 1982 Jan;255(1):37-48

Mirzoian RS, Gan'shina TS, Shmullovich LM: Vliianie izonikotinoilamida GAMK na mozgovoe krovoobrashchenie. Biull Eksp Biol Med 1981 Nov;92(11):573-4 (Eng. Abstr.) (Rus)

Misgeld U, Wagner A, Ohno T: Depolarizing IPSPs and Depolarization by GABA of rat neostriatum cells in vitro. Exp Brain Res 1982; 45(1-2):108-14

Mishra R, Sulser F: Cyclic AMP response to norepinephrine in the limbic forebrain of male and female rats: effect of desipramine. Biochem Pharmacol 1981 Nov 15;30(22):3126-8

Misra CH, Shelat H, Smith RC: Influence of age on the effects of chronic fluphenazine on receptor binding in rat brain. Eur J Pharmacol 1981 Dec 17;76(4):317-24

Misra CH, Smith RC: Effects of age on dopaminergic supersensitivity induced by chronic fluphenazine. Commun Psychopharmacol 1980; 4(5):411-5

Mitchell R, Fleetwood-Walker S: Substance P, but not TRH, modulates the 5-HT autoreceptor in ventral lumbar spinal cord. Eur J Pharmacol 1981 Nov 19;76(1):119-20

Mittag T, Tormay A: Desensitization of the beta-adrenergic receptor-adenylate cyclase complex in rabbit iris-ciliary body induced by topical epinephrine. Exp Eye Res 1981 Nov;33(5):497-503

Miyahara S, Oomura Y: Inhibitory action of the ventral noradrenergic bundle on the lateral hypothalamic neurons through alpha-noradrenergic mechanisms in the rat. Brain Res 1982 Feb 25; 234(2):459-63

Miyake A, Yen SS: Direct in vitro stimulation of pituitary LH release by alpha melanocyte stimulating hormone. Life Sci 1981 Dec 21; 29(25):2637-40

Mizuchi A, Saruta S, Kitagawa N, et al: Development of radioimmunoassay for sultopride and sulpiride. Arch Int Pharmacodyn Ther 1981 Dec;254(2):317-26

Mizukoshi H, Itoh M, Matsukawa S, et al: Tryptophan fluorescence of human hemoglobin. II. Effect of inositol hexaphosphate on the T-R transition. Biochim Biophys Acta 1982 Jan 18;700(2):143-7

Mocchetti I, De Angelis L, Racagni G: Postmortem changes of normetanephrine determined by a mass-fragmentographic technique in different rat brain areas. J Neurochem 1981 Dec;37(6):1607-9

Möhler H, Richards JG: Agonist and antagonist benzodiazepine receptor interaction in vitro. Nature 1981 Dec 24;294(5843):763-5

Molander L, Birkhed D: Effect of single oral doses of various neuroleptic drugs on salivary secretion rate, pH, and buffer capacity in healthy subjects. Psychopharmacology (Berlin) 1981;75(2):114-8

Molcan J, Novotny V, Korinkova V, et al: Tofizopam in the therapy of anxious-depressive syndromes. Agressologie 1981 Nov;22(D):23-4

Molcan J, Zucha I, Heretik A, et al: Subjective and psychometric assessment of effect in single application of clobazam. Agressologie 1981 Oct;22(C):43-5

Molčan J, Koníková M, Zucha I: Niektoré vztahy psychohygieny a psychofarmakológie. Cesk Psychiatr 1981 Jun;77(3):173-5 (Eng. Abstr.) (Slo)

Molcan J, Zucha I: Some dissociations in the anxiety and mental tension. Agressologie 1981 Oct;22(C):17-8

Moleman P, Borstrok JJ: Analysis of urinary 3-methoxy-4-hydroxyphenylglycol by high-performance liquid chromatography and electrochemical detection. J Chromatogr 1982 Feb 12;227(2):391-405

Momose K, Otsuka H, Higashikawa S, et al: Studies on isolated smooth muscle cells. VII. Response to agonists and the contraction velocity of taenia coli of guinea pig and the single smooth muscle cells. J Pharmacobiodyn 1981 Sep;4(9):670-6

Monaco F, Mutani R, Piredda S, et al: Brain uptake of carbamazepine in the cat. Epilepsia 1982 Feb;23(1):19-22

Mondadori C: Pharmacological modulation of memory: trends and problems. Acta Neurol Scand [Suppl] 1981;89:129-43

Mondal M, Banerjee PK: Role of cholinesterase in melanogenesis: search for a control mechanism. Indian J Biochem Biophys 1981 Dec; 18(6):448-9

Montagu A: The adolescent's unreadiness for pregnancy and motherhood. Pediatr Ann 1981 Dec;10(12):52-6

Montogomery SA, Rani SJ, Roy D, et al: Miansérine: synthèse et discussion des études en double-aveugle versus nomifensine. Encephale 1981;7(4 Suppl):485-94 (Eng. Abstr.) (Fre)

Moore KE, Stretton RJ: The effect of pH, temperature and certain media constituents on the stability and activity of the preservative, bronopol. J Appl Bacteriol 1981 Dec;51(3):483-94

Morad M, Tung L, Greenspan AM: Effect of diltiazem on calcium transport and development of tension in heart muscle. Am J Cardiol 1982 Feb 18;49(3):595-601

Morel A, Lauber M, Cohen P: Selective processing of the 15 000 Mr prosomatostatin by mouse hypothalamic extracts releases the tetradecapeptide. FEBS Lett 1981 Dec 28;136(2):316-8

Morelock S, Hingson R, Kayne H, et al: Bendectin and fetal development. A study of Boston City Hospital. Am J Obstet Gynecol 1982 Jan 15; 142(2):209-13

Morgan IG, Oliver J, Chubb IW: Discrete distributions of putative cholinergic and somatostatinergic amacrine cell dendrites in chicken retina. Neurosci Lett 1981 Nov 18;27(1):55-60

Morgan JB, York DA, Wasilewska A, et al: A study of the thermic responses to a meal and to a sympathomimetic drug (ephedrine) in relation to energy balance in man. Br J Nutr 1982 Jan;47(1):21-32

Morgan K: Effect of low-dose nitrazepam on performance in the elderly [letter] Lancet 1982 Feb 27;1(8270):516

Morgenstern R, Fink H, Bluth R: Computer-aided calculation of dose response curves in behavioral pharmacology by using a nonlinear regression procedure. Pharmacol Biochem Behav 1981 Dec; 15(6):987-91

Mori H, Tanaka T, Nishikawa A, et al: Enhancing effect of barbital on N-2-fluorenylacetamide-induced rat liver lesions. Gan 1981 Oct; 72(5):798-801

Mori K: Automated measurement of catecholamines in urine, plasma and tissue homogenates by high-performance liquid chromatography with fluorometric detection. J Chromatogr 1981 Nov 20;218:631-7

Mori M, Prasad C, Wilber JF: Regional dissociation of histidyl—proline diketopiperazine (cyclo-(His—Pro)) and thyrotropin-releasing hormone (TRH) in the rat brain. Brain Res 1982 Jan 14;231(2):451-3

Morihara K: [Peptide bond synthesis catalyzed by various proteases (author's transl)] Tanpakushitsu Kakusan Koso 1981 Oct;26(13):1979-98 (78 ref.) (Jpn)

Morikawa H, Okamura H, Takenaka A, et al: Histamine concentration and its effect on ovarian contractility in humans. Int J Fertil 1981; 26(4):283-6

Morita I, Masujima T, Yoshida H, et al: Enrichment and high-performance liquid chromatography analysis of tryptophan metabolites in plasma. Anal Biochem 1981 Nov 15;118(1):142-6

Moroji T, Watanabe N, Aoki N, et al: Antipsychotic effects of ceruletide (caerulein) on chronic schizophrenia [letter] Arch Gen Psychiatry 1982 Apr;39(4):485-6

Moroni F, Bianchi C, Moneti G, et al: Release of GABA from the guinea-pig neocortex induced by electrical stimulation of the 'locus coeruleus' or by norepinephrine. Brain Res 1982 Jan 28;232(1):216-21

Mory G, Ricquier D, Nechad M, et al: Impairment of trophic response of brown fat to cold in guanethidine-treated rats. Am J Physiol 1982 Mar;242(3):C159-65

Mostovoi VS: Vliianie tireoidnykh gormonov na nekotorye pokazateli vodno-solevogo obmena i funktsii pochek u krys. Fiziol Zh 1981 Nov-Dec;27(6):826-9 (Rus)

Motta M, Martini L: Neurotensin inhibits LH release. Proc Soc Exp Biol Med 1981 Oct;168(1):62-4

AUTHOR SECTION

Mounsey I, Brady KA, Carroll J, et al: K+-evoked [3H]-5-HT release from rat frontal cortex slices: the effect of 5-HT agonists and antagonists. Biochem Pharmacol 1982 Jan 1;31(1):49-53

Müller-Oerlinghausen B, Schmidt L, Rüther E: Drug monitoring in psychiatry. Mod Probl Pharmacopsychiatry 1981;16:101-8

Murakami K, Murakami K, Ueno T, et al: Simultaneous determination of chlorpromazine and levomepromazine in human plasma and urine by high-performance liquid chromatography using electrochemical detection. J Chromatogr 1982 Jan 8;227(1):103-12

Muraki T, Uzumaki H, Nakadate T, et al: Involvement of alpha 1-adrenergic receptors in the inhibitory effect of catecholamines on the thyrotropin-induced release of thyroxine by the mouse thyroid. Endocrinology 1982 Jan;110(1):51-4

Muramatsu I, Miura A, Fujiwara M, et al: Rat isolated mesenteric artery: a sensitive preparation for the bioassay of urotensin I. Gen Comp Endocrinol 1981 Dec;45(4):446-52

Murase K, Nedeljkov V, Randic M: The actions of neuropeptides on dorsal horn neurons in the rat spinal cord slice preparation: an intracellular study. Brain Res 1982 Feb 18;234(1):170-6

Murray J: Long-term psychotropic drug-taking and the process of withdrawal. Psychol Med 1981 Nov;11(4):853-8

Muto K, Toshima N, Yokoo H, et al: The chronic effect of nomifensine on rat stereotyped behavior. Kurume Med J 1981;28(2):173-5

Myers RD, Ross DH: Radiation and brain calcium: a review and critique. Neurosci Biobehav Rev 1981 Winter;5(4):503-43 (355 ref.)

N

Nabeshima T, Ho IK: Acute and chronic effects of pentobarbital on 5-hydroxytryptamine in mouse brain. Prog Neuropsychopharmacol 1981;5(4):373-81

Nadler JV: Desensitization-like changes in GABA receptor binding of rat fascia dentata after entorhinal lesion. Neurosci Lett 1981 Nov 4;26(3):275-81

Naess O, Cusan L, Brekke I, et al: Effects of castration, sex steroids, LHRH and glucocorticoids on LHRH binding in the anterior pituitary of male rats. Int J Androl 1981 Dec;4(6):685-90

Nag S, Sanyal S, Ghosh KK, et al: Prolactin suppression and spermatogenic developments in maturing rats. A quantitative study. Horm Res 1981;15(2):72-7

Nagakawa T, Ikemi Y: A new model of integrating Occidental and Oriental approaches. J Psychosom Res 1982;26(1):57-62

Nagnibeda NN, Vorobel IM: Izmenenie ékskretsii katekholaminov u podrostkov v usloviiakh vysokogor'ia. Fiziol Zh 1982 Jan-Feb;28(1):91-2 **(Rus)**

Náhunek K, Svestka J, Rysánek R, et al: K postavení pyrazidolu ve skupině antidepresiv v léčbě endogenní deprese. Cesk Psychiatr 1981 Oct;77(5):315-21 (Eng. Abstr.) **(Cze)**

Náhunek K, Svestka J, Cesková E, et al: Srovnání účinnosti tranylcyprominu, nortriptylinu, thioridazinu a amitriptylinu u dvou syndromologických typu endogenní deprese. Cesk Psychiatr 1981;77(4):245-52 (Eng. Abstr.) **(Cze)**

Nahunek K, Svestka J, Ceskova E: Influence of different psychotropic drugs on psychotic anxiety. Agressologie 1981 Nov;22(D):11-3

Nakai T, Yamada R: [Urinary excretion of catecholamines by various age groups and plasma catecholamine concentrations measured by new radioenzymatic assay (author's transl)] Horumon To Rinsho 1981 Aug;29(8):909-14 **(Jpn)**

Nakajima H, Shigehara R, Shimada M, et al: [Effect of alpha-methyl-para-tyrosine on 'methamphetamine-induced sterotype and hypermotility' of reserpinized rats (author's transl)] Nippon Yakurigaku Zasshi 1981 Dec;78(6):557-69 (Eng. Abstr.) **(Jpn)**

Nakamura GR, Noguchi TT: Fatalities from cocaine overdoses in Los Angeles County. Clin Toxicol 1981 Aug;18(8):895-905

Nakata H, Fujisawa H: Purification and properties of tryptophan 5-monooxygenase from rat brain-stem. Eur J Biochem 1982 Feb;122(1):41-7

Nakata Y, Kusaka Y, Yajima H, et al: Active uptake of substance P carboxy-terminal heptapeptide (5-11) into rat brain and rabbit spinal cord slices. J Neurochem 1981 Dec;37(6):1529-34

Napoleone P, Sancesario G, Amenta F: 5-hydroxytryptophan uptake in indoleaminergic nerve fibers within rat cerebrovascular tree. Neurosci Lett 1982 Jan 22;28(1):57-60

Nappi C, Mercorio F: Stimolazione della lattazione con metoclopramide: osservazioni sperimentali (nota preventiva). Arch Ostet Ginecol 1980 May-Jun;85(3):153-4 **(Ita)**

Narasinga Rao BS, Krishnaswamy K: Effect of leucine on tryptophan metabolism [letter] Am J Clin Nutr 1982 Jan;35(1):178-80

Narhi LO, Fulco AJ: Phenobarbital induction of a soluble cytochrome P-450-dependent fatty acid monooxygenase in Bacillus megaterium. J Biol Chem 1982 Mar 10;257(5):2147-50

Natelson BH, DeRoshia C, Levin BE: Physiological effects of bed rest [letter] Lancet 1982 Jan 2;1(8262):51

Nau H, Löscher W: Valproic acid: brain and plasma levels of the drug and its metabolites, anticonvulsant effects and gamma-aminobutyric acid (GABA) metabolism in the mouse. J Pharmacol Exp Ther 1982 Mar;220(3):654-9

Navakatikyan AO, Karpenko AV: Possibility of information analysis of the periodic structure of the human cardiac rhythm during work. Hum Physiol 1981 Mar-Apr;7(2):86-92

Naylor GG, Smith AH: Reduction of vanadate, a possible explanation of the effect of phenothiazines in manic-depressive psychosis [letter] Lancet 1982 Feb 13;1(8268):395-6

Naylor PH, Gilani SS, Milholland RJ, et al: In vivo antiglucocorticoids: Comparison between in vivo activity and in vitro competition of progestins for the glucocorticoid receptor. J Steroid Biochem 1981 Dec;14(12):1303-9

Nazian SJ: Temporal relationship between the development of the self-priming effect of LHRH and changes in serum concentrations of testosterone and androstenedione during the sexual maturation of the male rat. Biol Reprod 1981 Dec;25(5):977-82

Neal MJ, Cunningham JR, James TA, et al: The effect of 2-amino-4-phosphonobutyrate (APB) on acetylcholine release from the rabbit retina: evidence for on-channel input to cholinergic amacrine cells. Neurosci Lett 1981 Nov 4;26(3):301-5

Neale EA, Matthew E, Zimmerman EA, et al: Substance P-like immunoreactivity in neurons in dissociated cell cultures of mammalian spinal cord and dorsal root ganglia. J Neurosci 1982 Feb;2(2):169-77

Neborsky RJ, Janowsky DS, Perel JM: Red blood cell/plasma haloperidol ratios and antipsychotic efficacy [letter] Psychiatry Res 1982 Feb;6(1):123-4

Nechifor M, Munglu OC: Interacţiuni între unele benzodiazepine şi derivaţi pirazolonici. Rev Med Chir Soc Med Nat Iasi 1981 Jul-Sep;85(3):493-4 (Eng. Abstr.) **(Rum)**

Nedelmann C: Psychotherapie in der psychiatrischen Praxis. Nervenarzt 1982 Jan;53(1):33-8 **(Ger)**

Nedergaard J: Catecholamine sensitivity in brown fat cells from cold-acclimated hamsters and rats. Am J Physiol 1982 Mar;242(3):C250-7

Nedopil N, Dieterle D: Detoxication treatment of schizophrenic patients: a possible role of endorphins? Mod Probl Pharmacopsychiatry 1981;17:263-5

Nedopil N, Rüther E: Initial improvement as predictor of outcome of neuroleptic treatment. Pharmacopsychiatria 1981 Nov;14(6):205-7

Neirinckx RD, Kronauge JF, Gennaro GP, et al: Evaluation of inorganic adsorbents for the rubidium-82 generator: I. Hydrous SnO2. J Nucl Med 1982 Mar;23(3):245-9

Nencini P, Paroli E: Lipolytic and enkephalinase inhibitory activities of polypeptides from placental autolysate prepared for therapeutic purposes. Int J Tissue React 1981 Dec;3(3-4):167-72

Nesselhut T, Osborne NN: Is noradrenaline a major catecholamine in the bovine retina? Neurosci Lett 1982 Jan 22;28(1):41-5

Neuzil E, Cassaigne A: Les peptides opioïdes. Expos Annu Biochim Med 1982;35:161-214 (287 ref.) **(Fre)**

Nguyen-Legros J, Berger B, Vigny A, et al: Tyrosine hydroxylase-like immunoreactive interplexiform cells in the rat retina. Neurosci Lett 1981 Dec 23;27(3):255-9

Nicholson AN, Stone BM: Hypnotic activity and effects on performance of lormetazepam and camazepam--analogues of temazepam. Br J Clin Pharmacol 1982 Mar;13(3):433-9

Nicol SE, Senogles SE, Caruso TP, et al: Postmortem stability of dopamine-sensitive adenylate cyclase, guanylate cyclase, ATPase, and GTPase in rat striatum. J Neurochem 1981 Dec;37(6):1535-9

Nicolas P, Bewley TA, Gráf L, et al: beta-Endorphin: demonstration of a tertiary structure in aqueous solution. Proc Natl Acad Sci USA 1981 Dec;78(12):7290-3

Nicoletti F, Patti F, Condorelli DF, et al: Comparative effects of chronic haloperidol and sulpiride treatment on nigral and striatal GABA content. J Neurochem 1981 Oct;37(4):1048-51

Nicoletti F, Patti F, Ferrara N, et al: Comparative effects of estrogens and prolactin on nigral and striatal GAD activity. Brain Res 1982 Jan 28;232(1):238-41

Nicoletti F, Canonico PL, Patti F, et al: Sulpiride effects on nigral and striatal glutamic acid decarboxylase activity: a possible involvement of prolactin. Eur J Pharmacol 1982 Jan;77(2-3):131-5

Nicoll RA, Jahr CE: Self-excitation of olfactory bulb neurones. Nature 1982 Apr 1;296(5856):441-4

Niederlehner JR, DiFazio CA, Foster J, et al: Cerebral monoamines and lidocaine toxicity in rats. Anesthesiology 1982 Mar;56(3):184-7

Nielsen JA, Moore KE: Measurement of metabolites of dopamine and 5-hydroxytryptamine in cerebroventricular perfusates of unanesthetized, freely-moving rats: selective effects of drugs. Pharmacol Biochem Behav 1982 Jan;16(1):131-7

Niemegeers CJ, Heykants JJ, Janssen PA: Antiemetic effect of haloperidol in the dog as related to plasma level and dose. Psychopharmacology (Berlin) 1981;75(3):240-4

Nikol'skaia EB: Reguliatsiia kholinésteraznogo gidroliza kholinovymi i tiokholinovymi éfirami. Dokl Akad Nauk SSSR 1982;262(1):233-7 **(Rus)**

Nilius B: Properties of an acetylcholine-induced conductance in the rabbit atrial myocardium. Acta Biol Med Ger 1981;40(7-8):1031-42

AUTHOR SECTION

Nillius SJ: Peptid kontraception—nya principer för födelsekontroll. Lakartidningen 1981 Aug 19;78(34):2845–8 (Eng. Abstr.) (Swe)

Nilova TN: Farmakoprofilaktika éksperimental'nogo neirogennogo povrezhdeniia podzheludochnoi zhelezy. Farmakol Toksikol 1982 Jan–Feb;45(1):62–5 (Eng. Abstr.) (Rus)

Ninkovic M, Hunt SP, Kelly JS: Effect of dorsal rhizotomy on the autoradiographic distribution of opiate and neurotensin receptors and neurotensin-like immunoreactivity within the rat spinal cord. Brain Res 1981 Dec 28;230(1–2):111–9

Nishigori H, Iwatsuru M: Effects of sex hormones and glucocorticoids on the induction of a drug metabolizing enzyme by phenobarbital in chick embryo. Life Sci 1982 Feb 1;30(5):433–9

Nisticò G, De Sarro A, Richetti A, et al: Evidence for the existence of a dopamine-sensitive adenylate cyclase in chick optic tectum. Res Commun Chem Pathol Pharmacol 1981 Sep;33(3):387–93

Nisticò G, Di Giorgio RM, De Luca G, et al: Effects of intraventricular gamma-acetylenic-GABA on GABA concentrations, GABA-T and GAD in several areas of the chick brain. Monogr Neural Sci 1981;5:34–9

Nistrup Madsen S, Christensen SE, Hansen AP, et al: Influence of somatostatin on plasma cyclic AMP and metabolic substrate responses to i.v. adrenaline and glucagon in humans. Clin Endocrinol (Oxf) 1981 Nov;15(5):431–7

Niu XY, Wang WJ, Jin YC: [Dualistic action of scopolamine on avoidance conditioned response in dogs (author's transl)] Chung Kuo Yao Li Hsueh Pao 1981 Mar;2(1):4–8 (Eng. Abstr.) (Chi)

Nock B, Feder HH: Neurotransmitter modulation of steroid action in target cells that mediate reproduction and reproductive behavior. Neurosci Biobehav Rev 1981 Winter;5(4):437–47

Noda M, Furutani Y, Takahashi H, et al: Cloning and sequence analysis of cDNA for bovine adrenal preproenkephalin. Nature 1982 Jan 21;295(5846):202–6

Noguchi K: [Studies on the feedback regulation of gonadotropin concentrations in male rats (I). The effects of hypothalamic implantation of testosterone and its metabolites on gonadotropin release in castrated male rats (author's transl)] Nippon Naibunpi Gakkai Zasshi 1981 Aug 20;57(8):1139–47 (Eng. Abstr.) (Jpn)

Noguchi T, Diesterhaft M, Granner D: Evidence for a dual effect of dibutyryl cyclic AMP on the synthesis of tyrosine aminotransferase in rat liver. J Biol Chem 1982 Mar 10;257(5):2386–90

Nohta H, Ohtsubo K, Zaitsu K, et al: Assay for dopamine beta-hydroxylase in rat serum and adrenal medulla by high-performance liquid chromatography with fluorescence detection. J Chromatogr 1982 Feb 12;227(2):415–22

Nomura Y, Kajiyama H, Segawa T: Alteration in sensitivity to isoproterenol and acetylcholine in the rat heart after repeated administration of isoproterenol. J Pharmacol Exp Ther 1982 Feb;220(2):411–6

Nomura Y, Oki K, Segawa T: Ontogenetic development of the striatal [3H]spiperone binding: regulation by sodium and guanine nucleotide in rats. J Neurochem 1982 Apr;38(4):902–8

Norman TR, Fulton A, Burrows GD, et al: Pharmacokinetics of N-desmethyldiazepam after a single oral dose of clorazepate: the effect of smoking. Eur J Clin Pharmacol 1981;21(3):229–33

Nousiainen U, Hänninen O: On the inducibility of cytosolic and microsomal carboxylesterase by phenobarbital in rat tissues. Acta Pharmacol Toxicol (Copenh) 1981 Jul;49(1):77–80

Novitskaia NA, Aksentsev SL, Lyskova TI, et al: O prirode tsentrov, otvetstvennykh za stimuliatsiiu serotoninom Na,K-ATPazy mozga. Biokhimiia 1981 Nov;46(11):1981–3 (Eng. Abstr.) (Rus)

Nunez EA, Gershon MD, Silverman AJ: Uptake of 5-hydroxytryptamine by gonadotrophs of the bat's pituitary: A combined immunocytochemical radioautographic analysis. J Histochem Cytochem 1981 Nov;29(11):1336–46

Nussdorfer GG, Neri G, Belloni AS, et al: Effects of ACTH on the zona glomerulosa of sodium-loaded timolol maleate-treated rats: stereology and plasma hormone concentrations. Acta Endocrinol (Copenh) 1982 Feb;99(2):256–62

Nyman JV, Fritz WL: A review of the antiemetic use of delta-9-tetrahydrocannabinol and prescribing requirements. Ariz Med 1982 Jan;39(1):38–43

O

Oades RD: Dopaminergic agonistic and antagonistic drugs in the ventral tegmentum of rats inhibit and facilitate changes of food-search behaviour. Neurosci Lett 1981 Nov 18;27(1):75–80

Obregón MJ: Thyroxine radioimmunoassay for population surveys using dried blood: modifications of a highly sensitive method. Ann Clin Biochem 1982 Jan;19(Pt 1):29–34

Ochoa EL, Brusco A, Idoyaga-Vargas VP, et al: Postnatal changes in the activity ratio of specific and nonspecific cholinesterases from neuronal perikarya. J Neurochem 1982 May;38(5):1236–40

O'Connor EF, Watson WH 3d, Wyse GA: Identification and localization of catecholamines in the nervous system of Limulus polyphemus. J Neurobiol 1982 Jan;13(1):49–60

Offerhaus L: Drug interactions at excretory mechanisms. Pharmacol Ther 1981;15(1):69–78 (64 ref.)

Ogata N, Abe H: Substance P decreases membrane conductance in neurons of the guinea pig hypothalamus in vitro. Neuropharmacology 1982 Feb;21(2):187–9

Ogiso T, Iwaki M, Mori K: Fluidity of human erythrocyte membrane and effect of chlorpromazine on fluidity and phase separation of membrane. Biochim Biophys Acta 1981 Dec 7;649(2):325–35

Ohmiya Y, Mehendale HM: Metabolism of chlorpromazine by pulmonary microsomal enzymes in the rat and rabbit. Biochem Pharmacol 1982 Jan 15;31(2):157–62

Ohnhaus EE, Bürgi H, Burger A, et al: The effect of antipyrine, phenobarbitol and rifampicin on thyroid hormone metabolism in man. Eur J Clin Invest 1981 Oct;11(5):381–7

Ohnishi H, Ito C, Suzuki K, et al: [Effects of tofisopam on the physiological changes induced by stress loading and hypothalamic stimulation (author's transl)] Nippon Yakurigaku Zasshi 1981 Sep;78(3):139–44 (Eng. Abstr.) (Jpn)

Ohnishi ST, Devlin MT, Sato T, et al: Possible use of non-neuroleptic isomers of anti-psychotics in anti-sickling therapy. Eur J Pharmacol 1981 Oct 22;75(2–3):121–5

Ohtaki S, Nakagawa H, Nakamura M, et al: Reactions of purified hog thyroid peroxidase with H2O2, tyrosine, and methylmercaptoimidazole (goitrogen) in comparison with bovine lactoperoxidase. J Biol Chem 1982 Jan 25;257(2):761–6

Oikarinen J: The bone inductive capacity of decalcified bone matrix modified by diphenylhydantoin. Acta Orthop Scand 1981 Oct;52(5):505–11

Ojeda SR, Negro-Vilar A, McCann SM: Evidence for involvement of alpha-adrenergic receptors in norepinephrine-induced prostaglandin E2 and luteinizing hormone-releasing hormone release from the median eminence. Endocrinology 1982 Feb;110(2):409–12

Okuma Y, Osumi Y: Neurotensin-induced release of endogenous noradrenaline from rat hypothalamic slices. Life Sci 1982 Jan 4;30(1):77–84

Okuno S, Fujisawa H: Purification and some properties of tyrosine 3-monooxygenase from rat adrenal. Eur J Biochem 1982 Feb;122(1):49–55

Olesen OV, Thomsen K: A comparison between the natriuretic response to potassium in lithium- and amiloride-treated rats. Acta Pharmacol Toxicol (Copenh) 1981 May;48(5):382–9

Oliver C, Giraud P, Lissitzky JC, et al: Influence of endogenous somatostatin on growth hormone and thyrotropin secretion in neonatal rats. Endocrinology 1982 Mar;110(3):1018–22

Ong H, du Souich P, Marchand C: In vivo study of propranolol and metabolite(s) disposition in rat liver. Drug Metab Dispos 1981 Nov–Dec;9(6):529–34

Ongini E, Parravicini L, Bamonte F: Effects of physostigmine on benzodiazepine toxicity. Arch Int Pharmacodyn Ther 1981 Sep;253(1):164–76

Opdyke DF, Carroll RG, Keller NE: Catecholamine release and blood pressure changes induced by exercise in dogfish. Am J Physiol 1982 Mar;242(3):R306–10

O'Reilly HM, Coleman GJ, Armstrong S: Endogenous corticosterone alterations and appetitive learning in the rat. Physiol Behav 1981 Sep;27(3):515–22

Oriowo MA: Direct and indirect actions of 5-hydroxytryptamine in the rat anococcygeus muscle. Arch Int Pharmacodyn Ther 1981 Nov;254(1):13–9

Ortega-Corona BG, Carranza J, Sosa A, et al: Brain monoamine oxidase activity after in vivo-chronic iprindole treatment. Pharmacol Biochem Behav 1981 Dec;15(6):951–4

Osborn DE, George NJ, Rao PN, et al: Prostatodynia—physiological characteristics and rational management with muscle relaxants. Br J Urol 1981 Dec;53(6):621–3

O'Shanick GJ, Ellinwood EH Jr: Persistent elevation of thyroid-stimulating hormone in women with bipolar affective disorder. Am J Psychiatry 1982 Apr;139(4):513–4

Overton DA: Multiple drug training as a method for increasing the specificity of the drug discrimination procedure. J Pharmacol Exp Ther 1982 Apr;221(1):166–72

Owasoyo JO: Comparative effects of phenobarbital and picrotoxin on the choline acetyltransferase activity of specific rat brain areas. Gen Pharmacol 1982;13(1):71–3

Oyehaug E, Ostensen ET, Salvesen B: Determination of the antidepressant agent citalopram and metabolites in plasma by liquid chromatography with fluorescence detection. J Chromatogr 1982 Jan 8;227(1):129–35

P

Pacifici GM, Rane A: Inhibition of morphine glucuronidation by oxazepam in human fetal liver microsomes. Drug Metab Dispos 1981 Nov–Dec;9(6):569–72

Padbury JF, Diakomanolis ES, Hobel CJ, et al: Neonatal adaptation:

sympatho-adrenal response to umbilical cord cutting. Pediatr Res 1981 Dec;15(12):1483-7

Padmanabhan V, Leung K, Convey EM: Ovarian steroids modulate the self-priming effect of luteinizing hormone-releasing hormone on bovine pituitary cells in vitro. Endocrinology 1982 Mar;110(3):717-21

Pajer KA, Palmer GC, Manián AA: Actions of chlorpromazine metabolites on brain guanylate cyclase. Eur J Pharmacol 1981 Oct 22;75(2-3):137-9

Palmieri B, Gasparini Cesari M, Di Blasio P: Azione protettiva della prostenoglicina sulla intossicazione sperimentale in vitro di emazie. Clin Ter 1981 Dec 31;99(6):623-7 (Eng. Abstr.) **(Ita)**

Panasiuk LV, Arefolov VA, Andreeva NI, et al: Vliianie tetratsiklicheskikh antidepressantov pirazidola i inkazana na adrenergicheskuiu neiroperedachu vas deferans krysy. Farmakol Toksikol 1982 Jan-Feb; 45(1):13-7 (Eng. Abstr.) **(Rus)**

Pang SF, Tang PL, Yu HS, et al: The level of N-acetylserotonin and melatonin in the brain of male rats: diurnal variations and effects of pinealectomy. J Exp Zool 1982 Feb 20;219(3):271-6

Panten U, Langer J: Mechanism of 3-phenylpyruvate-induced insulin release from isolated pancreatic islets. Biochem J 1981 Aug 15; 198(2):353-6

Pantuck EJ, Pantuck CB, Anderson KE, et al: Cigarette smoking and chlorpromazine disposition and actions. Clin Pharmacol Ther 1982 Apr; 31(4):533-8

Pape BE: Enzyme immunoassay and two fluorometric methods compared for the determination of quinidine in serum. Ther Drug Monit 1981; 3(4):357-63

Papka RE, Furness JB, Della NG, et al: Depletion by capsaicin of substance P-immunoreactivity and acetylcholinesterase activity from nerve fibres in the guinea-pig heart. Neurosci Lett 1981 Nov 18; 27(1):47-53

Pappas BA, Vickers G, Buxton M, et al: Infant rat hyperactivity elicited by home cage bedding is unaffected by neonatal telencephalic dopamine or norepinephrine depletion. Pharmacol Biochem Behav 1982 Jan; 16(1):151-4

Paris MD: Interpersonal issues in prescribing medication [letter] Arch Gen Psychiatry 1982 Feb;39(2):235

Parker A, Maw B, Fedor L: The beta-glucuronidase catalyzed hydrolysis of a glucopyranosiduronamide and a glucopyranoside: evidence for the oxocarbonium ion mechanism for bovine liver beta-glucuronidase. Biochem Biophys Res Commun 1981 Dec 31;103(4):1390-4

Parnas I, Dudel J: Transmitter release in crayfish neuromuscular junction: comments on the article by Staggs et al. (1980). J Neurobiol 1982 Jan; 13(1):75-7

Parnavelas JG, Blue ME: The role of the noradrenergic system on the formation of synapses in the visual cortex of the rat. Brain Res 1982 Jan;255(1):140-4

Pascalis G: Psychose unipolaire dépressive périodique et traitement antidépresseur tricyclique chronique. Ann Med Psychol (Paris) 1981 Nov;139(9):965-9 (Eng. Abstr.) **(Fre)**

Pastukhov VA: Vliianie tsentral' nykh kholinergicheskikh struktur na deiatel'nost' serdechno-sosudistoi sistemy. Fiziol Zh SSSR 1981 Nov; 67(11):1661-9 (Eng. Abstr.) **(Rus)**

Patel AJ, Barochovsky O, Lewis PD: Psychotropic drugs and brain development: effects on cell replication in vivo and in vitro. Neuropharmacology 1981 Dec;20(12B):1243-9 (34 ref.)

Patrick KS, Kilts CD, Breese GR: Synthesis and pharmacology of hydroxylated metabolites of methylphenidate. J Med Chem 1981 Oct; 24(10):1237-40

Patrono C, Pugliese F, Ciabattoni G, et al: Evidence for a direct stimulatory effect of prostacyclin on renin release in man. J Clin Invest 1982 Jan;69(1):231-9

Patterson M, Heazelwood R, Smithurst B, et al: Plasma protein binding of phenytoin in the aged: in vivo studies. Br J Clin Pharmacol 1982 Mar;13(3):423-5

Paul SM, Kempner ES, Skolnick P: In situ molecular weight determination of brain and peripheral benzodiazepine binding sites. Eur J Pharmacol 1981 Dec 17;76(4):465-6

Paulos MA, Tessel RE: Excretion of beta-phenethylamine is elevated in humans after profound stress. Science 1982 Feb 26;215(4536):1127-9

Pax RA, Siefker C, Hickox T, et al: Schistosoma mansoni: neurotransmitters, longitudinal musculature and effects of electrical stimulation. Exp Parasitol 1981 Dec;52(3):346-55

Paxton JW: Phenytoin intoxication and sulphonamides [letter] NZ Med J 1981 Nov 25;94(696):396-7

Pazo JH, Medina JH, O'Donnell P, et al: Study of the neural basis of circling behavior induced by L-dopa in lesioned entopeduncular cats. Brain Res 1982 Feb 11;233(2):337-45

Pearce BR, Dutton GR: K+-stimulated release of endogenous glutamate, GABA and other amino acids from neuron- and glia-enriched cultures of the rat cerebellum. FEBS Lett 1981 Nov 30;135(1):215-8

Pearce RB, Cronshaw J, Holmes WN: Changes in corticotropic responsiveness and mitochondrial ultrastructure of adrenocortical cells from the inner zone of the duck (Anas platyrhynchos) adrenal gland: the effects of cycloheximide, puromycin, and chloramphenicol. Cell Tissue Res 1981;221(1):45-57

Pecquery R, Giudicelli Y: Catecholamine binding to the alpha-adrenergic receptors of hamster adipocytes. Evidence that guanine nucleotides regulate this binding to the alpha 2-receptor subtype. Biochim Biophys Acta 1982 Jan 12;714(1):14-25

Pedersen RC, Ling N, Brownie AC: Immunoreactive gamma-melanotropin in rat pituitary and plasma: a partial characterization. Endocrinology 1982 Mar;110(3):825-34

Peet M: Is propranolol antischizophrenic? Neuropharmacology 1981 Dec; 20(12B):1303-7 (36 ref.)

Pennefather P, Quastel DM: Relation between subsynaptic receptor blockade and response to quantal transmitter at the mouse neuromuscular junction. J Gen Physiol 1981 Sep;78(3):313-44

Pepine CJ, Feldman RL: Intracoronary propylene glycol [letter] N Engl J Med 1982 Apr 8;306(14):868-9

Pérez-López FR, Abós MD: Pituitary hormonal response to the orthopramides clebopride, bromopride, metoclopramide, and sulpiride. Fertil Steril 1982 Mar;37(3):445-8

Perry PJ, Stambaugh RL, Tsuang MT, et al: Sedative-hypnotic tolerance testing and withdrawal comparing diazepam to barbiturates. J Clin Psychopharmacol 1981 Sep;1(5):289-96

Perry PJ, Dunner FJ, Hahn RL, et al: Lithium kinetics in single daily dosing. Acta Psychiatr Scand 1981 Oct;64(4):281-94

Peselow ED, Dunner DL, Fieve RR, et al: Course and relationship of lithium side effects to plasma lithium levels. Psychiatr Clin (Basel) 1981; 14(3):178-83

Peter T, Fujimoto T, Hamamoto H, et al: Electrophysiologic effects of diltiazem in canine myocardium, with special reference to conduction delay during ischemia. Am J Cardiol 1982 Feb 18;49(3):602-5

Peterova E, Vencovsky E: The therapeutic effect of Trazodon with endogenous depressions. Agressologie 1981 Nov;22(E):25

Petersen EN, Lassen JB: A water lick conflict paradigm using drug experienced rats. Psychopharmacology (Berlin) 1981;75(3):236-9

Petersen OH, Iwatsuki N, Philpott HG, et al: Membrane potential and conductance changes evoked by hormones and neurotransmitters in mammalian exocrine gland cells. Methods Cell Biol 1981;23:513-30 (56 ref.)

Petraglia F, Facchinetti F, Parrini D, et al: Effetto dello stress da freddo nel coniglio sulle concentrazioni ipotalamiche, ipofisarie e plasmatiche di beta lipotropina e beta endorfina. Boll Soc Ital Biol Sper 1981 Sep 30;57(18):1862-8 (Eng. Abstr.) **(Ita)**

Pettibone DJ, Mueller GP: Evidence for independent secretion of beta-endorphin immunoreactivity from rat pars distalis in vivo. Endocrinology 1982 Feb;110(2):469-73

Petty F, Schlesser MA: Plasma GABA in affective illness. A preliminary investigation. J Affective Disord 1981 Dec;3(4):339-43

Petursson H, Bhattacharya SK, Glover V, et al: Urinary monoamine oxidase inhibitor and benzodiazepine withdrawal. Br J Psychiatry 1982 Jan;140:7-10

Peyrin L, Cottet-Emard JM, Gonnet C, et al: Urinary excretion of catecholamines in the night monkey (Aotus trivirgatus) (Primates, Cebidae). Arch Int Physiol Biochim 1981 Nov;89(4):345-56

Pfeifer S, Borchert HH, Schuster S, et al: Metabolische Wechselwirkungen von Promethazin 1,2. Pharmazie 1981 Dec;36(12):815-8 (Eng. Abstr.) **(Ger)**

Pfeiffer A, Herz A: Mixed type inhibition of [D-Ala2, D-Leu5]enkephalin binding to mu-opiate binding sites by mu-, but not by kappa-opiate ligands. Eur J Pharmacol 1982 Feb 5;77(4):359-61

Philips SR, Robson AM, Boulton AA: Unstimulated and amphetamine-stimulated release of endogenous noradrenaline and dopamine from rat brain in vivo. J Neurochem 1982 Apr;38(4):1106-10

Phillips M, Tashjian AH Jr: Characterization of an early inhibitory effect of glucocorticoids on stimulated adrenocorticotropin and endorphin release from a clonal strain of mouse pituitary cells. Endocrinology 1982 Mar;110(3):892-900

Phillips R, Plaa GL: Biliary excretion of diazepam in rats: influence of the route of administration and dosage. Arch Int Pharmacodyn Ther 1981;253(2):180-91

Phillips RH: Mood, creativity, and psychotherapeutic participation of patients receiving lithium. Psychosomatics 1982 Jan;23(1):81-7

Phillipson OT, Pycock CJ: Dopamine neurones of the ventral tegmentum project to both medial and lateral habenula. Some implications for habenular function. Exp Brain Res 1982;45(1-2):89-94

Phillis JW, Wu PH: Phenothiazines inhibit adenosine uptake by rat brain synaptosomes. Can J Physiol Pharmacol 1981 Oct;59(10):1108-10

Phillis JW, Wu PH: Catecholamines and the sodium pump in excitable cells. Prog Neurobiol 1981;17(3):141-84 (320 ref.)

Pi EH, Simpson GM: The treatment of refractory schizophrenia: pharmacotherapy and clinical implications of blood level measurement of neuroleptics. Int Pharmacopsychiatry 1981;16(3):154-61

Pickar D, Lake CR, Cohen RM, et al: Alterations in noradrenergic function during clorgyline treatment. Commun Psychopharmacol 1980; 4(5):379-86

Pickar D, Naber D, Post RM, et al: Measurement of endorphins in CSF. Relationship to psychiatric diagnosis. Mod Probl Pharmacopsychiatry 1981;17:246-62

Pickens RW, Heston LL: Personality factors in human drug self-administration. Natl Inst Drug Abuse Res Monogr Ser 1981 Jul;

(37):45–62

Pickoff AS, Kessler KM, Singh S, et al: Age-related differences in the protein binding of quinidine. Dev Pharmacol Ther 1981;3(2):108–15

Piekut DT, Knigge KM: Immunocytochemical analysis of the rat pineal gland using antisera generated against analogs of luteinizing hormone-releasing hormone (LHRH). J Histochem Cytochem 1982 Feb;30(2):106–10

Pieper DR, Gala RR, Regiani SR, et al: Dependence of pituitary gonadotropin-releasing hormone (GnRH) receptors on GnRH secretion from the hypothalamus. Endocrinology 1982 Mar;110(3):749–53

Piepho RW, Bloedow DC, Lacz JP, et al: Pharmacokinetics of diltiazem in selected animal species and human beings. Am J Cardiol 1982 Feb 18;49(3):525–8

Pinchasi I, Michaelson DM: Adenylate cyclase of Torpedo synaptosomes is inhibited by calcium and not affected by muscarinic ligands. J Neurochem 1982 May;38(5):1223–9

Pinder RM: Pharmacologie prévisionnelle d'un antidépresseur. Encephale 1981;7(4 Suppl):371–80 (Eng. Abstr.) (Fre)

Pitts FN Jr, Allen RE, Aniline O, et al: Occupational intoxication and long-term persistence of phencyclidine (PCP) in law enforcement personnel. Clin Toxicol 1981;18(9):1015–20

Pivovarov AS, Bespalova ZhD, Bakalkin GIa: Tormozhenie élektricheskoĭ aktivnosti zritel'noĭ kory levogo i pravogo polushariĭ énkefalinami. Dokl Akad Nauk SSSR 1981;261(1):240–4 (Rus)

Pizarro M, Puente J, Sapag-Hagar M: Calmodulin and cyclic nucleotide-phosphodiesterase activities in rat mammary gland during the lactogenic cycle. FEBS Lett 1981 Dec 21;136(1):127–30

Plech A: Psychopharmacological effects of cholinomimetic agents administered into hippocampus and various hypothalamic areas in the rat. Thesis. Pol J Pharmacol Pharm 1981;33(4):415–20

Plech A, Stachura Z, Wieloch-Depta L, et al: Effect of neuroleptics on release on acetylcholine to the lateral cerebral ventricle in the rat. Pol J Pharmacol Pharm 1981;33(4):393–400

Plevova J, Boleloucky Z, Bastecky J: Anxiety and placebo reaction in neurotic patients. Agressologie 1981 Oct;22(C):47–9

Plevova J, Boleloucky Z, Bastecky J: Anxiety and placebo reaction in neurotic patients. Agressologie 1981 Nov;22(E):31–2

Plotsky PM, Neill JD: The decrease in hypothalamic dopamine secretion induced by suckling: comparison of voltammetric and radioisotopic methods of measurement. Endocrinology 1982 Mar;110(3):691–6

Pohl M, Mares P: Effects of thalamic spreading depression on the rhythmic ECoG activity induced by metrazol in the rat. Act Nerv Super (Praha) 1981;23(4):295–6

Poikolainen K: Mortality related to psychotropic substances: current knowledge and research problems. Br J Addict 1981 Dec;76(4):363–74

Poláček J: Léčba schizofrenních psychóz depotními neurolptiky v psychiatrické ambulanci. Cesk Psychiatr 1982 Feb;78(1):49–55 (Eng. Abstr.) (Cze)

Polák L, Skoricová M, Dimová N, et al: Treatment of enuresis with sydnocarb. Act Nerv Super (Praha) 1981;23(4):263–4

Polenov SA, Cherniavskaia GV: Sravnitel'naia kharakteristika reaktsiĭ sosudov tonkogo kishechnika pri neĭrogennykh vliianiiakh i primenenii katekholaminov. Fiziol Zh SSSR 1981 Dec;67(12):1845–52 (Eng. Abstr.) (Rus)

Polleri A, Masturzo P, Murialdo G, et al: Circadian rhythmicity of prolactin secretion in elderly subjects: changes during bromocriptine treatment. J Endocrinol Invest 1981 Jul–Sep;4(3):317–21

Pollock RJ, Kapatos G, Kaufman S: Effect of cyclic AMP-dependent protein phosphorylating conditions on the pH-dependent activity of tyrosine hydroxylase from beef and rat striata. J Neurochem 1981 Oct;37(4):855–60

Polson JB, Krzanowski JJ, Anderson WH, et al: Effects of ketotifen, a benzocycloheptathiophene, on metacholine- and acetylcholine-induced contractions of canine respiratory smooth muscle. Immunopharmacology 1982 Feb;4(1):69–72

Poncelet PF: Sémiologie et clinique de l'urgence psychiatrique. Rev Med Liege 1981 Dec 1;36(23):850–5 (Fre)

Ponte CD: A suspected case of trimipramine-induced salivary adenitis. Drug Intell Clin Pharm 1982 Mar;16(3):248–9

Ponzio F, Achilli G, Perego C, et al: Differential effects of certain dopaminergic drugs on the striatal concentration of dopamine metabolites, with special reference to 3-methoxytramine. Neurosci Lett 1981 Nov 18;27(1):61–7

Poort C, Kramer MF: The proportion of ribosomes engaged in rat pancreatic polysomal structures as influenced by pilocarpine injection. J Cell Sci 1981 Aug;50:165–9

Popolow HB, King JC, Gerall AA: Rostral medial preoptic area lesions' influence on female estrous processes and LHRH distribution. Physiol Behav 1981 Nov;27(5):855–61

Popovic P, Popovic V, Honeycutt C: Levodopa and aspirin pretreatment beneficial in experimental decompression sickness. Proc Soc Exp Biol Med 1982 Jan;169(1):140–3

Porot M, Becamel G: Etude comparée de l'action hypnogène du bromazépam et du flunitrazépam. Ann Med Psychol (Paris) 1981;139(8):919–23 (Fre)

Porot M, Maillot S, Becamel G: Les benzodiazépines sont-elles anxiolytiques ou hypnotiques? Ann Med Psychol (Paris) 1981;139(8):915–9 (Fre)

Potter WZ, Calil HM, Sutfin TA, et al: Active metabolites of imipramine and desipramine in man. Clin Pharmacol Ther 1982 Mar;31(3):393–401

Pozdniakov OM, Polgar AA, Zinkevich VA, et al: Izmenenie sootnosheniia kvantovo-vezikuliarnykh parametrov pri narushenii sekretsii sinapticheskogo peredatchika v nervno-myshechnom soedinenii mlekopitaiushchego. Biull Eksp Biol Med 1981 Dec;92(12):738–40 (Eng. Abstr.) (Rus)

Pradayrol L, Bommelaer G, Fourmy D, et al: Inhibition de la libération d'hormone de croissance chez l'homme: effets comparés des somatostatines 14 et 28. Gastroenterol Clin Biol 1982 Feb;6(2):166–9 (Eng. Abstr.) (Fre)

Prakash R: Lithium and glycine levels [letter] Am J Psychiatry 1982 Jan;139(1):132

Pringuey D, Yzombard G, Tatossian A: La monothérapie antidépressive: efficacité et confort de la miansérine (Athymil). Ann Med Psychol (Paris) 1981 Nov;139(9):1003–14 (Fre)

Prinz PN, Vitiello MV, Roehrs TA, et al: Effect of phenobarbital on sleep and nighttime plasma growth hormone and cortisol levels. Can J Physiol Pharmacol 1981 Nov;59(11):1139–45

Proll MA, Kamp CW, Morgan WW: Use of liquid chromatography with electrochemistry to measure effects of varying intensities of white light on DOPA accumulation in rat retinas. Life Sci 1982 Jan 4;30(1):11–9

Przekop F: Rola podwzgórza w regulacji sekrecji hormonu luteinizującego (LH) i procesie owulachji. Acta Physiol Pol 1981;32(5 Suppl 23):87–128 (117 ref.) (Pol)

Publicover SJ: Inhibition of spontaneous transmitter release by the membrane ligand cationized ferritin. Naunyn Schmiedebergs Arch Pharmacol 1982 Feb;318(3):246–8

Puech AJ: En quoi les antidépresseurs sont-ils différents? Encephale 1981;7(4 Suppl):401–3 (Eng. Abstr.) (Fre)

Puech AJ, Rioux P, Poncelet M, et al: Pharmacological properties of new antipsychotic agents: use of animal models. Neuropharmacology 1981 Dec;20(12B):1279–84

Puglisi CV, de Silva JA: Determination of the anxiolytic agent 8-chloro-6-(2-chlorophenyl)-4H-imidazo-[1,5-alpha][1,4]-benzodiazepine-3-carboxamide in whole blood, plasma or urine by high-performance liquid chromatography. J Chromatogr 1981 Nov 13;226(1):135–46

Purshottam T, Kaveeshwar U: Effect of phenobarbitol pretreatment on regeneration of plasma cholinesterase activity inhibited by parathion or dichlorovos. Arch Environ Health 1982 Jan–Feb;37(1):53–8

Puzhin'skiĭ S, Bidzin'skiĭ A, Gauptmann M, et al: Katekholaminergicheskaia i serontoninergicheskaia sistemy pri depressii. Vestn Akad Med Nauk SSSR 1982;(1):66–8 (Eng. Abstr.) (Rus)

Pyke J, Page J: Long term care for the chronic schizophrenic patient. Can Nurse 1982 Jan;78(1):37–44

Q

Quednow B, Walther H, Genz A, et al: Amitriptyline levels and clinical effects. Agressologie 1981 Nov;22(E):15–8

Quirce CM, Odio M, Maickel RP: Stress-modulated alteration of brain biogenic amines in the rat: effects of L-tryptophan. Commun Psychopharmacol 1980;4(5):371–7

Quirion R, Rice KC, Skolnick P, et al: Stereospecific displacement of [3H]phencyclidine (PCP) receptor binding by an enantiomeric pair of PCP analogs. Eur J Pharmacol 1981 Aug 27;74(1):107–8

Quirion R, Pert CB: Dynorphins: similar relative potencies on mu, delta- and kappa-opiate receptors. Eur J Pharmacol 1981 Dec 17;76(4):467–8

Quitkin FM, Rabkin JG: Methodological problems in studies of depressive disorder: utility of the discontinuation design. J Clin Psychopharmacol 1981 Sep;1(5):283–8

R

Rabey JM, Passeltiner P, Bystritsky A, et al: The regulation of striatal DOPA synthesis by alpha 2-adrenoreceptors. Brain Res 1981 Dec 28;230(1–2):422–6

Raboch J Jr, Smolik P, Souček K, et al: Spermiologic findings during longterm lithium therapy. Act Nerv Super (Praha) 1981;23(4):274–5

Rafaelsen OJ: Perturbations biologiques humaines dans les troubles de l'humeur. Encephale 1981;7(4 Suppl):413–9 (Eng. Abstr.) (Fre)

Rägo LK, Allikmets LH, Zarkovsky AM: Effects of piracetam on the central dopaminergic transmission. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(1):36–7

Rahman R, Clayton RB: Sexual differentiation of hepatic metabolism of corticosterone and testosterone in the rat. J Biochem (Tokyo) 1981 Dec;90(6):1567–75

Rainaut J: Prescription des anti-dépresseurs. Encephale 1981;7(4 Suppl):513–22 (Eng. Abstr.) (Fre)

Rainbow TC, Biegon A, McEwen BS: Autoradiographic localization of imipramine binding in rat brain. Eur J Pharmacol 1982 Feb 5;77(4):363–4

AUTHOR SECTION

Raïs R, Girard C, Gipouloux JD: Mise en évidence de catécholamines dans la corde dorsale des embryons d'amphibiens anoures. relations possibles avec l'activité adénylate-cyclasique de cet organe et la migration des cellules germinales primordiales.
Arch Anat Microsc Morphol Exp 1981;70(3):149–60 (Eng. Abstr.) **(Fre)**

Ramade F, Bayle JD: Thalamic-hypothalamic interrelationships and stress-induced rebounding adrenocortical response in the pigeon.
Neuroendocrinology 1982 Jan;34(1):7–13

Randall WC, Rinkema LE, Jones SB, et al: Overdrive suppression of atrial pacemaker tissues in the alert, awake dog before and chronically after excision of the sinoatrial node. Am J Cardiol 1982 Apr 1;49(5):1166–75

Randic M, Carstens E, Zimmermann M, et al: Dual effects of substance P on the excitability of single cutaneous primary afferent C- and A-fibers in the cat spinal cord. Brain Res 1982 Feb 11;233(2):389–93

Rankin LI, Henry DP, Weinberger MH, et al: Sodium intake alters the effects of norepinephrine on the renin system and the kidney.
Am J Kidney Dis 1981 Nov;1(3):177–84

Rao GH, White JG: Epinephrine potentiation of arachidonate-induced aggregation of cyclooxygenase-deficient platelets. Am J Hematol 1981; 11(4):355–66

Rapp MS, Kaplan A: Polypsychopharmacy revisited. Can J Psychiatry 1981 Dec;26(8):569–73

Rappaport PL, Thiessen JJ: High-pressure liquid chromatographic analysis of indocyanine green. J Pharm Sci 1982 Feb;71(2):157–61

Rappay G, Makara GB: A quantitative approach to trace the corticotrophs in culture after adrenalectomy. Histochemistry 1981;73(1):131–6

Rarey KE, Ross MD, Smith CB: Distribution and significance of norepinephrine in the lateral cochlear wall of pigmented and albino rats. Hear Res 1982 Jan;6(1):15–23

Rarey KE, Ross MD, Smith CB: Quantitative evidence for cochlear, non-neuronal norepinephrine. Hear Res 1981 Sep;5(1):101–8

Rasmussen KJ, Schneider HH, Petersen EN: Sodium valproate exerts anti-conflict activity in rats without any concomitant rise in forebrain GABA level. Life Sci 1981 Nov 23;29(21):2163–70

Rastogi RB, Singhal RL, Lapierre YD: Comparative effects of short- and long-term treatment with neuroleptics on behavioural activity as well as dopamine turnover in striatum. Gen Pharmacol 1982;13(1):35–40

Ratge D, Knoll E, Diener U, et al: Altered circadian rhythm of catecholamines in patients with apallic syndrome. Experientia 1981 Nov 15;37(11):1207–9

Rausch JL, Shah NS, Burch EA, et al: Platelet serotonin uptake in depressed patients: circadian effect. Biol Psychiatry 1982 Jan;17(1):121–3

Rawls WN: Trazodone (Desyrel, Mead-Johnson Pharmaceutical Division). Drug Intell Clin Pharm 1982 Jan;16(1):7–13 (50 ref.)

Ray DB, Horst IA, Jansen RW, et al: Glucocorticoid regulation of alpha-lactalbumin production in long-term cultures of normal rat mammary cells. Endocr Res Commun 1981;8(3):165–78

Reavill C, Leigh N, Jenner P, et al: Critical role of midbrain reticular formation in the expression of dopamine-mediated circling behaviour. Adv Biochem Psychopharmacol 1981;30:187–204

Reavill C, Leigh PN, Jenner P, et al: Drug-induced circling after unilateral 6-hydroxydopamine lesions of the nigro-striatal pathway is mediated via the midbrain periaqueductal grey and adjacent reticular formation (angular complex). Life Sci 1981 Dec 7;29(23):2357–65

Redburn DA, Thomas TN: Evidence for a serotonin neurotransmitter system in bovine retina. Vision Res 1981;21(11):1673–6

Redgrave P, Dean P: Intracranial self-stimulation. Br Med Bull 1981 May; 37(2):141–6 (71 ref.)

Redgrave P, Dean P: Collicular picrotoxin alleviates akinesia but not sensory neglect in rats with bilateral 6-hydroxydopamine lesions of ventral midbrain. Psychopharmacology (Berlin) 1981;75(2):204–9

Redgrave P, Dean P, Souki W, et al: Gnawing and changes in reactivity produced by microinjections of picrotoxin into the superior colliculus of rats. Psychopharmacology (Berlin) 1981;75(2):198–203

Redmond O, Tuffery AR: Thyroid proliferation, body weight, thyrotropin and thyroid hormones in chronic antithyroid (carbimazole) treatment in rats. J Anat 1981 Aug;133(Pt 1):37–47

Regan JW, Roeske WR, Malick JB, et al: gamma-Aminobutyric acid enhancement of CL 218,872 affinity and evidence of benzodiazepine receptor heterogeneity. Mol Pharmacol 1981 Nov;20(3):477–83

Reginaldi D, Tondo L, Floris G, et al: Poor prophylactic lithium response due to antidepressants. Int Pharmacopsychiatry 1981;16(2):124–8

Regléro A, Calvo P, Ortiz de la Tabla V, et al: Separation and properties of two enzyme forms of beta-glucuronidase from the mollusc Helicella ericetorum. Int J Biochem 1981;13(11):1185–9

Rehavi M, Skolnick P, Brownstein MJ, et al: High-affinity binding of [3H]desipramine to rat brain: a presynaptic marker for noradrenergic uptake sites. J Neurochem 1982 Apr;38(4):889–95

Reichelt KL: Peptider som informasjonsoverfører ved psykiatriske sykdommer. Nord Med 1980 Nov;95(11):283–6 **(Nor)**

Reimer F: Psychopharmaka in der Hand des Nichtpsychiaters. HNO 1981 Dec;29(12):415–7 (Eng. Abstr.) **(Ger)**

Reinstein DK, Isaacson RL: Behavioral and temperature changes induced by clonidine in the developing rat. Neurosci Lett 1981 Nov 4;26(3):251–7

Reisine T, Soubrie P, Artaud F, et al: Sensory stimuli differentially affect in vivo nigral and striatal [3H]serotonin release in the cat.
Brain Res 1982 Jan 28;232(1):77–87

Reiter EO, Duckett GE, Root AW: Further studies of the effects of intravenous infusion or intramuscular injection of gonadotropin-releasing hormone during childhood and adolescence.
J Adolesc Health Care 1981 Jun;1(4):275–81

Reith ME, Sershen H, Lajtha A: Binding of [3H]cocaine in mouse brain: kinetics and saturability. J Recept Res 1981;2(3):233–43

Rettori V, Siler-Khodr TM, Pauerstein CJ, et al: Effects of porcine follicular fluid on gonadotropin concentrations in rhesus monkeys.
J Clin Endocrinol Metab 1982 Mar;54(3):500–3

Reveley AM, Reveley MA, Clifford CA, et al: Cerebral ventricular size in twins discordant for schizophrenia. Lancet 1982 Mar 6;1(8271):540–1

Reveley AM, Reveley MA, Murray RM: Effects of neuroleptic drugs on MAO activity [letter] Br J Psychiatry 1981 Nov;139:475–6

Revuelta AV, Cheney DL: Simultaneous reduction in the turnover rates of septal gamma-aminobutyric acid and hippocampal acetylcholine following administration of nabilone. Neuropharmacology 1981 Nov; 20(11):1111–4

Rey E, d'Athis P, Richard MO, et al: Pharmacokinetics of tiapride and absolute bioavailability of three extravascular forms.
Int J Clin Pharmacol Ther Toxicol 1982 Feb;20(2):62–7

Ribak CE: The GABAergic neurons of the extrapyramidal system as revealed by immunocytochemistry. Adv Biochem Psychopharmacol 1981;30:23–36

Ricevuti G, Rizzo SC: Aplastic anaemia treated with lithium carbonate [letter] Br J Haematol 1982 Jan;50(1):173–4

Richardson PD, Kane RL, Agarwal K: Effects of drugs on adhesion of human platelets. Trans Am Soc Artif Intern Organs 1981;27:203–7

Richens A, Makki K, Monks A, et al: Effects of sodium valproate on the serum protein binding of phenytoin, and on liver enzyme activity. Monogr Neural Sci 1981;5:221–8

Riches DW, Morris CJ, Stanworth DR: Studies on the possible involvement of complement component C3 in the initiation of acid hydrolase secretion by macrophages. Immunology 1982 Mar; 45(3):473–81

Rickels K: Benzodiazepines: clinical use patterns.
Natl Inst Drug Abuse Res Monogr Ser 1980;(33):43–60

Rickels K: Recent advances in anxiolytic therapy. J Clin Psychiatry 1981 Nov;42(11 Pt 2):40–4

Rifkin A: Maprotiline versus imipramine [letter] J Clin Psychiatry 1981 Mar;43(3):122

Riker DK, Zito RA Jr, Roth RH: Lidocaine selectively diminishes medullary serotonin metabolism in the rat. Neuropharmacology 1981 Dec;20(12A):1233–6

Rindler MJ, McRoberts JA, Saier MH Jr: (Na+,K+)-cotransport in the Madin-Darby canine kidney cell line. Kinetic characterization of the interaction between Na+ and K+. J Biol Chem 1982 Mar 10; 257(5):2254–9

Rindt W, Lücker PW, Treitz P, et al: Klinische Aspekte der tageszeitlich unterschiedlichen Beeinflussbarkeit des Prolaktinsystems.
Methods Find Exp Clin Pharmacol 1981;3 Suppl 1:115S–118S **(Ger)**

Rintamäki H, Lahti H, Hissa R: Feather position of the pigeon after intrahypothalamic injections of noradrenaline, 5-hydroxytryptamine and carbachol. Experientia 1981 Nov 15;37(11):1173–5

Riou F, Cespuglio R, Jouvet M: Propriétés hypnogènes du 'vasoactive intestinal polypeptide' chez le rat. C R Seances Acad Sci [III] 1981 Nov 30;293(12):679–82 (Eng. Abstr.) **(Fre)**

Ritschel WA, Banarer M: Lithium dosage regimen design by the repeated one-point method. Arzneimittelforsch 1982;32(2):98–102

Rittelmeyer LF Jr: Minor tranquilizers: prescribing practices of primary physicians. Psychosomatics 1982 Jan;23(1):23–6

Ritter S, Bellin SI, Pelzer NL: The role of gustatory and postingestive signals in the termination of delayed glucoprivic feeding and hypothalamic norepinephrine turnover. J Neurosci 1981 Dec; 1(12):1354–60

Ritzler BA: Paranoia--prognosis and treatment: a review.
Schizophr Bull 1981;7(4):710–28 (89 ref.)

Riva R, Albani F, Baruzzi A: Quantitative determination of camazepam and its metabolite temazepam in man by gas-liquid chromatography with electron-capture detection. Farmaco [Prat] 1982 Jan;37(1):15–9

Rivas-Suárez E, Cilento G: Quenching of enzyme-generated acetone phosphorescence by indole compounds: stereospecific effects of D- and L-tryptophan. Photochemical-like effects. Biochemistry 1981 Dec 22; 20(26):7329–33

Rivier C, Vale W: Interaction of gonadotropin-releasing hormone agonist and antagonist with progesterone, prolactin, or human chorionic gonadotropin during pregnancy in the rat. Endocrinology 1982 Feb; 110(2):347–51

Rivier C, Brownstein M, Spiess J, et al: In vivo corticotropin-releasing factor-induced secretion of adrenocorticotropin, beta-endorphin, and corticosterone. Endocrinology 1982 Jan;110(1):272–8

Robbins RJ, Sutton RE, Reichlin S: Sodium- and calcium-dependent somatostatin release from dissociated cerebral cortical cells in culture. Endocrinology 1982 Feb;110(2):496–9

Robbins RJ, Sutton RE, Reichlin S: Effects of neurotransmitters and cyclic

AUTHOR SECTION

AMP on somatostatin release from cultured cerebral cortical cells. Brain Res 1982 Feb 25;234(2):377–86

Roberts CJ, Daneshmend TK, Macfarlane D, et al: Anticonvulsant intoxication precipitated by azapropazone. Postgrad Med J 1981 Mar; 57(665):191–2

Roberts DC, Bloom FE: Adrenal steroid–induced changes in beta–adrenergic receptor binding in rat hippocampus. Eur J Pharmacol 1981 Aug 27;74(1):37–41

Roberts MS, Cossum PA, Kowaluk EA, et al: Plastic syringes and intravenous infusions [letter] Med J Aust 1981 Nov 28;2(11):580–1

Robertson HA, Baker GB, Coutts RT, et al: Interactions of beta–carbolines with the benzodiazepine receptor: structure–activity relationships. Eur J Pharmacol 1981 Dec 3;76(2–3):281–4

Robertson J, Weston R, Lewis MJ, et al: Evidence for the potentiation of the antinociceptive action of morphine by bromocriptine. Neuropharmacology 1981 Nov;20(11):1029–32

Robertson MM, Trimble MR: Neuroleptics as antidepressants. Neuropharmacology 1981 Dec;20(12B):1335–6

Rock MH, Goldberger L: Level of ego development and psychotherapy outcome in phobic patients. Br J Med Psychol 1981 Dec;54(Pt 4):319–28

Rockoff S, Baselt RC: Severe carbamazepine poisoning. Clin Toxicol 1981 Aug;18(8):935–9

Rodríguez–Sierra JF, Blake CA: Catecholestrogens and release of anterior pituitary gland hormones. II. Prolactin. Endocrinology 1982 Feb; 110(2):325–9

Rodríguez–Sierra JF, Blake CA: Catecholestrogens and release of anterior pituitary gland hormones. I. Luteinizing hormone. Endocrinology 1982 Feb;110(2):318–24

Rogeness GA, Riester AE, Wicoff JS: Unusual presentation of manic depressive disorder in adolescence. J Clin Psychiatry 1982 Jan; 43(1):37–9

Rogeness GA, Hernandez JM, Macedo CA, et al: Biochemical differences in children with conduct disorder socialized and undersocialized. Am J Psychiatry 1982 Mar;139(3):307–11

Rogóż Z, Skuza G, Sowińska H: Central action of ketotifen. Pol J Pharmacol Pharm 1981;33(5):503–15

Rolls ET: Central nervous mechanisms related to feeding and appetite. Br Med Bull 1981 May;37(2):131–4 (61 ref.)

Romagna F, Zbinden G: Distribution of nuclear size and DNA content in serial liver biopsies of rats treated with N–nitrosomorpholine, phenobarbital and butylated hydroxytoluene. Exp Cell Biol 1981; 49(6):294–305

Romagnano MA, Pilcher WH, Bennett–Clarke C, et al: Distribution of somatostatin in the mouse brain: effects of neonatal MSG treatment. Brain Res 1982 Feb 25;234(2):387–98

Rooke GA, Feigl EO: Work as a correlate of canine left ventricular oxygen consumption, and the problem of catecholamine oxygen wasting. Circ Res 1982 Feb;50(2):273–86

Roquebert J, Gomond P, Demichel P: Activité antinoradrénergique de la raubasine sur l'aorte thoracique et le canal déférent isolés de rat. J Pharmacol 1981 Nov–Dec;12(4):393–403 (Eng. Abstr.) **(Fre)**

Rorie DK, Tyce GM: Regulation of norepinephrine levels in synaptic clefts of dog vascular tissue. Am J Physiol 1982 Feb;242(2):H233–9

Rosen AJ, Wirtshafter D, Pandey GN, et al: Platelet monoamine oxidase activity and behavioral response to pharmacotherapy in psychiatric patients. Psychiatry Res 1982 Feb;6(1):49–59

Rosen H: Therapies of depression. Curr Psychiatr Ther 1981;20:301–11

Rosenbaum JF: The drug treatment of anxiety. N Engl J Med 1982 Feb 18;306(7):401–4 (24 ref.)

Rosenberg R: A kinetic analysis of L–tryptophan transport in human red blood cells. Biochim Biophys Acta 1981 Dec 7;649(2):262–8

Rosenblatt JE: Lorazepam and desipramine serum concentration [letter] Am J Psychiatry 1982 Apr;139(4):536–7

Rosson D, Dunlap RB: Modification of tyrosine residues in dihydrofolate reductase from Lactobacillus casei. Biochim Biophys Acta 1982 Feb 4;701(1):49–56

Rothwell NJ, Stock MJ, Wyllie MG: Dopaminergic mechanisms in diet–induced thermogenesis and brown adipose tissue metabolism. Eur J Pharmacol 1982 Jan 8;77(1):45–8

Rothwell NJ, Stock MJ: Effects of early overnutrition and undernutrition in rats on the metabolic responses to overnutrition in later life. J Nutr 1982 Mar;112(3):426–35

Rotsztejn WH, Dussaillant M, Nobou F, et al: Rapid glucocorticoid inhibition of vasoactive intestinal peptide–induced cyclic AMP accumulation and prolactin release in rat pituitary cells in culture. Proc Natl Acad Sci USA 1981 Dec;78(12):7584–8

Rowe BP, Nasjletti A: The effect of angiotensin II infusion on plasma catecholamines in the conscious rabbit. Proc Soc Exp Biol Med 1981 Oct;168(1):110–3

Rowe JW, Minaker KL, Sparrow D, et al: Age–related failure of volume–pressure–mediated vasopressin release. J Clin Endocrinol Metab 1982 Mar;54(3):661–4

Royet JP, Pager J: Lesions of the olfactory pathways affecting neophobia and learned aversion differentially. Behav Brain Res 1982 Mar; 4(3):251–62

Rozanov VA: Sezonnye izmeneniia v sisteme gamma–aminomaslianoi kisloty golovnogo mozga myshei. Ukr Biokhim Zh 1982;54(1):36–40 (Eng. Abstr.) **(Rus)**

Rudorfer MV, Raichman JA: Questions about combined lithium and haloperidol treatment [letter] Am J Psychiatry 1982 Apr;139(4):537–8

Ruffalo RL, Thompson JF: More on cimetidine–benzodiazepine drug interactions [letter] South Med J 1982 Mar;75(3):382

Rump S, Ilczuk I, Walczyna K, et al: Preliminary pharmacological investigations of N–amino–diphenyl–hydantoin, a new hydantoin derivative with prolonged action. Monogr Neural Sci 1981;5:163–7

Rump S, Ilczuk I, Rabsztyn T, et al: Pharmacological properties of N–aminodiphenylhydantoin, a new hydantoin derivative with anticonvulsant activity. Pharmazie 1981 Nov;36(11):780–1

Rurak A, Melzacka M, Danek L: Pharmacokinetics of trazodone after different routes of administration. Pol J Pharmacol Pharm 1981; 33(3):341–8

Rush ME, Blake CA: Serum testosterone concentrations during the 4–day estrous cycle in normal and adrenalectomized rats. Proc Soc Exp Biol Med 1982 Feb;169(2):216–21

Russell RW, Carson VG, Booth RA, et al: Mechanisms of tolerance to the anticholinesterase, DFP: acetylcholine levels and dynamics in the rat brain. Neuropharmacology 1981 Dec;20(12A):1197–201

Russo–Marie F, Seillan C, Duval D: Glucocorticoids as inhibitors of prostaglandin synthesis. Bull Eur Physiopathol Respir 1981;17(4):587–94 (38 ref.)

Ruwe WD, Myers RD: 5–HT receptors and hyper– or hypothermia: elucidation by catecholamine antagonists injected into the cat hypothalamus. Brain Res Bull 1982 Jan;8(1):79–86

Ryżewska M, Targońska I, Staff–Zielińska E, et al: The effect of TRH and its analogues, (Pro–NH–NH2)3TRH and (2–Picolyl)1–TRH on TSH level in rat serum. Mater Med Pol 1980 Jan–Jun;12(1–2):136–9

S

Saady JJ, Bloom VL, Narasimhachari N, et al: A comparison of plasma and serum levels of two tricyclic antidepressants: imipramine and desipramine. Psychopharmacology (Berlin) 1981;75(2):173–4

Sábato UC, Aguilar JS, Medina JH, et al: Changes in rat hippocampal benzodiazepine receptors and lack of changes in muscarinic receptors after fimbria–fornix lesions. Neurosci Lett 1981 Dec 11;27(2):193–7

Sable DL, Brammell HL, Sheehan MW, et al: Attenuation of exercise conditioning by beta–adrenergic blockade. Circulation 1982 Apr; 65(4):679–84

Sachs JR: Internal potassium stimulates the sodium–potassium pump by increasing cell ATP concentration. J Physiol (Lond) 1981;319:515–28

Sadowski J, Gellert R, Kurkus J, et al: Denervated and intact kidney responses to exercise in the dog. J Appl Physiol 1981 Dec;51(6):1618–24

Sagar SM, Landry D, Millard WJ, et al: Depletion of somatostatin–like immunoreactivity in the rat central nervous system by cysteamine. J Neurosci 1982 Feb;2(2):225–31

Sahyoun HA, Costall B, Naylor RJ: On the ability of domperidone to selectively inhibit catecholamine–induced relaxation of circular smooth muscle of guinea–pig stomach. J Pharm Pharmacol 1982 Jan;34(1):27–33

Saji M, Miura M: Transmitter sensitivities among various types of cultured brain stem neurons. Brain Res 1982 Feb 4;233(1):83–96

Sakahira K, Tsunoda Y, Takegawa K, et al: The effects of catecholamines on hemorrhagic shock in dogs. Bull Tokyo Med Dent Univ 1981 Dec; 28(4):125–34

Sakamoto S, Ichikawa S, Komabayashi T, et al: [Effects of adrenaline, noradrenaline and pilocarpine on the oxygen uptake in rat submandibular gland (author's transl)] Nippon Seirigaku Zasshi 1981; 43(10):469–78 (Eng. Abstr.) **(Jpn)**

Sakanaka M, Shiosaka S, Takatsuki K, et al: Evidence for the existence of a substance P–containing pathway from the nucleus laterodorsalis tegmenti (Castaldi) to the lateral septal area of the rat. Brain Res 1981 Dec 28;230(1–2):351–5

Sakoguchi T, Kobayashi K, Kimura M, et al: [Inhibition of serum choline esterase by fatty acids and the recovery by human serum albumin (author's transl)] Rinsho Byori 1981 Sep;29(9):925–8 **(Jpn)**

Sakurai J, Komura K: [Secular change of background activity in Ge(Li) detector (author's transl)] Radioisotopes 1981 Aug;30(8):471–4 **(Jpn)**

Saladini M, Gabana MA, Bracco F, et al: Effect of antiepileptic drugs on the cerebral amino acid uptake in vitro. Ital J Neurol Sci 1981 Dec; 2(4):351–60

Salers P, Benoit V, Boyer J: Activation of hormone–sensitive lipase: disparity between evaluations in intact and disrupted fat cells. Biochem Biophys Res Commun 1981 Dec 15;103(3):813–8

Saletu B, Grünberger J, Amrein R, et al: Assessment of pharmacodynamics of a new 'controlled release' form of diazepam (Valium CR Roche) by quantitative EEG and psychometric analysis in neurotic subjects. J Int Med Res 1981;9(6):408–33

Saletu B, Grünberger J, Linzmayer L, et al: Anxiolytics and beta blockers: evaluation of pharmacodynamics by quantitative EEG, psychometric and physiological variables. Agressologie 1981 Oct;22(C):5–16

Saligaut C, Moore N, Daoust M, et al: Piribedil–induced anti–hypoxic protection in rats. Aviat Space Environ Med 1982 Jan;53(1):35–9

AUTHOR SECTION

Salomon NW, Plachetka JR, Copeland JG: Comparison of dopamine and dobutamine following coronary artery bypass grafting. Ann Thorac Surg 1982 Jan;33(1):48-54

Salzman C: Basic principles of psychotropic drug prescription for the elderly. Hosp Community Psychiatry 1982 Feb;33(2):133-6

Sánchez-Cuadrado MC, Boada J, Bayo JM: Acción del propranolol, nifenalol y pirindolol sobre el efecto lipolítico de la adrenalina en epidídimo de rata. Arch Farmacol Toxicol 1981 Apr;7(1):181-2 **(Spa)**

Sandberg BE, Hanley MR, Watson SP, et al: Synthesis and metabolic stability of a tritium-labelled substance P analogue. FEBS Lett 1982 Jan 25;137(2):236-40

Sander GE, Giles TD, Kastin AJ, et al: Cardiopulmonary pharmacology of enkephalins in the conscious dog. Peptides (Fayetteville) 1981 Winter; 2(4):403-7

Sandyk R: Phenytoin toxicity induced by antituberculosis drugs [letter] S Afr Med J 1982 Mar 13;61(11):382

Sannita WG, Cabri M, Montano VF, et al: Quantitative EEG and behavioral effects in volunteers of a new benzodiazepine (SAS 643) in relation to drug plasma concentration. Ther Drug Monit 1981; 3(4):341-9

Santana MA, Beck G: Caractérisation de la tyrosine aminotransférase par une technique d'immunoadsorption. Application à la mesure de l'ARN messager spécifique. C R Soc Biol (Paris) 1981;175(6):859-65 (Eng. Abstr.) **(Fre)**

Santidrián S: Effect of corticosterone on the urinary output of Nt-methylhistidine in mature male rats. Arch Farmacol Toxicol 1981 Aug;7(2):283-8

Sarthy PV: The uptake of [3H]gamma-aminobutyric acid by isolated glial (Müller) cells from the mouse retina. J Neurosci Methods 1982 Jan; 5(1-2):77-82

Sartorius N: WHO-coordinated collaborative studies in the effects of psychopharmacological drugs in different populations. Mod Probl Pharmacopsychiatry 1981;16:83-93

Sastry BV, Statham CN, Meeks RG, et al: Changes in phospholipid methyltransferases and membrane microviscosity during induction of rat liver microsomal cytochrome P-450 by phenobarbital and 3-methylcholanthrene. Pharmacology 1981;23(4):211-22

Satli MA, Aron C: Role played by serotonin in the control of estrous receptivity. Ovarian activity and ovulation in the cyclic female rat. Psychoneuroendocrinology 1981;6(2):121-9

Satoh S, Ohyama Y, Hayashi M: Effects of renal nerve stimulation, norepinephrine and angiotensin II on renal blood flow in relation to release of PG-like substances in anesthetized dogs. Arch Int Pharmacodyn Ther 1981 Dec;254(2):304-16

Saul'skaya NB: Correlation between the rate of avoidance conditioning and the brain catecholamine level in rats. Neurosci Behav Physiol 1981 May-Jun;11(3):221-6

Scandling J, Spital A: Amphetamine-associated myoglobinuric renal failure. South Med J 1982 Feb;75(2):237-40

Scatton B, Zivkovic B, Dedek J, et al: gamma-Aminobutyric acid (GABA) receptor stimulation. III. Effect of progabide (SL 76002) on norepinephrine, dopamine and 5-hydroxytryptamine turnover in rat brain areas. J Pharmacol Exp Ther 1982 Mar;220(3):678-88

Scatton B, Bartholini G: gamma-Aminobutyric acid (GABA) receptor stimulation. IV. Effect of progabide (SL 76002) and other GABAergic agents on acetylcholine turnover in rat brain areas. J Pharmacol Exp Ther 1982 Mar;220(3):689-95

Seelsi R, Arrigoni E, Moglia A, et al: Effects of lithium administration on central and peripheral nervous system in rats. Biochemical and morphological findings. Pharmacopsychiatria 1981 Nov;14(6):213-6

Schachner ER, Oster ZH, Cicale NR, et al: The effect of diphenylhydantoin (Dilantin) on thallium-201 chloride uptake. Eur J Nucl Med 1981 Dec;6(12):585-6

Schäfer-Korting M, Mutschler E: Pharmacokinetics of bendroflumethiazide alone and in combination with propranolol and hydralazine. Eur J Clin Pharmacol 1982;21(4):315-23

Schanbacher BD: Responses of ram lambs to active immunization against testosterone and luteinizing hormone-releasing hormone. Am J Physiol 1982 Mar;242(3):E201-5

Schatzberg AF, Orsulak PJ, Rosenbaum AH, et al: Toward a biochemical classification of depressive disorders IV: Pretreatment urinary MHPG levels as predictors of antidepressant response to imipramine. Commun Psychopharmacol 1980;4(5):441-5

Schatzberg AF, Orsulak PJ, Rosenbaum AH, et al: Toward a biochemical classification of depressive disorders. V: Heterogeneity of unipolar depressions. Am J Psychiatry 1982 Apr;139(4):471-5

Scheel-Krüger J, Magelund G, Olianas MC: Role of GABA in the striatal output system: globus pallidus, nucleus entopeduncularis, substantia nigra and nucleus subthalamicus. Adv Biochem Psychopharmacol 1981; 30:165-86 (92 ref.)

Schell NB: Juggling act on a tightrope: using psychotropics in the elderly [editorial] NY State J Med 1981 Nov;81(12):1737

Scherber A, Richter K, Feller K: The distribution of drugs between blood and cerebro-spinal fluid man. Agressologie 1981 Nov;22(E):37-8

Scherman D, Roisin MP, Henry JP, et al: Ionophore mediated catecholamine release from chromaffin granules. Comparison of X-537 A and X-14547 A effects. Biochem Pharmacol 1981 Dec 15; 30(24):3277-83

Schichtl H: Behandlung von akuten psychischen Ausnahmezuständen im ambulanten Notarztdienst. Ther Ggw 1982 Jan;121(1):46-50 **(Ger)**

Schlesinger C: Zur Ontogenese des Acetylcholin-Systems im Gehirn des Südafrikanischen Krallenfrosches (Xenopus laevis Daudin). J Hirnforsch 1981;22(5):543-53 (Eng. Abstr.) **(Ger)**

Schlicker E, Göthert M: Antagonistic properties of quipazine at presynaptic serotonin receptors and alpha-adrenoceptors in rat brain cortex slices. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov; 317(3):204-8

Schmidt M, Imbs JL, Schwartz J: The vascular dopamine receptor : a review. J Pharmacol 1981 Nov-Dec;12(4):355-82 (183 ref.)

Schmidt P: Neuroleptics in the treatment of anxiety. Agressologie 1981 Nov;22(D):19-20

Schmidt RH, Ingvar M, Lindvall O, et al: Functional activity of substantia nigra grafts reinnervating the striatum: neurotransmitter metabolism and [14C]2-deoxy-D-glucose autoradiography. J Neurochem 1982 Mar; 38(3):737-48

Schmidt WF 3d, Asakura T, Schwartz E: Effect of cetiedil on cation and water movements in erythrocytes. J Clin Invest 1982 Mar;69(3):589-94

Schmitt BD: Nocturnal enuresis: an update on treatment. Pediatr Clin North Am 1982 Feb;29(1):21-36

Schneider F, Mihalaş G, Petroiu A, et al: Electrocardiographic and metabolic investigations concerning the exhaustive exercise under conditions of adrenergic blocking in rats. Physiologie 1982 Jan-Mar; 19(1):31-3

Schoffelmeer AN, Mulder AH: 3H-Noradrenaline and 3H-5-hydroxytryptamine release from rat brain slices and its presynaptic alpha-adrenergic modulation after long-term desipramine pretreatment. Naunyn Schmiedebergs Arch Pharmacol 1982 Feb; 318(3):173-80

Schofield JG, Sa'th S: Potentiation of bovine growth hormone release by an inhibitor of potassium channels. Eur J Pharmacol 1981 Dec 17; 76(4):431-4

Schorderet-Slatkine S, Schorderet M, Baulieu EE: Cyclic AMP-mediated control of meiosis: effects of progesterone, cholera toxin, and membrane-active drugs in Xenopus laevis oocytes. Proc Natl Acad Sci USA 1982 Feb;79(3):850-4

Schreiber V, Stěpán J, Stárka L: Digoxin-like immunoreactivity of certain steroid and other hormones. Physiol Bohemoslov 1981;30(6):569-71

Schreiber V, Přibyl T, Gregorová I: Faktor aktivující influx 86Rb+ do erytrocytu in vitro jako znečištěnina komerčního preparátu testosteronu. Sb Lek 1981;83(11-12):305-8 (Eng. Abstr.) **(Cze)**

Schreier HA: Mania responsive to lecithin in a 13-year-old girl. Am J Psychiatry 1982 Jan;139(1):108-10

Schreurs AJ, Nijkamp FP: Haemophilus influenzae induced loss of lung beta-adrenoceptor binding sites and modulation by changes in peripheral catecholaminergic input. Eur J Pharmacol 1982 Jan;77(2-3):95-102

Schuckit MA: Current therapeutic options in the management of typical anxiety. J Clin Psychiatry 1981 Nov;42(11 Pt 2):15-26

Schulman JA, Finger TE, Brecha NC, et al: Enkephalin immunoreactivity in Golgi cells and mossy fibers of mammalian, avian, amphibian and teleost cerebellum. Neuroscience 1981;6(11):2407-16

Schultz HD, Zehr JE, Livnat A: Central and peripheral adrenergic modulation of carotid sinus-induced renin release. Am J Physiol 1982 Mar;242(3):R318-25

Schultz S: The Boston State Hospital case: a conflict of civil liberties and true liberalism. Am J Psychiatry 1982 Feb;139(2):183-8

Schulze G, Tetzner M, Topolinski H: Operant thermoregulation of rats with anterior hypothalamic lesions. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(1):43-8

Schuster CR, Fischman MW, Johanson CE: Internal stimulus control and subjective effects of drugs. Natl Inst Drug Abuse Res Monogr Ser 1981 Jul;(37):116-29 (46 ref.)

Schuster DI, Holden WL, Narula AP, et al: Irreversible blockade of striatal dopamine receptors in vivo by a derivative of alpha-flupenthixol. Eur J Pharmacol 1982 Feb 5;77(4):313-6

Schwarcz G: Case report of inhibition of ejaculation and retrograde ejaculation as side effects of amoxapine. Am J Psychiatry 1982 Feb; 139(2):233-4

Schwille PO, Engelhardt W, Wolf U, et al: Infusion of somatostatin antiserum in the rat—failure to raise stress induced low gastric acid secretion. Horm Metab Res 1981 Dec;13(12):710-1

Schwyzer R: Peptides and the new endocrinology. Naturwissenschaften 1982 Jan;69(1):15-20

Scott PJ, Reid JL: The effect of age on the responses of human isolated arteries to noradrenaline. Br J Clin Pharmacol 1982 Feb;13(2):237-9

Scuvée-Moreau J, Dresse A: Monoamines et dépressions endogènes. Aspects biochimique et pharmacologique. Rev Med Liege 1982 Jan 1;37(1):1-7 **(Fre)**

Sedivec V: Vliv ročních období průběh a léčebné výsledky depresivních fázi maniomelancholie. Cesk Psychiatr 1981 Oct;77(5):326-30 (Eng. Abstr.) **(Cze)**

Séguin C, Bélanger A, Labrie F, et al: Study of the direct action of luteinizing hormone-releasing hormone agonists at the testicular level in intact rats treated with an antiluteinizing hormone serum. Endocrinology 1982 Feb;110(2):524-30

Seideman P, Ericsson O, Gröningsson K, et al: Effect of pentobarbital on the formation of diastereomeric oxazepam glucuronides in man: analysis by high performance liquid chromatography. Acta Pharmacol Toxicol (Copenh) 1981 Sep;49(3):200-4

Seiler N, Knödgen B, Gittos MW, et al: On the formation of amino acids deriving from spermidine and spermine. Biochem J 1981 Oct 15; 206(1):123-32

Selemon LD, Sladek JR Jr: Aging of tuberoinfundibular (A-12) dopamine neurons in the C57Bl/6N male mouse. Brain Res Bull 1981 Nov; 7(5):585-94

Selinger D, Hailer AW, Nurnberger JI Jr, et al: A new method for the use of salivary lithium concentrations as an indicator of plasma lithium levels. Biol Psychiatry 1982 Jan;17(1):99-102

Selking O, Gustavsson S, Johansson H, et al: Effect of parathyroid hormone on gastrin and somatostatin release from the gastric antrum. Ups J Med Sci 1981;86(3):259-67

Seliers JC, Wit LC, Ganjam VK, et al: Seasonal plasma T4 titers in the hibernating lizard Cnemidophorus sexlineatus. Gen Comp Endocrinol 1982 Jan;46(1):24-8

Semenkova GN, Kravchenko LM, Cherenkevich SN, et al: Opredelenie kontsentratsii adrenalina v sliune cheloveka. Lab Delo 1982;(1):15-7 (Eng. Abstr.) **(Rus)**

Semenov EV: Znachenie ionov Ca2+ i Mg2+ v mekhanizme presinapticheskogo deistviia tsentral'nykh M- i N-kholinolitikov. Vopr Med Khim 1982 Jan-Feb;28(1):67-71 **(Rus)**

Semerdjian-Rouquier L, Bossi L, Scatton B: Determination of 5-hydroxytryptophan, serotonin and 5-hydroxyindoleacetic acid in rat and human brain and biological fluids by reversed-phase high-performance liquid chromatography with electrochemical detection. J Chromatogr 1981 Nov 20;218:663-70

Serafini-Cessi F, Campadelli-Fiume G: Studies on benzhydrazone, a specific inhibitor of herpesvirus glycoprotein synthesis. Size distribution of glycopeptides and endo-beta-N-acetylglucosaminidase-H treatment. Arch Virol 1981;70(4):331-43

Serbanescou T, Lutrand JC, Balzamo E: Sommeil de nuit de psychotiques en traitement au long cours sous flupentixol. Encephale 1981;7(5):623-9 (Eng. Abstr.) **(Fre)**

Seredenin SB, Zin'kovskiĭ VG, Badyshtov BA, et al: Izuchenie geneticheskikh razlichii v protivosudorozhnom éffekte i skorosti metabolizma fenazepama. Biull Eksp Biol Med 1981 Oct;91(10):450-3 (Eng. Abstr.) **(Rus)**

Sergeenko NI, Chirkin AA, Kavtsevich IuP: Izmenenie soderzhaniia 11-oksikortikosteroidov u bol'nykh, poluchavshikh droperidol i oksibutirat natriia i podvergavshikhsia élektrostimuliatsii. Vestn Khir 1981 Nov;127(11):114-6 **(Rus)**

Setchell KD, Lawson AM, Conway E, et al: The definitive identification of the lignans trans-2,3-bis(3-hydroxybenzyl)-gamma-butyrolactone and 2,3-bis(3-hydroxybenzyl)butane-1,4-diol in human and animal urine. Biochem J 1981 Aug 1;197(2):447-58

Seth RV, Clarke VS, Lewis RA, et al: Effect of propranolol on the airway response to prostaglandin E2 in normal man. Br J Clin Pharmacol 1981 Nov;12(5):731-5

Sethy VH, Harris DW: Effect of norepinephrine uptake blocker on beta-adrenergic receptors of the rat cerebral cortex. Eur J Pharmacol 1981 Oct 15;75(1):53-6

Severina IS, Klimova GI, Nersisian AA: Vliianie soliubilizatsii mitokhondrial'noĭ monoaminoksidazy pecheni krysy metilétilketonom na tormozhenie khlorgilinom i deprenilom aktivnosti fermenta. Biokhimiia 1981 Nov;46(11):2043-55 (Eng. Abstr.) **(Rus)**

Seydoux J, Assimacopoulos-Jeannet F, Jeanrenaud B, et al: Alterations of brown adipose tissue in genetically obese (ob/ob) mice. I. Demonstration of loss of metabolic response to nerve stimulation and catecholamines and its partial recovery after fasting or cold adaptation. Endocrinology 1982 Feb;110(2):432-8

Shader RI, Ciraulo DA, Greenblatt DJ, et al: Steady-state plasma desmethyldiazepam during long-term clorazepate use: effects of antacids. Clin Pharmacol Ther 1982 Feb;31(2):180-3

Shader RI, Greenblatt DJ, Ciraulo DA, et al: Effect of age and sex on disposition of desmethyldiazepam formed from its precursor clorazepate. Psychopharmacology (Berlin) 1981;75(2):193-7

Shader RI, Greenblatt DJ: Amoxapine, an observation, and a perspective on MAOIs and their safety [editorial] J Clin Psychopharmacol 1981 Sep;1(5):263

Shah DS, Chambon P, Guidotti A: Binding of (3H)-5,5 diphenylhydantoin to rat brain membranes. Neuropharmacology 1981 Nov;20(11):1115-9

Shaker N, Eldefrawi AT, Miller ER, et al: Interaction of tricyclic antidepressants with the ionic channel of the acetylcholine receptor of Torpedo electric organ. Mol Pharmacol 1981 Nov;20(3):511-8

Shanbaky NM, Emran A, Borowitz JL: Identification of subcellular organelles involved in Ba2+- and Cd2+-induced adrenomedullary secretion. Toxicol Appl Pharmacol 1982 Jan;62(1):167-71

Shani J, Givant Y, Goldhaber G, et al: Suppression of mammotropic development and prolactin release by sympathomimetic drugs in rats. Arch Farmacol Toxicol 1981 Aug;7(2):201-8

Shanming Y: Lithium therapy in China. Brief communication. Acta Psychiatr Scand 1981 Sep;64(3):270-2

Sheehan KL, Casper RF, Yen SS: Induction of luteolysis by luteinizing hormone-releasing factor (LRF) agonist: sensitivity, reproducibility, and reversibility. Fertil Steril 1982 Feb;37(2):209-12

Shekim WO, Javaid J, Dekirmenjian H, et al: Effects of d-amphetamine on urinary metabolites of dopamine and norepinephrine in hyperactive boys. Am J Psychiatry 1982 Apr;139(4):485-8

Shellenberger MK: Persistent alteration of rat brain monoamine levels by carbon monoxide exposure: sex differences and behavioral correlation. Neurotoxicology (Park Forest Il) 1981 Nov;2(3):431-41

Shibagaki M, Seo M, Asano T, et al: Environmental enrichment to alleviate maze performance deficits in rats with microcephaly induced by x-irradiation. Physiol Behav 1981 Nov;27(5):797-802

Shibata K, Kataoka Y, Gomita Y, et al: Localization of the site of the anticonflict action of benzodiazepines in the amygdaloid nucleus of rats. Brain Res 1982 Feb 25;234(2):442-6

Shiino M: Ultrastructural evidence of gonadotrophin release from castration cells following injection of LHRH in the rat. Cell Tissue Res 1982 Jan;222(1):213-22

Shima F, Hassler R: Circling behavior produced by unilateral lesions of the central vestibular system. Appl Neurophysiol 1982 May-Jun; 45(3):255-60

Shimai S, Hoshishima K: Effects of bilateral amygdala lesions on neophobia and conditioned taste aversion in mice. Percept Mot Skills 1982 Feb;54(1):127-30

Shimamine M, Takahashi K, Ono M: [Identification of psychotropic drugs. Analysis of beta-carboline derivatives (author's transl)] Eisei Shikenjo Hokoku 1981;99:79-83 (Eng. Abstr.) **(Jpn)**

Shimeno H, Fukumoto Y, Toda A, et al: Effect of dl-3-pyridylalanine on serotonin concentration and tryptophan-serotonin metabolizing enzymes in rats. Chem Pharm Bull (Tokyo) 1981 Oct;29(10):2940-8

Shimizu Y, Kuwayama Y, Fukuda M, et al: Localization of substance P-like immunoreactivity in the anterior eye segment of squirrels: an immunohistochemical analysis. Invest Ophthalmol Vis Sci 1982 Feb; 22(2):259-63

Shin SH, Bates L, Jellinck PH: Temporal and other effects of catechol estrogens on prolactin secretion in the rat. Neuroendocrinology 1981 Dec;33(6):352-7

Shiosaka S, Takatsuki K, Sakanaka M, et al: Ontogeny of somatostatin-containing neuron system of the rat: immunohistochemical analysis. II. Forebrain and diencephalon. J Comp Neurol 1982 Jan 20; 204(3):211-24

Shirai K, Jackson RL: Lipoprotein lipase-catalyzed hydrolysis of p-nitrophenyl butyrate. Interfacial activation by phospholipid vesicles. J Biol Chem 1982 Feb 10;257(3):1253-8

Shires TK, Hargrove JL: Growth hormone inhibition of tyrosine aminotransferase in primary cultures of rat liver cells. Biochim Biophys Acta 1982 Jan 12;714(1):170-2

Shiu GK, Nemoto EM: Simple, rapid and sensitive reversed-phase high-performance liquid chromatographic method for thiopental and pentobarbital determination in plasma and brain tissue. J Chromatogr 1982 Jan 8;227(1):207-12

Shnaiderman R, Avi-Dor Y: The uptake and extrusion of salts by the halotolerant bacterium, Ba1. Arch Biochem Biophys 1982 Jan; 213(1):177-85

Showell HJ, Glovsky MM, Ward PA: C3a-induced lysosomal enzyme secretion from human neutrophils: lack of inhibition by f met-leu-phe antagonists and inhibition by arachidonic acid antagonists. Int Arch Allergy Appl Immunol 1982 Mar;67(3):227-32

Shukla R, Srimal RC, Dhawan BN: The effect of intracerebroventricular administration of catecholamines and their antagonists on rectal temperature of Mastomys natalensis. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(1):38-42

Shulgin AT, Carter MF: N, N-Diisopropyltryptamine (DIPT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT). Two orally active tryptamine analogs with CNS activity. Commun Psychopharmacol 1980;4(5):363-9

Shute CC: Subjective colours and brain function. Endeavour 1981; 5(4):141-6

Sia RL, Boonstra S, Westra P, et al: An electroencephalographic study of 4-aminopyridine. Anesth Analg (Cleve) 1982 Apr;61(4):354-7

Siever L, Cohen R, Pert A: Assessing pharmacologically induced dopamine receptor sensitivity changes with the Ungerstedt turning model. Psychopharmacology (Berlin) 1981;75(2):212-3

Sievers J, Mangold U, Berry M, et al: Experimental studies on cerebellar foliation. I. A qualitative morphological analysis of cerebellar fissuration defects after neonatal treatment with 6-OHDA in the rat. J Comp Neurol 1981 Dec 20;203(4):751-69

Sikri KL, Hoyes AD, Barber P, et al: Substance P-like immunoreactivity in the intramural nerve plexuses of the guinea-pig ureter: a light and electron microscopical study. J Anat 1981 Oct;133(Pt 3):425-42

Silva Carvalho L, Silva Carvalho J, Moniz de Bettencourt JM: L'action de la phentolamine sur les réflexes carotidiens déclenchés par l'acétylcholine. C R Soc Biol (Paris) 1981;175(6):913-5 (Eng. Abstr.) **(Fre)**

AUTHOR SECTION

Silverman AY, Darnell BJ, Montiel MM, et al: Response of rhesus monkey lymphocytes to short-term administration of THC. Life Sci 1982 Jan 4;30(1):107-15

Silverman HI, Lewis GP: Phenylpropanolamine [letter] JAMA 1982 Jan 22-29;247(4):460-1

Simantov R: Localization and modulation of enkephalins, endorphins and opiate receptors in the CNS and the pituitary gland. Mod Probl Pharmacopsychiatry 1981;17:38-48

Simler S, Puglisi-Allegra S, Mandel P: gamma-Aminobutyric acid in brain areas of isolated aggressive or non-aggressive inbred strains of mice. Pharmacol Biochem Behav 1982 Jan;16(1):57-61

Simon-Trompler E, Maksay G, Lukovits I, et al: Lorazepam and oxazepam esters. Hydrophobicity, hydrolysis rates and brain appearance. Arzneimittelforsch 1982;32(2):102-5

Simpson GM, White KL, Boyd JL, et al: Relationship between plasma antidepressant levels and clinical outcome for inpatients receiving imipramine. Am J Psychiatry 1982 Mar;139(3):358-60

Singh P, Muldoon TG: A direct effect on LHRH on anterior pituitary estrogen receptors in the female rat. J Steroid Biochem 1982 Jan; 16(1):31-7

Sinha YN, Gilligan TA: Estrogen in high doses inhibits perphenazine-induced prolactin release. Endocrinology 1982 Jan; 110(1):126-30

Siris SG, Cooper TB, Rifkin AE, et al: Plasma imipramine concentrations in patients receiving concomitant fluphenazine decanoate. Am J Psychiatry 1982 Jan;139(1):104-6

Sirotkin AV, Kisliuk SM: Vliianie arginin-vazototsina, oksitotsina i ikh fragmentov na soderzhanie kortikosterona v plazme krovi kur razlichnykh vozrastov. Fiziol Zh SSSR 1982 Jan;68(1):112-5 (Eng. Abstr.) **(Rus)**

Skagerberg G, Emson PC, Björklund A: Transplantation of irides or sensory ganglia to the anterior eye chamber of the rat: survival and sprouting of substance P-containing neurones. Neurosci Lett 1982 Jan 22;28(1):29-34

Skallgård F: Agranulocytose under behandling med mianserin (Tolvon)] Ugeskr Laeger 1981 Nov 9;143(46):3057 (Eng. Abstr.) **(Dan)**

Skarin G, Nillius SJ, Wide L: Early follicular phase luteinizing hormone-releasing hormone agonist administration - effects on follicular maturation and corpus luteum function in women. Contraception 1982 Jan;25(1):31-9

Skirboll L, Hökfelt T, Rehfeld J, et al: Coexistence of substance P- and cholecystokinin-like immunoreactivity in neurons of the mesencephalic periaqueductal central gray. Neurosci Lett 1982 Jan 22;28(1):35-9

Skliarov AIa: Vliianie atsetilkholina na sekretornuiu frnktsiiu zheludka i tonus ego sosudov. Fiziol Zh SSSR 1982 Jan;68(1):90-9 (Eng. Abstr.) **(Rus)**

Skov Olsen P, Kirkegaard P, Petersen B, et al: The effect of a synthetic met-enkephalin analogue (FK 33-824) on gastric acid secretion and serum gastrin in man. Scand J Gastroenterol 1981;16(4):531-3

Skovronsky O, boleloucky Z, Bastecky J: Anxiety and other neurotic symptoms in patients suffering from dans la conception des états limitrophes et des mécanismes d'action clinique des tranquillisants. Agressologie 1981 Oct;22(C):25-6

Skul'skiĭ IA, Krestinskaia TV, Pisareva LN, et al: Vliianie strukturnoĭ sokhrannosti preparatov Na,K-ATFazy na sposobnost' litiia zameshchat' natriĭ v aktivatsii fermenta. Tsitologiia 1982 Jan;24(1):95-8 (Eng. Abstr.) **(Rus)**

Slater P, Bennett MW: Effects of putative endogenous benzodiazepine receptor ligands on the potentiation of adenosine by benzodiazepines in isolated smooth muscle. J Pharm Pharmacol 1982 Jan;34(1):42-4

Slaunwhite WR Jr: Inhibitors of prolactin secretion: a mini-review. Prog Clin Biol Res 1981;75B:19-29 (42 ref.)

Smart L: Competitive inhibition of sodium-dependent high affinity choline uptake by harmala alkaloids. Eur J Pharmacol 1981 Nov 5;75(4):265-9

Smeds S, Allenmark S, Lamke LO, et al: LCEC analysis of 5-hydroxytryptamine and norepinephrine in the human gastrointestinal tract. Acta Chir Scand 1981;147(5):361-2

Smith A: Use of 2-allyl-2-isopropylacetamide as a catalytic site probe for rabbit cytochrome P-450. Res Commun Chem Pathol Pharmacol 1981 Sep;33(3):475-85

Smith CC, Lewis ME, Tallman JF: Effect of benzodiazepines on cyclic GMP formation in rat cerebellar slices. Pharmacol Biochem Behav 1982 Jan;16(1):29-33

Smith CU: Don Juan and the vision of Vision. Perception 1981; 10(4):435-53

Smith DC, El-Hage A: Chronic exercise does not alter the chronotropic response of isolated rat atria to catecholamines. Experientia 1982 Feb 15;38(2):260-1

Smith DM, Shelley SA, Balis JU: Ultrastructural stereologic analysis of fetal rabbit type II alveolar epithelial cells following maternal pilocarpine treatment or fasting. Anat Rec 1982 Jan;202(1):23-31

Smith EM, Blalock JE: Human lymphocyte production of corticotropin and endorphin-like substances: association with leukocyte interferon. Proc Natl Acad Sci USA 1981 Dec;78(12):7530-4

Smith GC, Courtney PG, Wreford NG, et al: Further studies on the effects of intravenously administered 6-hydroxydopamine on the median eminence of the rat. Brain Res 1982 Feb 18;234(1):101-10

Smith JP, Emptage MH, Orme-Johnson WH: Magnetic susceptibility studies of native and thionine-oxidized molybdenum-iron protein from Azotobacter vinelandii nitrogenase. J Biol Chem 1982 Mar 10; 257(5):2310-3

Smith JR, Simon EJ: Endorphins, opiate receptors and their evolving biology. Pathobiol Annu 1981;11:87-126 (212 ref.)

Smith MK, Hazelwood RL: Alpha- and beta-adrenergic control of pancreatic polypeptide and insulin secretion in adult chickens. Proc Soc Exp Biol Med 1981 Dec;168(3):319-24

Smith MS: Effect of pulsatile gonadotropin-releasing hormone on the release of luteinizing hormone and follicle-stimulating hormone in vitro by anterior pituitaries from lactating and cycling rats. Endocrinology 1982 Mar;110(3):882-91

Smith RE, Helms PM: Adverse effects of lithium therapy in the acutely ill elderly patient. J Clin Psychiatry 1981 Mar;43(3):94-9

Smith RJ, Bowman BJ, Iden SS: Effects of trifluoperazine on human neutrophil function. Immunology 1981 Dec;44(4):677-84

Smith SG 3d, Matt KS, Prestowitz WF, et al: Regulation of tonic gonadotropin release in prepubertal female hamsters. Endocrinology 1982 Apr;110(4):1262-7

Smotherman WP, Burt G, Kimble DP, et al: Behavioral and corticosterone effects in conditioned taste aversion following hippocampal lesions. Physiol Behav 1981 Oct;27(4):569-74

Smulevitch A: Differentiated psychopharmacotherapy in anxiety states of slowly progressive schizophrenia. Agressologie 1981 Nov;22(D):31-2

Smythies JR: An hypothesis of the molecular structure of the dopamine receptor. Med Hypotheses 1981 Dec;7(12):1449-56

Snape BM, Badawy AA: Enhancement of rat brain tyrosine aminotransferase activity by cortisol. Biochem J 1981 Aug 15; 198(2):417-20

Snow AE, Horita A: Interaction of apomorphine and stressors in the production of hyperthermia in the rabbit. J Pharmacol Exp Ther 1982 Feb;220(2):335-9

Sobolev VI, Chirva GI: Vliianie myshechnoĭ raboty na sledovye éffekty kholodovoĭ akklimatsii. Fiziol Zh SSSR 1981 Nov;67(11):1710-6 **(Rus)**

Sokolova ZP: Osobennosti gormonal'nykh sootnoshenii v poslerodovom periode. Akush Ginekol (Mosk) 1981;(11):3-6 (43 ref.) **(Rus)**

Solov'ev MM, Ignatov IuD, Kiseleva EG, et al: Kharakteristika psikhoémotsional'nogo sostoianiia deteĭ pri lechenii zubov. Stomatologiia (Mosk) 1982 Jan-Feb;61(1):77-82 (Eng. Abstr.) **(Rus)**

Solow EB: Determination of phenobarbital and phenytoin by gas-liquid chromatography with on-column methylation. Clin Chem 1982 Jan; 28(1):216-8

Somei K: [The blocking potencies and the mode of blockade by pentobarbital and phenobarbital, examined on various types of ACh-receptor activities (author's transl)] Nippon Seirigaku Zasshi 1981; 43(11):529-31 (Eng. Abstr.) **(Jpn)**

Sominskiĭ VN, Kuznetsova VA, Sanzhara TS, et al: Fliuorimetricheskoe opredelenie serotonina i gistamina v odnom obraztse. Lab Delo 1982; (2):104-7 (Eng. Abstr.) **(Rus)**

Sominskiĭ VN, Tkacheva ET, Ivkina TM, et al: Spektrofliuorimetricheskoe opredelenie katekholaminov i dioksibenilalanina v odnom obraztse. Lab Delo 1982;(1):11-5 (Eng. Abstr.) **(Rus)**

Sommer H, Kasper H: Effect of acetylcholine, gastrin, and glucagon alone and in combination with secretin and cholecystokinin on the secretion of the isolated perfused rat pancreas. Res Exp Med (Berl) 1981; 179(3):239-47

Somogyi P, Cowey A, Halász N, et al: Vertical organization of neurones accumulating 3H-GABA in visual cortex of rhesus monkey. Nature 1981 Dec 24;294(5843):761-3

Sorimachi M, Yamagami K: Nitriphenol compound induces Ca-dependent exocytotic secretion of catecholamines by a direct effect on the plasma membranes of the adrenal medullary cells. Brain Res 1982 Jan 28; 232(1):242-6

Sorimachi M, Nishimura S: Calcium-dependent secretion of catecholamines from the perfused bovine adrenal medulla by sodium deprivation. Jpn J Physiol 1981;31(5):753-56

Sorrell JM, Weiss L: Development of the embryonic chick phagocytic system: intraembryonic erythrophagocytosis induced by phenylhydrazine. J Morphol 1982 Feb;171(2):183-94

Soucek K, Zatecka I, Vencovsky E: The use of the antidepressant tradozone in outpatient psychiatric practice. Agressologie 1981 Nov;22(D):27

Soustre H, Rakotonirina A: Electrophysiological and mechanical studies of frog heart adrenoceptor stimulation by epinine. Cardiovasc Res 1981 Dec;15(12):700-10

Sowers JR, Berg G, Martin VS, et al: Dopaminergic modulation of aldosterone secretion in the rhesus monkey: evidence that dopamine affects the late pathway of aldosterone biosynthesis by inhibiting the conversion of corticosterone to 18-hydroxycorticosterone. Endocrinology 1982 Apr;110(4):1173-7

Specian RD, Neutra MR: Regulation of intestinal goblet cell secretion. I. Role of parasympathetic stimulation. Am J Physiol 1982 Apr; 242(4):G370-9

Spedding M, Berg C: Stereospecific blockade of alpha 2-adrenoceptors

AUTHOR SECTION

by (+)–butaclamol: implications for the characterization of dopamine receptors. J Pharm Pharmacol 1982 Jan;34(1):56–8

Speight A, Fink G: Comparison of steroid and LH–RH effects on the responsiveness of hemipituitary glands and dispersed pituitary cells. Mol Cell Endocrinol 1981 Dec;24(3):267–81

Sperk G: Simultaneous determination of serotonin, 5–hydroxindoleacetic acid, 3,4–dihydroxyphenylacetic acid and homovanillic acid by high performance liquid chromatography with electrochemical detection. J Neurochem 1982 Mar;38(3):840–3

Spiegel D, Detrick D, Frischholz E: Hypnotizability and psychopathology. Am J Psychiatry 1982 Apr;139(4):431–7

Springer DL, Krivak BM, Broderick DJ, et al: Metabolic fate of hydrazine. J Toxicol Environ Health 1981 Jul–Aug;8(1–2):21–9

Spyraki C, Fibiger HC: Behavioural evidence for supersensitivity of postsynaptic dopamine receptors in the mesolimbic system after chronic administration of desipramine. Eur J Pharmacol 1981 Sep 11; 74(2–3):195–206

Sridaran R, Rodriguez–Sierra JF, Blake CA: Effects of hypothalamic arcuate nucleus lesions on pulsatile luteinizing hormone concentration in ovariectomized rats. Proc Soc Exp Biol Med 1981 Oct;168(1):38–44

Sroczyński J, Węgiel A, Wydra A: Wydalanie noradrenaliny w moczu u osób narażonych na drgania mechaniczne i halas przemyslowy. Pol Tyg Lek 1981 Sep 7;36(36):1387–8 (Eng. Abstr.) (Pol)

Stafford JE, Jackson LS, Forrest TJ, et al: Haloperidol pharmacokinetics: a preliminary study in rhesus monkeys using a new radioimmunoassay procedure. J Pharmacol Methods 1981 Dec;6(4):261–79

Stancer HC, Persad E: Treatment of intractable rapid–cycling manic–depressive disorder with levothyroxine. Clinical observations. Arch Gen Psychiatry 1982 Mar;39(3):311–2

Standaert FG: Release of transmitter at the neuromuscular junction. Br J Anaesth 1982 Feb;54(2):131–45 (82 ref.)

Stanton TL, Winokur A, Beckman AL: Seasonal variation in thyrotropin–releasing hormone (TRH) content of different brain regions and the pineal in the mammalian hibernator, Citellus lateralis. Regul Pept 1982 Feb;3(2):135–44

Starke K, Hedler L, Steppeler A: Metabolism of endogenous and exogenous noradrenaline in guinea–pig atria. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov;317(3):193–8

Starr M, Kilpatrick I: Comparison of content with synthesis, uptake and breakdown of GABA in substantia nigra of unoperated, hemitransected and kainate–treated rats. Life Sci 1981 Nov 30;29(22):2281–7

Stavchansky S, Loper A: Nitrogen–phosphorous detection of phencyclidine in blood serum. J Pharm Sci [illegible] Feb;71(2):194–6

Stefanova D: Kolksazepin—nevro–farmakologic[illegible] prouchvaniia. Eksp Med Morfol 1981;20(4):208–13 (Eng. Abstr.) (Bul)

Stein K, Portig J, Noack G: Neuropharmacological effects of isomers of hexachlorocyclohexane—3. An account of the convulsant activity of the gamma–isomer in rats. Neuropharmacology 1981 Nov; 20(11):1017–24

Steinacker A, Zuazaga DC: Changes in neuromuscular junction endplate current time constants produced by sulfhydryl reagents. Proc Natl Acad Sci USA 1981 Dec;78(12):7806–9

Steinhoff J, Migalla H, Buhr N, et al: Zur Pharmakokinetik von Propranolol beim gesunden Menschen. Pharmazie 1981 Nov; 36(11):785–6 (Ger)

Steinsapir J, Rojas AM, Alarcón O, et al: Effect of insulin and epinephrine on some early oestrogenic responses in the rat uterus. Acta Endocrinol (Copenh) 1982 Feb;99(2):263–71

Stengaard–Pedersen K, Larsson LI: Comparative immunocytochemical localization of putative opioid ligands in the central nervous system. Histochemistry 1981;73(1):89–114 (50 ref.)

Stephenson RK, Sole MJ, Baines AD: Neural and extraneural catecholamine production by rat kidneys. Am J Physiol 1982 Mar; 242(3):F261–6

Steranka LR: Stereospecific long–term effects of amphetamine on striatal dopamine neurons in rats. Eur J Pharmacol 1981 Dec 17;76(4):443–6

Steranka LR: Long–term decreases in striatal dopamine, 3,4–dihydroxyphenylacetic acid, and homovanillic acid after a single injection of amphetamine in iprindole–treated rats: time course and time–dependent interactions with amfonelic acid. Brain Res 1982 Feb 18;234(1):123–36

Sternberg DE, Charney DS, Heninger GR, et al: Impaired presynaptic regulation of norepinephrine in schizophrenia. Effects of clonidine in schizophrenic patients and normal controls. Arch Gen Psychiatry 1982 Mar;39(3):285–9

Stier CT Jr, Cowden EA, Allison ME: Effects of bromocriptine on single nephron and whole–kidney function in rats. J Pharmacol Exp Ther 1982 Feb;220(2):366–70

Stine SM, Yang HY, Costa E: Evidence for ascending and descending intraspinal as well as primary sensory somatostatin projections in the rat spinal cord. J Neurochem 1982 Apr;38(4):1144–50

Stjärne L: Ionic mechanisms of alpha–autoinhibition of [3H]noradrenaline secretion in guinea–pig vas deferens: possible role of extracellular sodium. Neuroscience 1981;6(12):2759–71

Stjernschantz J, Gregerson D, Bausher L, et al: Enzyme–linked immunosorbent assay of substance P: a study in the eye. J Neurochem 1982 May;38(5):1323–8

Stone DN, Dujardin JP: The effects of phenoxybenzamine on the aortic pressure–diameter relationship in dogs. Experientia 1982 Feb 15; 38(2):257–8

Stone WE, Javid MJ: Muscimol as an antagonist of chemical convulsants. Arch Int Pharmacodyn Ther 1981 Oct;253(2):294–300

Straughan J: Erythromycin–carbamazepine interaction? [letter] S Afr Med J 1982 Mar 20;61(12):420–1

Stripling JS: Origin of cocaine– and lidocaine–induced spindle activity within the olfactory forebrain of the rat. Electroencephalogr Clin Neurophysiol 1982 Feb;53(2):208–19

Stumbo D, Good MJ, Good BJ: Diagnostic profile of a family practice clinic: patients with psychosocial diagnoses. J Fam Pract 1982 Feb; 14(2):281–5

Su TP: Psychotomimetic opioid binding: specific binding of [3H]SKF–10047 to etorphine–inaccessible sites in guinea–pig brain. Eur J Pharmacol 1981 Oct 15;75(1):81–2

Subbaraj R: Effect of lithium chloride on the circadian rhythm in the flight activity of the microchiropteran bat, Taphozous melanopogon. Z Naturforsch [C] 1981 Nov–Dec;36(11–12):1068–71

Sudo K, Tachizawa H, Sano M: Disposition of timiperone, 4'–fluoro–4–[4–(2–thioxo–1–benzimidazolinyl)piperidino]butyrophenon a neuroleptic, in the rat on repeated oral dosage. Xenobiotica 1981 Oct; 11(10):683–91

Sugden MC, Ashcroft SJ: Cyclic nucleotide phosphodiesterase of rat pancreatic islets. Effects of Ca2+, calmodulin and trifluoperazine. Biochem J 1981 Aug 1;197(2):459–64

Sullivan SN: Inhibition of salivary and lacrimal secretion by an enkephalin analogue [letter] Am J Psychiatry 1982 Mar;139(3):385–6

Sum CY, Kasper CB: Mixed–function amine oxidase of the rat hepatocyte nuclear envelope. Demonstration and effects of phenobarbital and 3–methylcholanthrene. Biochem Pharmacol 1982 Jan 1;31(1):69–73

Summers C, de Vries JB, Horn AS: Behavioural and neurochemical studies on apomorphine–induced hypomotility in mice. Neuropharmacology 1981 Dec;20(12A):1203–8

Sundaram K, Connell KG, Bardin CW, et al: Inhibition of pituitary–testicular function with [D–Trp6] luteinizing hormone–releasing hormone in rhesus monkeys. Endocrinology 1982 Apr;110(4):1308–14

Sutton CA, Martin TF: Thyrotropin–releasing hormone (TRH) selectively and rapidly stimulates phosphatidylinositol turnover in GH pituitary cells: a possible second step of TRH action. Endocrinology 1982 Apr; 110(4):1273–80

Suva J, Svejnohová D, Janousek I: Study of lithium levels in the serum and sex organs of female rats. Act Nerv Super (Praha) 1981;23(4):280–1

Suzuki H, Itoh T, Kuriyama H: Effects of diltiazem on smooth muscles and neuromuscular junction in the mesenteric artery. Am J Physiol 1982 Mar;242(3):H325–36

Suzuki T, Yoshii T, Yanaura S, et al: Effect of parachlorophenylalanine on the incidence of abnormal behaviors observed following diazepam withdrawal. Prog Neuropsychopharmacol 1981;5(4):415–7

Svendsen K, Christensen PG: Duration of REM sleep latency as predictor of effect of antidepressant therapy. A preliminary report. Acta Psychiatr Scand 1981 Sep;64(3):238–43

Svensson L, Ahlenius S: Functional importance of nucleus accumbens noradrenaline in the rat. Acta Pharmacol Toxicol (Copenh) 1982 Jan; 50(1):22–4

Svestka J, Bártová D, Cesková E, et al: Depotní neuroleptika v psychiatrické praxi. Cesk Psychiatr 1981 Jun;77(3):187–97 (Eng. Abstr.) (Cze)

Svet–Moldavsky I, Svet–Moldavsky G, Zinzar S, et al: The extracerebral dopamine antagonist domperidone block the suppressive effect of bromocriptine on prolactin and TSH secretion in man. Biomedicine 1981 Oct;35(5):142–4

Swann AC, Grant SJ, Maas JW: Brain (Na+, K+)–ATPase and noradrenergic activity: effects of hyperinnervation and denervation on high–affinity ouabain binding. J Neurochem 1982 Mar;38(3):836–9

Swenson RP, Williams CH Jr, Massey V: Chemical modification of D–amino acid oxidase. Amino acid sequence of the tryptic peptides containing tyrosine and lysine residues modified by fluorodinitrobenzene. J Biol Chem 1982 Feb 25;257(4):1937–44

Symons AM, Arendt J: Lack of effect of melatonin on the pituitary response to LH–RH in the ewe. J Reprod Fertil 1982 Jan;64(1):103–6

Sypniewska M, Przegaliński E: The effect of pyrazidol on the central serotonergic system. Pol J Pharmacol Pharm 1981;33(3):313–9

Szabó G, Endröczi E: LH–RH induced changes in cAMP content of the anterior pituitary gland in male and female rats in vivo and in vitro. Acta Physiol Acad Sci Hung 1981;57(4):343–53

Szabo GK, Browne TR: Improved isocratic liquid–chromatographic simultaneous measurement of phenytoin, phenobarbital, primidone, carbamazepine, ethosuximide, and N–desmethylmethsuximide in serum. Clin Chem 1982 Jan;28(1):100–4

Szabolcs I, Szilágyi G, Góth M, et al: Plasma triiodothyronine response to thyrotropin releasing hormone, thyrotropin and propranolol in old age. Exp Gerontol 1981;16(4):309–16

Szafarczyk A, Ixart G, Alonso G, et al: Effects de la destruction des noyaux suprachiasmatiques sur les rythmes circadiens de l'ACTH, de la corticostérone et de l'activité générale chez des rattes soumises à un environnement apériodique. C R Soc Biol (Paris) 1981;175(6):801-10 (Eng. Abstr.) (Fre)

Szajner-Milart I, Rubaj B, Zajęczkowska M: Role of some biogenic amines in the pathomechanism of glomerulonephritis. I. Histological examinations of kidneys in acute and chronic serum sickness in rabbits. Acta Physiol Pol 1981;32(4):349-62

Szara SI: Benzodiazepines: a review of research results, 1980. Introduction. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):1-3

Szebeni J: The Ca2+-sensitive K+ transport in inside-out red cell membrane vesicles. Acta Biochim Biophys Acad Sci Hung 1981; 16(1-2):77-82

Székelyhidi L, Hornyák I: A tofizopam fotolumineszcencián alapuló meghatározási lehetöségeinek vizsgálata. Acta Pharm Hung 1981 Nov; 51(6):270-4 (Eng. Abstr.) (Hun)

Szewczyk H: Medizinische Psychologie - traditionsbeladenes Gebiet oder Ausdruck einer neuen Entwicklungs-richtung in der Medizin? Psychiatr Neurol Med Psychol (Leipz) 1981 Oct;33(10):589-96 (Eng. Abstr.) (Ger)

Sziegoleit W, Schmidt C, Lohse M, et al: Wirkung von Allopurinol auf die durch Noradrenalin oder adrenokortikotropes Hormon stimulierte Fettsäurefreisetzung aus isoliertem Ratten- und Kaninchenfettgewebe. Acta Biol Med Ger 1981;40(6):881-3 (Ger)

Szmuszkovicz J, Von Voigtlander PF, Kane MP: A new nontricyclic antidepressant agent. Synthesis and activity of N-[trans-2-(dimethylamino)cyclopentyl]-N-(3,4-dichlorophenyl)propa and related compounds. J Med Chem 1981 Oct;24(10):1230-6

Szyszko E, Wejman W: Gas chromatographic determination of noxyptyline in substance, tablets and in biological material. J Chromatogr 1981 Dec 4;219(2):291-6

T

Taché Y, Collu R: CNS mediated inhibition of gastric secretion by bombesin: independence from interaction with brain catecholaminergic, and serotoninergic pathways and pituitary hormones. Regul Pept 1982 Jan;3(1):51-9

Tachi N, Tomogane H, Yokoyama A: Diurnal patterns of food intake and plasma corticosterone levels in lactating rats. Physiol Behav 1981 Sep; 27(3):481-6

Tachibana S, Araki K, Ohya S, et al: Isolation and structure of dynorphin, an opioid peptide, from porcine duodenum. Nature 1982 Jan 28; 295(5847):339-40

Takeda M, Takeda F, Matsumoto F, et al: Divalent cation, ATP-dependent [3H]leu-enkephalin uptake by synaptic vesicle fraction isolated from bovine caudate nucleus. Brain Res 1982 Feb 25; 234(2):319-26

Takemura S, Miki Y, Hoshida M, et al: Synthesis and selective activity of cholinergic agents with rigid skeletons. II. Chem Pharm Bull (Tokyo) 1981 Oct;29(10):3019-25

Takemura S, Miki Y, Uono M, et al: Synthesis and selective activity of cholinergic agents with rigid skeletons. III. Chem Pharm Bull (Tokyo) 1981 Oct;29(10):3026-32

Tallman JF: Benzodizepines: biochemistry of function. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):4-11

Tamásy V, Korányi L, Phelps CP: The role of dopaminergic and serotonergic mechanisms in the development of swimming ability of young rats. Dev Neurosci 1981;4(5):389-400

Tan CT, Ong TC, Chee KT: The use of fluphenazine decanoate (Modecate)depot therapy in outpatient schizophrenics-a retrospective study. Singapore Med J 1981 Aug;22(4):214-8

Tan CT, Chan SW, Hsia JC: Membrane immunoassay: a spin membrane immunoassay for thyroxine. Methods Enzymol 1981;74 Pt C:152-61

Tanabe T, Tabata K: [Determination of urinary catecholamine by high performance liquid chromatography (author's transl)] Rinsho Byori 1981 Sep;29(9):874-8 (Jpn)

Tanaka I, Nakai Y, Nakao K, et al: Presence of immunoreactive gamma-melanocyte-stimulating hormone, adrenocorticotropin, and beta-endorphin in human gastric antral mucosa. J Clin Endocrinol Metab 1982 Feb;54(2):39[illegible]-6

Taniguchi H, Murakami K, Tsutou A, et al: A role of endogenous somatostatin and glucagon in insulin release from pancreatic islets. Kobe J Med Sci 1981 Dec;27(6):213-24

Taniguchi K, Yamashita M, Ishida K, et al: [Effects of intrathecal beta-endorphin and morphine on post-operative pain (author's transl)] Masui 1981 Oct;30(10):1105-11 (Eng. Abstr.) (Jpn)

Tank AW, Weiner H, Thurman JA: Enzymology and subcellular localization of aldehyde oxidation in rat liver. Oxidation of 3,4-dihydroxyphenylacetaldehyde derived from dopamine to 3,4-dihydroxyphenylacetic acid. Biochem Pharmacol 1981 Dec 15; 30(24):3265-75

Tarr JB: Measurement of urinary tryptophan metabolites by reverse-phase high-pressure liquid chromatography. Biochem Med 1981 Dec; 26(3):330-8

Tassin JP, Simon H, Hervé D, et al: Non-dopaminergic fibres may regulate dopamine-sensitive adenylate cyclase in the prefrontal cortex and nucleus accumbens. Nature 1982 Feb 25;295(5851):696-8

Taylor CA Jr, Smith HE, Goldberg MR, et al: (alpha S)-erythro-alpha-methylepinephrine: preparation and stereoselective binding to adrenergic receptors in rat forebrain. J Med Chem 1981 Oct; 24(10):1261-3

Taylor EA, Harrison J, Turner P: Propranolol in experimentally induced stress. Br J Psychiatry 1981 Dec;139:545-9

Tayo FM: Prejunctional inhibitory dopamine receptors in the rat isolated vas deferens. Arch Int Pharmacodyn Ther 1981 Nov;254(1):28-37

Tenner TE Jr, Mukherjee A, Hester RK: Reserpine-induced supersensitivity and the proliferation of cardiac beta-adrenoceptors. Eur J Pharmacol 1982 Jan 8;77(1):51-5

Terry LC, Crowley WR, Johnson MD: Regulation of episodic growth hormone secretion by the central epinephrine system. Studies in the chronically cannulated rat. J Clin Invest 1982 Jan;69(1):104-12

Tessitore V, Buscemi M, Gerbino A, et al: Distribution and activity of adrenergic and cholinergic innervation of the extrahepatic biliary system in the rabbit. Cell Mol Biol 1981;27(5):527-37

Tessler A, Himes BT, Artymyshyn R, et al: Spinal neurons mediate return of substance P following deafferentation of cat spinal cord. Brain Res 1981 Dec 28;230(1-2):263-81

Thams P, Geisler A: On the mechanism of inhibition of rat fat cell adenylate cyclase by lithium. Acta Pharmacol Toxicol (Copenh) 1981 May;48(5):397-403

Thibault MC, Vallières J, LeBlanc J: Norepinephrine mobilization of free fatty acids in endurance trained rats. Eur J Applied Physiol 1981; 47(4):313-22

Thiede HM, Kehr W: Catecholamine metabolism in rat brain. The role of neutral and acidic catechol metabolites. Naunyn Schmiedebergs Arch Pharmacol 1981 Dec;318(1):29-35

Thiessen DD, Upchurch M: Haloperidol and clonidine increase, and apomorphine decreases ultrasonic vocalizations by gerbils. Psychopharmacology (Berlin) 1981;75(3):287-90

Thilmann J: Vergleichende Untersuchung zum Tranquilizereffekt von Fluspirilen und Bromazepam. Med Welt 1981 Dec 25;32(51-52):1959-61 (Ger)

Tholose A: Réflexions sur les conditions de la prescription prolongée des neuroleptiques à travers quelques cas cliniques. Ann Med Psychol (Paris) 1981;139(8):894-9 (Fre)

Thomas EM, Templeton D: Sites of noradrenergic innervation of the jejunal villus. Gen Pharmacol 1982;13(1):67-9

Thompson DM, Moerschbaecher JM: Phencyclidine in combination with pentobarbital: supra-additive effects on complex operant behavior in patas monkeys. Pharmacol Biochem Behav 1982 Jan;16(1):159-65

Thompson EM, Brodie HK: The psychodynamics of drug therapy. Curr Psychiatr Ther 1981;20:239-51

Thomson R: Side effects and placebo amplification. Br J Psychiatry 1982 Jan;140:64-8

Thornhill DP: The biological disposition and kinetics of lithium. Biopharm Drug Dispos 1981 Oct-Dec;2(4):305-22 (121 ref.)

Thornhill DP, Field SP: Distribution of lithium elimination rates in a selected population of psychiatric patients. Eur J Clin Pharmacol 1982; 21(4):351-4

Ticku MK, Davis WC: Molecular interactions of etazolate with benzodiazepine and picrotoxinin binding sites. J Neurochem 1982 Apr; 38(4):1180-2

Tidball JG: An ultrastructural and cytochemical analysis of the cellular basis for tyrosine-derived collagen crosslinks in Leptogorgia virgulata (Cnidaria: Gorgonacea). Cell Tissue Res 1982;222(3):635-45

Tijssen AM, de Koning J, van Rees GP: Release of LH in vitro from anterior pituitary glands of ovariectomized rats by LRH or elevated potassium concentration after pre-treatment with oestradiol benzoate in vivo. Acta Endocrinol (Copenh) 1982 Feb;99(2):206-10

Tikal K: Operant behaviour of rats after aminophylline and DH-ergotoxin in interaction with catecholamines. Act Nerv Super (Praha) 1981; 23(4):319-20

Tilakaratne N, Hill WG, Land RB: Direct and correlated responses to selection for plasma thyroxine levels in mice. Genet Res 1981 Oct; 38(2):157-69

Tilders FJ, Berkenbosch F, Smelik PG: Adrenergic mechanisms involved in the control of pituitary-adrenal activity in the rat: a beta-adrenergic stimulatory mechanism. Endocrinology 1982 Jan;110(1):114-20

Timsit-Berthier M: A propos de l'interprétation de la variation contingente négative en psychiatrie. Rev Electroencephalogr Neurophysiol Clin 1981 Nov;11(2):236-44 (Eng. Abstr.) (Fre)

Tintoré I: Evaluación cuantitativa automática de la actividad motora espontánea. Validación del método. Arch Farmacol Toxicol 1981 Apr; 7(1):79-82 (Spa)

Titeler M: Irreversible blockade of [3H]spiperone- but not [3H]dopamine-labeled dopamine receptors with phenoxybenzamine. Biochem Pharmacol 1981 Nov 15;30(22):3031-7

Tizabi Y, O'Donohue TL, Jacobowitz DM: Variations in plasma and adrenal catecholamines and related enzymes in isolated-aggressive mice. Commun Psychopharmacol 1980;4(5):433-9

AUTHOR SECTION

Tkachuk VN, Zaezhalkin VV, Ledovskaia SM: Ekskretsiia katekholaminov u bol'nykh khronicheskim pielonefritom. Sov Med 1982;(2):22-5 (Eng. Abstr.) **(Rus)**

Toda N, Konishi M, Okunishi H, et al: Influence of disopyramide, compared with procainamide and quinidine, on isolated dog arteries in response to transmural stimulation and norepinephrine. J Cardiovasc Pharmacol 1981 Nov-Dec;3(6):1332-41

Todorov S, Petkov V: On the interaction of histamine with the tryptaminergic smooth-muscle receptors. Acta Physiol Pharmacol Bulg 1980;6(4):47-54

Tokovic B, Sek S, Cusic S, et al: Odreadivanje aktivnosti holinesteraze u serumu i plazmi. Vojnosanit Pregl 1981 Sep-Oct;38(5):353-6 **(Scr)**

Tombaugh TN, Szostak C, Voorneveld P, et al: Failure to obtain functional equivalence between dopamine receptor blockade and extinction: evidence supporting a sensory-motor conditioning hypothesis. Pharmacol Biochem Behav 1982 Jan;16(1):67-72

Tondlova H, Kral J, Bastecky J, et al: Anxiety in climax and its pharmacological treatment. Agressologie 1981 Nov;22(E):7-8

Tondo L, Laddomada P, Serra G, et al: Rapid cyclers and antidepressants. Int Pharmacopsychiatry 1981;16(2):119-23

Tonoue T: Stimulation by thyrotropin-releasing hormone of vagal outflow to the thyroid gland. Regul Pept 1982 Jan;3(1):29-39

Tormey WP, Buckley MP, Taaffe W, et al: Prolactin responsiveness to repeated decremental doses of sulpiride. Horm Metab Res 1981 Aug;13(8):454-5

Tornqvist K, Mandahl A, Leander S, et al: Substance P-immunoreactive nerve fibres in the anterior segment of the rabbit eye. Distribution and possible physiological significance. Cell Tissue Res 1982;222(3):467-77

Toru M, Shibuya H, Nishikawa T, et al: [Biochemical analysis of dopaminergic nerve terminals of post-mortem brain from schizophrenic patients (author's transl)] Seishin Shinkeigaku Zasshi 1981;83(7):430-47 (Eng. Abstr.) **(Jpn)**

Trachtenberg MC, Packey DJ, Sweeney T: In vivo functioning of the Na+, K+-activated ATPase. Curr Top Cell Regul 1981;19:159-217 (269 ref.)

Tran MA, Dang TL, Berlan M: Effects of catecholamines on free fatty acid release from bone marrow adipose tissue. J Lipid Res 1981 Nov;22(8):1271-6

Treneer CM, Bernstein IL: Learned aversions in rats fed a tryptophan-free diet. Physiol Behav 1981 Nov;27(5):757-60

Tret'iakov AV: Antiéstrogeny i antiandrogeny na osnove atsilgidrazinov. Dokl Akad Nauk SSSR 1981;261(1):247-51 **(Rus)**

Trevisan M, Cooper R, Ostrow D, et al: Dietary sodium, erythrocyte sodium concentration, sodium-stimulated lithium efflux and blood pressure. Clin Sci [Suppl] 1981 Dec;61(7):29s-32s

Triebig G: Valid evaluation of plasma catecholamines [letter] Thorax 1981 Nov;36(11):880

Tsao SC, Iga T, Sugiyama Y, et al: Effect of chlorpromazine on isolated rat hepatocytes. Biochem Pharmacol 1982 Feb 15;31(4):491-7

Tse CK, Dolly JO, Hambleton P, et al: Preparation and characterisation of homogeneous neurotoxin type A from Clostridium botulinum. Its inhibitory action on neuronal release of acetylcholine in the absence and presence of beta-bungarotoxin. Eur J Biochem 1982 Mar 1;122(3):493-500

Tune LE, McHugh PR, Coyle JT: Drug management in chronic schizophrenia. Johns Hopkins Med J 1982 Jan;150(1):45-8

Türck M, Yeh H, Woodward DJ, et al: Beta-adrenergic receptors in rat cerebellum after neonatal X-irradiation: effect of prolonged imipramine and lithium treatment. Neurosci Lett 1981 Dec 23;27(3):357-62

Tureck RW, Mastroianni L Jr, Blasco L, et al: Inhibition of human granulosa cell progesterone secretion by a gonadotropin-releasing hormone agonist. J Clin Endocrinol Metab 1982 May;54(5):1078-80

Turkall RM, Denison RC, Tsan MF: Degradation and oxidation of methionine enkephalin by human neutrophils. J Lab Clin Med 1982 Mar;99(3):418-27

Turkanis SA, Karler R: Excitatory and depressant effects of delta 9-tetrahydrocannabinol and cannabidiol on cortical evoked responses in the conscious rat. Psychopharmacology (Berlin) 1981;75(3):294-8

Turkelson CM, Arimura A, Culler MD, et al: In vivo and in vitro release of ACTH by synthetic CRF. Peptides (Fayetteville) 1981 Winter;2(4):425-9

Turski L, Czuczwar SJ, Turski W, et al: Effect of antidepressant drugs on carbachol chloride-induced wet dog shake behaviour in rats. Neuropharmacology 1981 Dec;20(12A):1193-6

Tybring G, von Bahr C, Bertilsson L, et al: Metabolism of carbamazepine and its epoxide metabolite in human and rat liver in vitro. Drug Metab Dispos 1981 Nov-Dec;9(6):561-4

Tyrer P: Major common symptoms in psychiatry. Anxiety. Br J Hosp Med 1982 Feb;27(2):109-13

U

Al-Ubaidy SS, Al-Janabi NY, Al-Tai SA: Effect of phenytoin on mitotic activity of gingival tissue and cultured fibroblasts. J Periodontol 1981 Dec;52(12):747-9

Uddman R, Edvinsson L, Owman C, et al: Perivascular substance P: occurrence and distribution in mammalian pial vessels. J Cereb Blood Flow Metab 1981;1(2):227-32

Ueda H, Tatsumi K, Shiomi H, et al: Analgesic dipeptide, kyotorphin (Tyr-Arg), is highly concentrated in the synaptosomal fraction of the rat brain. Brain Res 1982 Jan 7;231(1):222-4

Ueda N, Muramatsu I, Sakakibara Y, et al: Noncholinergic, nonadrenergic contraction and substance P in rabbit iris sphincter muscle. Jpn J Pharmacol 1981 Dec;31(6):1071-9

Ueda S, Mutoh S, Yano S, et al: Effects of adrenergic drugs on miniature contractions of isolated dog urinary bladder. Eur Urol 1982 Jan-Feb;8(1):37-41

Uhlenhuth EH: Specific anxiety syndromes: current therapeutic options. J Clin Psychiatry 1981 Nov;42(11 Pt 2):27-34

Ulloa ER, Boado RJ, Beretervide RE, et al: Effectos de la ciproheptadina sobre la secreción y contenido pituitario de la tirotrofina en la rata. Medicina (B Aires) 1981;41(3):333-6 (Eng. Abstr.) **(Spa)**

Ulrich K, Auer LM, Kuschinsky W: Cat pial venoconstriction by topical microapplication of norepinephrine. J Cereb Blood Flow Metab 1982;2(1):109-11

Unger RM: A program for late twentieth-century psychiatry. Am J Psychiatry 1982 Feb;139(2):155-64

Unsworth CD, Hughes J, Morely JS: O-sulphated Leu-enkephalin in brain. Nature 1982 Feb 11;295(5849):519-22

Uphouse L, McLean S, Russell M: Stability of CNS bindings sites under various conditions. Neurotoxicology (Park Forest Il) 1981 Nov;2(3):533-40

Uratani Y: Dansyl chloride labeling of Pseudomonas aeruginosa treated with pyocin R1: change in permeability of the cell envelope. J Bacteriol 1982 Feb;149(2):523-8

Urban J, Dąbrowski M: Mechanizm wpływu dopaminy na kurczliwość isolowanych naczyń łożyska ludzkiego. Ginekol Pol 1981;52(9):757-62 (Eng. Abstr.) **(Pol)**

Usami H, Aida J, Nagatsuka S, et al: [Measurement of free thyroxine in serum using 'SPAC-T4' RIA kit (author's transl)] Horumon To Rinsho 1981 Sep;29(9):1167-72 **(Jpn)**

Ushakov GK, Maslova AF, Kostiunina ZG: Kliniko-biokhimicheskie paralleli pri pogranichnykh nervno-psikhicheskikh rasstroĭstvakh. Zh Nevropatol Psikhiatr 1981;81(11):1663-6 (Eng. Abstr.) **(Rus)**

V

Vadasz C, Baker H, Joh TH, et al: The inheritance and genetic correlation of tyrosine hydroxylase activities in the substantia nigra and corpus striatum in the C x B recombinant inbred mouse strains. Brain Res 1982 Feb 18;234(1):1-9

Val'dman AV: Novye dannye neĭrokhimicheskikh mekhanizmakh deĭstviia antidepressantov. Vestn Akad Med Nauk SSSR 1982;(1):3-8 (Eng. Abstr.) **(Rus)**

Valtorta S, Hahn L, Johnson HD: Effect of high ambient temperature (35 degrees), and feed intake on plasma T4 levels in sheep. Proc Soc Exp Biol Med 1982 Feb;169(2):260-5

Valzelli L, Bernasconi S, Dalessandro M: Effect of tryptophan administration on spontaneous and P-CPA-induced muricidal aggression in laboratory rats. Pharmacol Res Commun 1981 Oct;13(9):891-7

Vamvakides A: Evaluation de la vitesse de synthèse de la dopamine cérébrale de rat. Agressologie 1981;22(3):117-28 (Eng. Abstr.) **(Fre)**

van Boxtel CJ, Rane A, Brown RD, et al: The formation of carbamazepine epoxide by rat liver microsomes: an investigation of the biphasic kinetic profile. Life Sci 1981 Dec 21;29(25):2575-84

Van Buskirk R, Dowling JE: Isolated horizontal cells from carp retina demonstrate dopamine-dependent accumulation of cyclic AMP. Proc Natl Acad Sci USA 1981 Dec;78(12):7825-9

Van Dam LJ, Rolland R: Lactation-inhibiting and prolactin-lowering effect of lisuride and bromocriptine: a comparative study. Eur J Obstet Gynecol Reprod Biol 1981 Nov;12(5):323-30

Vandel B, Vandel S, Jounet JM, et al: Clomipramine et desméthylclomipramine. Relation entre les concentrations plasmatiques et l'effec clinique. Encephale 1981;7(5):601-8 (Eng. Abstr.) **(Fre)**

van den Broek JM, Teunissen MW, Breimer DD: Induction of hexobarbital and antipyrine metabolism by rifampicin treatment in the pig. Drug Metab Dispos 1981 Nov-Dec;9(6):541-4

van Dijk J, Hartog J, Hillen FC: Non-tricyclic antidepressants. Prog Med Chem 1978;15:261-320 (351 ref.)

van Dijken J, von Knorring AL, von Knorring L, et al: Antidepressiva läkemedel kan ge tandskador hos barn och vuxna. Lakartidningen 1981 Nov 25;78(48):4366-8 **(Swe)**

van Kammen DP, Sternberg DE, Hare TA, et al: CSF levels of gamma-aminobutyric acid in schizophrenia. Low values in recently ill patients. Arch Gen Psychiatry 1982 Jan;39(1):91-7

Van Nueten JM, Janssen PA, De Ridder A, et al: Interaction between 5-hydroxytryptamine and other vasoconstrictor substances in the isolated femoral artery of the rabbit; effect of ketanserin (R 41 468). Eur J Pharmacol 1982 Feb 5;77(4):281-7

van Praag HM, Verhoeven WM, van Ree JM, et al: The treatment of

AUTHOR SECTION

schizophrenic psychoses with gamma-type endorphins. Biol Psychiatry 1982 Jan;17(1):83-98

Van Putten T, May PR, Jenden DJ: Does a plasma level of chlorpromazine help? Psychol Med 1981 Nov;11(4):729-34

van Ree JM, De Wied D: Endorphins in schizophrenia. Neuropharmacology 1981 Dec;20(12B):1271-7 (93 ref.)

Van Ree JM, Verboeven WM, Van Praag HM, et al: Neuroleptic-like and antipsychotic effects of gamma-type endorphins. Mod Probl Pharmacopsychiatry 1981;17:266-78

Vargaftig BB, Lefort J: Enhancement by prostacyclin of the contractility of the guinea-pig airways smooth muscle. Eur J Pharmacol 1981 Sep 11;74(2-3):141-8

Vargas Fernández L: Componente psicológico del stress en seres humanos. Parte I. Rev Med Chil 1981 May;109(5):441-51 (Eng. Abstr.) **(Spa)**

Varnam MA: Psychotropic prescribing. What am I doing? J R Coll Gen Pract 1981 Aug;31(229):480-3

Vasil'eva VF, Gusev GP, Krestinskaia TV: Vliianie litiia na ékskretornuiu funktsiiu i Na, K--ATFaznuiu aktivnost' v pochkakh krys. Fiziol Zh SSSR 1981 Dec;67(12):1866-72 (Eng. Abstr.) **(Rus)**

Vaught JL: A characterization of dynorphin-(1-13) on the guinea pig ileal longitudinal muscle. Eur J Pharmacol 1981 Dec 17;76(4):453-6

Vellucci SV, Webster RA: Modification of diazepam's antileptazol activity by endogenous tryptophan-like compounds. Eur J Pharmacol 1981 Dec 3;76(2-3):255-9

Vencovský E: Uvod do kliniky psychických poruch v involuci. Cesk Psychiatr 1981;77(4):232-6 (Eng. Abstr.) **(Cze)**

Verbeeck RK, Tjandramaga TB, De Schepper PJ, et al: Impaired elimination of lorazepam following subchronic administration in two patients with renal failure [letter] Br J Clin Pharmacol 1981 Nov; 12(5):749-51

Verbeeck RK, Branch RA, Wilkinson GR: Drug metabolites in renal failure: pharmacokinetic and clinical implications. Clin Pharmacokinet 1981 Sep-Oct;6(5):329-45 (139 ref.)

Verbeuren TJ, Vanhoutte PM: Deamination of released 3H-noradrenaline in the canine saphenous vein. Naunyn Schmiedebergs Arch Pharmacol 1982 Feb;318(3):148-57

Verbruggen LA, Salomon DS, Greene RM: Inhibition of collagen and sulfated glycosaminoglycan synthesis in neonatal mouse dermal fibroblasts by corticosterone. Biochem Pharmacol 1981 Dec 15; 30(24):3285-9

Verhoef J, Wiegant VM, De Wied D: Regional distribution of alpha- and gamma-type endorphins in rat brain. Brain Res 1982 Jan 14; 231(2):454-60

Verhoeven WM, Westenberg HG, Gerritsen TW, et al: (Des-tyrosine1)-gamma-endorphin in schizophrenia: clinical, biochemical, and hormonal aspects. Psychiatry Res 1981 Dec; 5(3):293-309

Verimer T, Long JP, Flynn JR, et al: Subsensitivity of the presynaptic dopamine receptors in cat heart after the termination of chronic haloperidol treatment. Arch Int Pharmacodyn Ther 1981 Oct; 253(2):233-40

Verkleij AJ, De Maagd R, Leunissen-Bijvelt J, et al: Divalent cations and chlorpromazine can induce non-bilayer structures in phosphatidic acid-containing model membranes. Biochim Biophys Acta 1982 Jan 22; 684(2):255-62

Verma DS, Spitzer G, Gutterman JU, et al: Human leukocyte interferon-mediated granulopoietic differentiation arrest and its abrogation by lithium carbonate. Am J Hematol 1982 Feb;12(1):39-46

Vermes I, Berkenbosch F, Tilders FJ, et al: Hypothalamic deafferentation in the rat appears to discriminate between the anterior lobe and intermediate lobe response to stress. Neurosci Lett 1981 Nov 18; 27(1):89-93

Vernon AW: Classification of psychotherapeutic drugs. J Psychosoc Nur Ment Health Serv 1981 Nov;19(11):15-7

Versteeg DH, Kovács GL, Bohus B, et al: Effect of des-Tyr1-gamma-endorphin and des-Tyr1-alpha-endorphin on alpha-MPT-induced catecholamine disappearance in rat brain nuclei: a dose--response study. Brain Res 1982 Jan 14;231(2):343-51

Veselková A, Brodan V, Poslušný Z: Vliv intenzívního tréninku na močové vylučování katecholaminu a 17-OH kortikoidu při aerobním zatížení na ergometru. Cas Lek Cesk 1982 Jan 22;121(3):71-3 (Eng. Abstr.) **(Cze)**

Veselková A, Brodan V: Vylučování močových katecholaminu a jejich metabolitu po podání atropinu a alfa a beta sympatolytik u zdravých dobrovolníku. Cas Lek Cesk 1981;120(50):1533-6 (Eng. Abstr.) **(Cze)**

Vetro A, Pallag P, Szentistvanyi LI, et al: Treatment of childhood aggressivity with lithium. Agressologie 1981 Nov;22(E):27-30

Vetulani J, Lebrecht U, Pilc A: Enhancement of responsiveness of the central serotonergic system and serotonin-2 receptor density in rat frontal cortex by electroconvulsive treatment. Eur J Pharmacol 1981 Nov 19;76(1):81-5

Vierhapper H, Grubeck-Loebenstein B, Korn A, et al: Release and vasoactive actions of catecholamines during inhibition of prostaglandin synthesis in normal man. Hypertension 1982 Jan-Feb;4(1):112-7

Villalpando-Hernández S, Barrón-Uribe C, Junco-Lorenzana E, et al: Large single doses of oral TRH blockade the TSH response in children. Arch Invest Med (Mex) 1981;12(4):491-7 **(Eng. Spa)**

Vinar O: Drug treatment of anxiety. Agressologie 1981 Oct;22(C):35-8

Violon C, Pessemier L, Vercruysse A: High-performance liquid chromatography of benzophenone derivatives for the determination of benzodiazepines in clinical emergencies. J Chromatogr 1982 Feb 5; 236(1):157-68

Virgilio R, Cordano AM: Naturally occurring prototrophic strains of Salmonella typhi. Can J Microbiol 1981 Dec;27(12):1272-5

Viukari M, Salo H, Lamminsivu U, et al: Pharmacokinetics of diazepam administered rectally in geriatric patients: comparison of suppositories with rectal tubes in a cross-over study. Acta Pharmacol Toxicol (Copenh) 1981 Jul;49(1):59-64

Vlk J: Cholinesterases and postnatal development of the negative chronotropic effects of acetylcholine in albino rats. Physiol Bohemoslov 1981;30(6):497-503

von Kleist D, Zschiedrich M, Stopik D, et al: Das Verhalten der sekretin-pankreozymin-stimulierten Sekretion des Pankreas, der Gallenblasenkontraktion und der Cholerese unter Somatostatin. Dtsch Z Verdau Stoffwechselkr 1981;41(5):219-24 (Eng. Abstr.) **(Ger)**

von Knorring L: Changes in saliva secretion and accommodation width during short-term administration of imipramine and zimelidine in healthy volunteers. Int Pharmacopsychiatry 1981;16(2):69-78

Vorodaevskaia GI: Vliianie kholoda na fluorestsentsiiu katekholaminov v nekotroykh strukturakh golovnogo mozga krys. Fiziol Zh 1982 Jan-Feb;28(1):86-8 **(Rus)**

Vree TB, Baars AM, Booij LH, et al: Simultaneous determination and pharmacokinetics of midazolam and its hydroxymetabolites in plasma and urine of man and dog by means of high-performance liquid chromatography. Arzneimittelforsch 1981;31(12a):2215-9

Vyas S, Marchbanks RM: The effect of ouabain on the release of [14C]acetylcholine and other substances from synaptosomes. J Neurochem 1981 Dec;37(6):1467-74

Vysotskii ES, Zavoruev VV, Mezhevikin VV: Vliianie fenobarbitala na liuminestsentnuiu sistemu svetiashchikhsia bakterii. Mikrobiologiia 1981 Nov-Dec;50(6):985-91 (Eng. Abstr.) **(Rus)**

W

Wada S, Koizumi M, Sasahara K, et al: The lipid-lowering profile in rodents. AZ-1355, a new dibenzoxazepine derivative. Atherosclerosis 1981 Nov-Dec;40(3-4):263-71

Wagner GF, McKeown BA: Immunocytochemical localization of hormone-producing cells within the pancreatic islets of the rainbow trout (Salmo gairdneri). Cell Tissue Res 1981;221(1):181-92

Wagner J, Vitali P, Palfreyman MG, et al: Simultaneous determination of 3,4-dihydroxyphenylalanine, 5-hydroxytryptophan, dopamine, 4-hydroxy-3-methoxyphenylalanine, norepinephrine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, serotonin, and 5-hydroxyindoleacetic acid in rat cerebrospinal fluid and brain by high-performance liquid chromatography with electrochemical detection. J Neurochem 1982 May;38(5):1241-54

Wakade AR, Wakade TD: Release of noradrenaline by one pulse: modulation of such release by alpha-adrenoceptor antagonists and uptake blockers. Naunyn Schmiedebergs Arch Pharmacol 1981; 317(4):302-9

Wakade AR, Wakade TD: Release of 3H-norepinephrine by ammonium and its modification by changes in pH. Life Sci 1981 Dec 7;29(23):2381-9

Waldmeyer J, Korkidis K, Geacintov NE: Relative contributions of tryptophan and tyrosine to the phosphorescence emission of human serum albumin at low temperatures. Photochem Photobiol 1982 Mar; 35(3):299-304

Walker RG, Davies B, Holwill B, et al: Lithium nephrotoxicity: is there cause for concern? Drugs 1981 Dec;22(6):421-2

Wallace SM: Graphic methods of predicting phenytoin dosage and plasma concentrations [letter] Am J Hosp Pharm 1981 Dec;38(12):1879, 1882

Wallis DI, Stansfeld CE, Nash HL: Depolarizing responses recorded from nodose ganglion cells of the rabbit evoked by 5-hydroxytryptamine and other substances. Neuropharmacology 1982 Jan;21(1):31-40

Wallnau LB: The effects of quipazine, fenfluramine and apomorphine on the morphine potentiation of tonic immobility. Pharmacol Biochem Behav 1981 Dec;15(6):895-901

Wallwork JC, Botnen JH, Sandstead HH: Influence of dietary zinc on rat brain catecholamines. J Nutr 1982 Mar;112(3):514-9

Walmsley LM, Chasseaud LF: High-performance liquid chromatographic determination of lorazepam in monkey plasma. J Chromatogr 1981 Nov 13;226(1):155-63

Walsh JH, Lechago J, Wong HC, et al: Presence of ranatensin-like and bombesin-like peptides in amphibian brains. Regul Pept 1982 Jan; 3(1):1-13

Wang RY, Aghajanian GK: Correlative firing patterns of serotonergic neurons in rat dorsal raphe nucleus. J Neurosci 1982 Jan;2(1):11-6

Warburton DM: Neurochemistry of behaviour. Br Med Bull 1981 May; 37(2):121-5 (45 ref.)

Ward BJ, Charlton HM: Female sexual behaviour in the GnRH deficient, hypogonadal (hpg) mouse. Physiol Behav 1981 Dec;27(6):1107-9

Ward D, Trevor A: Phenylclindine-induced alteration in rat muscarinic cholinergic receptor regulation. Eur J Pharmacol 1981 Sep 11; 74(2-3):189-93

Ward DS, Bellville JW: Reduction of hypoxic ventilatory drive by dopamine. Anesth Analg (Cleve) 1982 Apr;61(4):333-7

Ward NG, Lampe TH: A trial of dextroamphetamine in patients with involutional agitated depression. J Clin Psychiatry 1982 Jan;43(1):35-6

Washburn DD, Kem DC, Orth DN, et al: Effect of beta-lipotropin on aldosterone production in the isolated rat adrenal cell preparation. J Clin Endocrinol Metab 1982 Mar;54(3):613-8

Wasiewska E, Maczugowska H, Święcka E, et al: Plasma dopamine-beta-hydroxylase activity during labour in women. Acta Physiol Pol 1981;32(4):399-405

Wassef M, Berod A, Sotelo C: Dopaminergic dendrites in the pars reticulata of the rat substantia nigra and their striatal input. Combined immunocytochemical localization of tyrosine hydroxylase and anterograde degeneration. Neuroscience 1981;6(11):2125-39

Waszczak BL, Bergstrom DA, Walters JR: Single unit responses of substantia nigra and globus pallidus neurons to GABA agonist and antagonist drugs. Adv Biochem Psychopharmacol 1981;30:79-94

Watanabe K, Narimatsu S, Yamamoto I, et al: Difference in tolerance development of hypothermia and pentobarbital-induced sleep prolonging effect of 11-hydroxy-delta 8-tetrahydrocannabinol and 11-oxo-delta 8-tetrahydrocannabinol in mice. Eur J Pharmacol 1982 Jan 8;77(1):53-6

Watanabe Y, Matsumiya T, Oka T: Effects of fusaric (5-butylpicolinic) acid on the monosynaptic reflex neural activity of cat spinal cord. Tokai J Exp Clin Med 1981 Oct;6(4):443-51

Watanabe YG: Immunohistochemical study of the responsiveness of LH cells of fetal rats to synthetic LHRH in vitro. Cell Tissue Res 1981; 221(1):59-66

Waters BG, Lapierre YD: Therapeutic use of the tricyclic-induced switch in bipolar manic-depression. Am J Psychiatry 1982 Feb;139(2):245-6

Watson SJ, Akil H, Fischli W, et al: Dynorphin and vasopressin: common localization in magnocellular neurons. Science 1982 Apr 2; 216(4541):85-7

Waud BE, Farrell L, Waud DR: Lithium and neuromuscular transmission. Anesth Analg (Cleve) 1982 May;61(5):399-402

Wauquier A, Clincke G, Fransen J: Brain reinforcement mechanisms: alpha-adrenergic and dopaminergic agonists and antagonists. Prog Clin Biol Res 1981;71:177-96

Wawrzyniak M, Cybulska R: The haloperidol effect on the histofluorescence in the caudate nucleus of the rat brain treated with agonistic and antagonistic acetylcholine compounds. Folia Histochem Cytochem (Krakow) 1981;19(3):143-8

Weber E, Roth KA, Barchas JD: Colocalization of alpha-neo-endorphin and dynorphin immunoreactivity in hypothalamic neurons. Biochem Biophys Res Commun 1981 Dec 15;103(3):951-8

Weber E, Evans CJ, Barchas JD: Acetylated and nonacetylated forms of beta-endorphin in rat brain and pituitary. Biochem Biophys Res Commun 1981 Dec 15;103(3):982-9

Wehr TA, Wirz-Justice A: Circadian rhythm mechanisms in affective illness and in antidepressant drug action. Pharmacopsychiatria 1982 Jan; 15(1):31-9 (59 ref.)

Weihe E, Reinecke M: Peptidergic innervation of the mammalian sinus nodes: vasoactive intestinal polypeptide, neurotensin, substance P. Neurosci Lett 1981 Nov 4;26(3):283-8

Weiler M, Roed IS, Whittaker VP: The kinetics of acetylcholine turnover in a resting cholinergic nerve terminal and the magnitude of the cytoplasmic compartment. J Neurochem 1982 May;38(5):1187-91

Weiner N, Arold N, Wesemann W: Possible hazards in serotonin binding assays in human and rat brain: effects of ascorbate, pargyline, and buffer concentration. J Neurosci Methods 1982 Jan;5(1-2):41-5

Weiner WJ: Abrupt versus gradual withdrawal of antiparkinsonians [letter] Am J Psychiatry 1982 Feb;139(2):256-7

Weingartner H, Kaye W, Gold P, et al: Vasopressin treatment of cognitive dysfunction in progressive dementia. Life Sci 1981 Dec 28;29(26):2721-6

Weir RL, Hruska RE, Silbergeld EK: Binding of antiparkinsonian ergot derivatives to the dopamine receptor. Psychopharmacology (Berlin) 1981;75(2):119-23

Weiss S, Drummond GI: Dopamine- and serotonin-sensitive adenylate cyclase in the gill of Aplysia californica. Mol Pharmacol 1981 Nov; 20(3):592-7

Welbel SL: Clinical investigations of some anxiolytics drugs. Agressologie 1981 Oct;22(C):39-40

Weld FM, Coromilas J, Rottman JN, et al: Mechanisms of quinidine-induced depression of maximum upstroke velocity in ovine cardiac Purkinje fibers. Circ Res 1982 Mar;50(3):369-76

Weller EB, Weller RA, Preskorn SH, et al: Steady-state plasma imipramine levels in prepubertal depressed children. Am J Psychiatry 1982 Apr; 139(4):506-8

Wells PG, Küpfer A, Lawson JA, et al: Relation of in vivo drug metabolism to stereoselective fetal hydantoin toxicology in mouse: evaluation of mephenytoin and its metabolite, nirvanol. J Pharmacol Exp Ther 1982 Apr;221(1):228-34

Wenk GL, Stemmer KL: The influence of ingested aluminum upon norepinephrine and dopamine levels in the rat brain. Neurotoxicology (Park Forest Il) 1981 Oct;2(2):347-53

Wennig R: Contribution à la recherche de drogeus toxicomanogènes dans les milieux biologiques. Bull Soc Sci Med Grand Duche Luxemb 1981; 118(1):41-5 (Fre)

Wennogle LP, Beer B, Meyerson LR: Human platelet imipramine recognition sites: biochemical and pharmacological characterization. Pharmacol Biochem Behav 1981 Dec;15(6):975-82

Werner S, Widström AM, Wahlberg V, et al: Immunoreactive calcitonin in maternal milk and serum in relation to prolactin and neurotensin. Early Hum Dev 1982 Jan;6(1):77-82

Wesemann W, Muschalek G, Stöltzing H, et al: Effect of 1-aminoadamantanes on adenine nucleotide and serotonin storage in blood platelets. Eur J Cell Biol 1981 Dec;26(1):158-67

West DP, Fillenz M: Control of noradrenaline release from hippocampal synaptosomes. J Neurochem 1981 Oct;37(4):1052-3

Westendorf JM, Schonbrunn A: Bombesin stimulates prolactin and growth hormone release by pituitary cells in culture. Endocrinology 1982 Feb; 110(2):352-8

Westerink BH, Spaan SJ: On the significance of endogenous 3-methoxytyramine for the effects of centrally acting drugs on dopamine release in the rat brain. J Neurochem 1982 Mar;38(3):680-6

Westermann KH, Funk KF: Receptor supersensitivity in mental disease. Agressologie 1981 Nov;22(E):33-5

Westermann KH, Schmidt J, Bucher U: Effects of nootropic drugs on dopaminergic systems in the CNS. Pol J Pharmacol Pharm 1981; 33(4):431-6

Wetzel HW, Briley MS, Langer SZ: 3H-WB 4101 binding in the rat vas deferens. Effects of chronic treatments with desipramine and prazosin. Naunyn Schmiedebergs Arch Pharmacol 1981 Nov;317(3):187-92

Whalen CK, Henker B, Finck D: Medication effects in the classroom: three naturalistic indicators. J Abnorm Child Psychol 1981 Dec; 9(4):419-33

Wharton J, Polak JM, McGregor GP, et al: The distribution of substrate P-like immunoreactive nerves in the guinea-pig heart. Neuroscience 1981;6(11):2193-204

Wheatley DN: Disposition of the acid-extractable amino acid pool in mammalian cells. Cytobios 1981;31(122):117-34

White WE Jr, Rock SG: Lack of comutagenicity by norharman and other compounds on revertants induced by photolabeling with 2-azido-9-fluorenone oxime. Mutat Res 1981 Dec;84(2):263-71

Whittle SR, Turner AJ: Effects of anticonvulsants on the formation of gamma-hydroxybutyrate from gamma-aminobutyrate in rat brain. J Neurochem 1982 Mar;38(3):848-51

Wick MM, Fitzgerald G: Inhibition of reverse transcriptase by tyrosinase generated quinones related to levodopa and dopamine. Chem Biol Interact 1981 Dec;38(1):99-107

Widelitz MM, Hable CP 2d: The effect of PEA on serotonin and catecholamines. Biochem Biophys Res Commun 1981 Dec 15; 103(3):1107-11

Wieczorek H, Gęsicka E, Stawska A: Ocena zależności między stężeniem kwasu migdałowego m moczu a stężeniem styrenu w powietrzu w warunkach ekspozycji zawodowej. Przegl Lek 1981;38(9):681-4 (Eng. Abstr.) (Pol)

Wightman PD, Dahlgren ME, Hall JC, et al: Identification and characterization of a phospholipase C activity in resident mouse peritoneal macrophages. Inhibition of the enzyme by phenothiazines. Biochem J 1981 Aug 1;197(2):523-6

Wiklund L, Toggenburger G, Cuénod M: Aspartate: possible neurotransmitter in cerebellar climbing fibers. Science 1982 Apr 2; 216(4541):78-80

Wildmann J, Dewair M, Matthaei H: Immunochemical evidence for exocytosis in isolated chromaffin cells after stimulation with depolarizing agents. J Neuroimmunol 1981 Sep;1(3):353-64

Wilkins JA, Salganicoff L: Participation of a transmembrane proton gradient in 5-hydroxytryptamine transport by platelet dense granules and dense-granule ghosts. Biochem J 1981 Jul 15;198(1):113-23

Wilkinson M, Bhanot R: A puberty-related attenuation of opiate peptide-induced inhibition of LH secretion. Endocrinology 1982 Mar; 110(3):1046-8

Williams M, Risley EA: Interaction of avermectins with [3H]beta-carboline-3-carboxylate ethyl ester and [3H]diazepam binding sites in rat brain cortical membranes. Eur J Pharmacol 1982 Feb 5; 77(4):307-12

Williams N, Clouet DH: The effect of acute opioid administration on the phosphorylation of rat striatal synaptic membrane proteins. J Pharmacol Exp Ther 1982 Feb;220(2):278-86

Williams RL, Pearson JE, Gonzalez FM: Comparison of effects of cyanide and acetylcholine on renal hemodynamics and sodium excretion. J Pharm Sci 1982 Jan;71(1):47-50

Williamson AM, Ng KT, Richdale A: Changes in corticosterone levels in iron deficient rats. Physiol Behav 1981 Dec;27(6):1085-8

Williamson R, Ward JB: Deficiency of autolytic activity in Bacillus subtilis and Streptococcus pneumoniae is associated with a decreased permeability of the wall. J Gen Microbiol 1981 Aug;125(Pt 2):325-34

AUTHOR SECTION

Wilson CM, Myhre MJ, Reynolds RC, et al: Regulation of mouse submaxillary gland renin by thyroxine. Endocrinology 1982 Mar; 110(3):982–9

Wilson LG, Roberts RW, Gerber CJ, et al: Pimozide versus chlorpromazine in chronic schizophrenia: a 52 week double-blind study of maintenance therapy. J Clin Psychiatry 1982 Feb;43(2):62–5

Wince LC, Rutledge CO: Developmental changes in the accumulation of norepinephrine and the chronotropic effects of catecholamines in isolated rat atria as influenced by dietary lipid.
J Pharmacol Exp Ther 1982 Feb;220(2):340–6

Winn P, Redgrave P: Dose-dependent feeding in the rat following substantia nigra acetylcholinesterase blockade. Eur J Pharmacol 1981 Dec 17;76(4):421–5

Winokur A, Amsterdam J, Caroff S, et al: Variability of hormonal responses to a series of neuroendocrine challenges in depressed patients.
Am J Psychiatry 1982 Jan;139(1):39–44

Winsnes M, Jeppsson R, Sjöberg B: Diazepam adsorption to infusion sets and plastic syringes. Acta Anaesthesiol Scand 1981 Apr;25(2):93–6

Withy RM, Mayer RJ, Strange PG: The distribution of radioligand binding activity and 5'-nucleotidase activity in bovine caudate nucleus subcellular fractions. J Neurochem 1982 May;38(5):1348–55

Witkin JM, Barrett JE: Effects of pentobarbital on punished behavior: persistent increases with chronic administration.
Psychopharmacology (Berlin) 1981;75(3):324–5

Witt R: Medication compliance among discharged psychiatric patients. Issues Ment Health Nurs 1981 Oct-Dec;3(4):305–17

Wolcott DL: Does protein synthesis decline in lithium-treated sea urchin embryos because RNA synthesis is inhibited? Exp Cell Res 1982 Feb; 137(2):427–31

Wollheim CB, Janjic D, Siegel EG, et al: Importance of cellular calcium stores in glucose-stimulated insulin release. Ups J Med Sci 1981; 86(2):149–64

Wong SH, McCauley T, Kramer PA: Determination of 2-hydroxydesipramine by high-performance liquid chromatography.
J Chromatogr 1981 Nov 13;226(1):147–54

Wong WC, Tan CK: Ultrastructural changes after intracisternal injection of 6-hydroxydopamine in the intermediolateral nucleus of the monkey (Macaca fascicularis). J Anat 1981 Oct;133(Pt 3):321–31

Wood D, Reimherr F, Wender PH: Effects of levodopa on attention deficit disorder, residual type. Psychiatry Res 1982 Feb;6(1):13–20

Wood JD, Kurylo E, Tsui SK: Interactions of di-n-propylacetate, gabaculine, and aminooxyacetic acid: anticonvulsant activity and the gamma-aminobutyrate system. J Neurochem 1981 Dec;37(6):1440–7

Woodman OL, Medgett IC, Lang WJ, et al: Agonistic actions of DPI (2-(3,4-dihydroxyphenylimino)-imidazolidine) on alpha-adrenoceptors and dopamine receptors. Eur J Pharmacol 1981 Oct 15;75(1):11–9

Woodruff ML, Baisden RH, Fish BS: Forebrain catecholamine concentrations in the rat after neocortical and hippocampal lesions.
Life Sci 1981 Dec 21;29(25):2603–7

Worms P, Willigens MT, Lloyd KG: The behavioural effects of systemically administered kainic acid: a pharmacological analysis.
Life Sci 1981 Nov 23;29(21):2215–25

Wray SD, Hassell TM, Phillips C, et al: Preliminary study of the effects of carbamazepine on congenital orofacial defects in offspring of A/J mice. Epilepsia 1982 Feb;23(1):101–10

Wurtman RJ: The effects of nutritional factors on memory.
Acta Neurol Scand [Suppl] 1981;89:145–54

Wyllie MG, Wood MD, Pheysey J, et al: Modulation of central noradrenaline release by postsynaptic receptors. J Pharm Pharmacol 1982 Jan;34(1):53–5

Wyroba E, Bottiroli G, Giordano P: Cycloheptaamylose-dansyl chloride complex as a fluorescent label of surface membranes in living ciliates.
Histochemistry 1981 Dec;73(3):459–67

Wysocki H, Czarnecki R, Wierusz-Wysocka B, et al: The selective polymorphonuclear neutrophils (PMN) degranulation as the probable additional mechanism of the hemodialysis (HD)-induced complement activation. Int J Artif Organs 1981 Jul;4(4):174–7

Y

Yahaba Y, Obata N, Hidano F, et al: [Bioavailability of two commercial phenytoin preparations (author's transl)] Seishin Shinkeigaku Zasshi 1981;83(9):582–96 (Eng. Abstr.) (Jpn)

Yamada M: Effects of atropine on nicotinic transmission in bullfrog sympathetic ganglia. Kurume Med J 1981;28(2):119–23

Yamada T, Chopra IJ, Kaplowitz N: Inhibition of rat hepatic thyroxine 5'-monodeiodinase by propylthiouracil: relation to site of interaction of thyroxine and glutathione. J Endocrinol Invest 1981 Oct-Dec; 4(4):379–87

Yamaguchi I, Akimoto Y, Nishiyama S, et al: [Effects of diltiazem on catecholamine release from cat adrenal glands (author's transl)]
Nippon Yakurigaku Zasshi 1981 Nov;78(5):501–9 (Eng. Abstr.) (Jpn)

Yamaguchi K, Goko H, Takashima S, et al: Abnormalities of insulin secretory and lipolytic response to epinephrine produced by a high fat diet and electric stress in rats. Endokrinologie 1981 Dec;78(2–3):253–61

Yamamura M, Ochiai T, Ishida R: [Effects of afloqualone, a new centrally acting muscle relaxant, on DRL response and CER in rats (author's transl)] Nippon Yakurigaku Zasshi 1981 Oct;78(4):381–92 (Eng. Abstr.) (Jpn)

Yamazumi S, Miura S: Haloperidol concentrations in saliva and serum: determination by the radioimmunoassay method.
Int Pharmacopsychiatry 1981;16(3):174–83

Yanofsky C, Platt T, Crawford IP, et al: The complete nucleotide sequence of the tryptophan operon of Escherichia coli. Nucleic Acids Res 1981 Dec 21;9(24):6647–68 (62 ref.)

Yasuda H, Shimada O, Nakajima A, et al: Cerebral protective effect and radical scavenging action. J Neurochem 1981 Oct;37(4):934–8

Yazulla S, Kleinschmidt J: Dopamine blocks carrier-mediated release of GABA from retinal horizontal cells. Brain Res 1982 Feb 4;233(1):211–5

Yehuda S, Mostofsky DI, Bracha T: Increased serotonin level via augmented tryptophan diet and its effect on escape learning.
Int J Neurosci 1981;15(4):193–6

Yesavage JA, Becker J, Werner PD, et al: Serum level monitoring of thiothixene in schizophrenia: acute single-dose levels at fixed doses.
Am J Psychiatry 1982 Feb;139(2):174–8

Yin ZZ, Zeng GY: [Pharmacology of puerarin. V. Effects of puerarin on platelet aggregation and release of 5-HT from platelets]
Chung Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao 1981 Jun;3 Suppl 1:44–7 (Eng. Abstr.) (Chi)

Yip BP, Lardy HA: The role of calcium in the stimulation of gluconeogenesis by catecholamines. Arch Biochem Biophys 1981 Dec; 212(2):370–7

Yoran C, Higginson L, Romero MA, et al: Reflex sympathetic augmentation of left-ventricular inotropic state in the conscious dog.
Am J Physiol 1981 Dec;241(6):H857–63

Yoshida M: The GABAergic systems and the role of basal ganglia in motor control. Adv Biochem Psychopharmacol 1981;30:37–52

Yu PH, Bowen R, Carlson K, et al: Comparison of biochemical properties of platelet monoamine oxidase in mentally disordered and healthy individuals. Psychiatry Res 1982 Feb;6(1):107–21

Yu PH, Barclay S, Davis B, et al: Deuterium isotope effects on the enzymatic oxidative deamination of trace amines.
Biochem Pharmacol 1981 Nov 15;30(22):3089–94

Yukimura T, Unger T, Rascher W, et al: Central peptidergic stimulation in blood pressure control: role of enkephalins in rats.
Clin Sci [Suppl] 1981 Dec;61(7):347s–350s

Yurkewicz L, Marchi M, Lauder JM, et al: Development and aging of noradrenergic cell bodies and axon terminals in the chicken.
J Neurosci Res 1981;6(5):621–41

Yuwiler A, Brammer GL: Neonatal hormone treatment and maturation of the pineal noradrenergic system: hydrocortisone and thyroxine.
J Neurochem 1981 Oct;37(4):985–92

Z

Zacur HA, Mitch WE, Tyson JE, et al: Autoregulation of rat pituitary prolactin secretion demonstrated by a new perfusion method.
Am J Physiol 1982 Apr;242(4):E226–33

Zaczek R, Coyle JT: Rapid and simple method for measuring biogenic amines and metabolites in brain homogenates by HPLC-electrochemical detection. J Neural Transm 1982;53(1):1–5

Zadina JE, Kastin AJ, Fabre LA, et al: Facilitation of sexual receptivity in the rat by an ovulation-inhibiting analog of LHRH.
Pharmacol Biochem Behav 1981 Dec;15(6):961–4

Zagrodzka J, Korczyński R, Fonberg E: The effects of imipramine on socio-emotional and alimentary motivated behavior in dogs.
Acta Neurobiol Exp (Warsz) 1981;41(4):363–72

Zajączkowska M, Gębala A, Szajner-Milart I: Role of some biogenic amines in the pathomechanism of glomerulonephritis.
Acta Physiol Pol 1981;32(4):375–82

Zakarian S, Smyth DG: beta-Endorphin is processed differently in specific regions of rat pituitary and brain. Nature 1982 Mar 18;296(5854):250–2

Zapletálek M, Zbytovský J, Libiger J, et al: Terapie endogenních depresí maprotilinem, clomipraminem, dibenzepinem a pyrlindolem.
Cesk Psychiatr 1981 Jun;77(3):198–203 (Eng. Abstr.) (Cze)

Zar MA, Ebong O, Bateman DN: Effect of metoclopramide in guinea-pig ileum longitudinal muscle: evidence against dopamine-mediation.
Gut 1982 Jan;23(1):66–70

Zarach-Krutysza M: Wrażliwość myszy albinotycznych i czarnych na niektóre leki mające powinowactwo do melanin. Acta Pol Pharm 1981; 38(4):513–8 (Eng. Abstr.) (Pol)

Zarifian E: Intérêt du site de liaison de l'imipramine tritiée dans la pharmacologie des antidépresseurs. Encephale 1981;7(4 Suppl):405–7 (Fre)

Zarifian E, Scatton B, Bianchetti G, et al: High doses of haloperidol in schizophrenia. A clinical, biochemical, and pharmacokinetic study.
Arch Gen Psychiatry 1982 Feb;39(2):212–5

Zarkowsky HS: Membrane-active agents and heat-induced erythrocyte fragmentation. Br J Haematol 1982 Feb;50(2):361–5

Zefirov AL: Analiz chastotnogo oblegcheniia v nervno-myshechnykh sinapsakh portniazhnoĭ myshtsy liagushki. Biull Eksp Biol Med 1981 Oct;91(10):389-92 (Eng. Abstr.) (Rus)

Zehavi U, Mechoulam R: O-and C-D-glucosyluronic acid derivatives of delta 1-tetrahydrocannabinol: synthesis and differential behavior to beta-glucuronidase. Carbohydr Res 1981 Dec 1;98(1):143-7

Zelis RF, Kinney EL: The pharmacokinetics of diltiazem in healthy American men. Am J Cardiol 1982 Feb 18;49(3):529-32

Zermatten A, Cumps J: Etude de la nomifensine dans le traitement des états dépressifs. Acta Psychiatr Belg 1981 Jul-Aug;81(4):379-98 (Eng. Abstr.) (Fre)

Zetin M: Combined use of trimipramine and phenelzine in depression. J Nerv Ment Dis 1982 Apr;170(4):246-7

Zetta L, Cabassi F: 270-MHz 1H nuclear-magnetic-resonance study of met-enkephalin in solvent mixtures. Conformational transition from dimethylsulphoxide to water. Eur J Biochem 1982 Feb;122(1):215-22

Zevenhuizen LP: Cellular glycogen, beta-1,2,-glucan, poly beta-hydroxybutyric acid and extracellular polysaccharides in fast-growing species of Rhizobium. Antonie Van Leeuwenhoek 1981; 47(6):481-97

Zhang YF: [Clinical observation on the effect of domestic fluphenazine decanoate in the treatment of schizophrenia---report of 431 cases (author's transl)] Chung Hua Shen Ching Ching Shen Ko Tsa Chih 1981 Aug;14(3):182-5 (Chi)

Zharkovskiĭ AM, Nurk AM: Vliianie vnutrikaudatnogo vvedeniia kainovoĭ kisloty na aktivnost' dofaminergicheskoĭ sistemy. Fiziol Zh SSSR 1981 Nov;67(11):1606-10 (Eng. Abstr.) (Rus)

Ziegler WH, Thurneysen JD, Crevoisier C, et al: Relations entre l'effet clinique et la pharmacocinétique du midazolam après administration i.m. et i.v. chez des volontaires. 1ère communication: Aspects cliniques. Arzneimittelforsch 1981;31(12a):2206-10 (Eng. Abstr.) (Fre)

Zimmermann H, Kaplan SL, Ganong WF: Evidence that the effects of 5-hydroxytryptophan on the secretion of ACTH and growth hormone in dogs are not mediated by central release of serotonin. Neuroendocrinology 1982 Jan;34(1):27-31

Zohar J, Spiro D, Novack A, et al: Lack of benefit from magnesium in lithium toxicity. Neuropsychobiology 1982 Jan-Feb;8(1):10-1

Zolovick AJ, Rossi J 3d, Davies RF, et al: An improved pharmacological procedure for depletion of noradrenaline: pharmacology and assessment of noradrenaline-associated behaviors. Eur J Pharmacol 1982 Feb 5; 77(4):265-71

Zozulia AA, Patsakova EK, Kost NV: Vzaimodeĭstvie metinioninénkefalina s limfotsitami cheloveka. Vestn Akad Med Nauk SSSR 1982;(1):28-33 (Eng. Abstr.) (Rus)

Zurgil N, Zisapel N: Induced neurotransmitter release from primary cultures of rat brain neurons. Life Sci 1981 Nov 30;29(22):2265-71

ANONYMOUS

Adv Biochem Psychopharmacol
GABA and the basal ganglia. Adv Biochem Psychopharmacol 1981; 30:1-241

Agressologie
3e symposium de psychopharrmacologie. (Smolenice, 20-22 octobre 1980) Psychopharmacologie de l'anxiété. Agressologie 1981 Oct;22(C):1-53 (Fre)

Am J Hosp Pharm
Physostigmine's use questioned for amoxapine overdose [letter] Am J Hosp Pharm 1981 Dec;38(12):1882, 1889

Arzneimittelforsch
Midazolam. Symposium, Geneva, 26-28 June 1980. Arzneimittelforsch 1981;31(12a):2177-287 (Eng, Mul)

Chir Dent Fr
Nouveautés industrielles et pharmaceutiques. Prontalgine. Chir Dent Fr 1981 Nov 19;51(134):55 (Fre)

Drug Ther Bull
Lormetazepam - yet another benzodiazepine. Drug Ther Bull 1982 Jan 8;20(1):3-4

J Am Geriatr Soc
Clinical conferences: Management of depression in older people. J Am Geriatr Soc 1982 Mar;30(3):219-23

JAMA
Nitrous oxide-oxygen sedation [letter] JAMA 1982 Jan 15;247(3):302-3

Lancet
Alpha 2 adrenergic receptors in depression [editorial] Lancet 1982 Apr 3;1(8275):781

Mod Probl Pharmacopsychiatry
The role of endorphins in neuropsychiatry. Mod Probl Pharmacopsychiatry 1981;17:1-290

N Engl J Med
beta-Adrenoceptor antagonists [letter] N Engl J Med 1982 Jan 21; 306(3):176-7

Natl Inst Drug Abuse Res Monogr Ser
Benzodiazepines: a review of research results, 1980. Natl Inst Drug Abuse Res Monogr Ser 1980;(33):1-96

Nurs Times
Christmas Eve. Nurs Times 1981 Dec 23-Jan 5;77(52):2246

Pharmacopsychiatria
Guidelines for the evaluation of drugs in the elderly neuropsychiatric patient (demented and non-demented). Pharmacopsychiatria 1981 Nov; 14(6):217-22

Prog Clin Biol Res
Psychopharmacology of clonidine. Prog Clin Biol Res 1981;71:1-320

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-379-151/104

The *Psychopharmacology Bulletin* is prepared by the Pharmacologic and Somatic Treatments Research Branch of the National Institute of Mental Health. Its purpose is to facilitate the dissemination and exchange of information among the national and international scientific community. The emphasis is on rapid, informal reporting of work which has not appeared in the more formal literature. We invite contributions such as original articles, brief reports, review articles, letters to the Editor, news items, books for review, and announcements appropriate for the *Bulletin*.

All material published in the *Psychopharmacology Bulletin* is in the public domain unless otherwise noted. Publication in the *Bulletin* therefore does not preclude publication elsewhere.

Individuals interested in submitting material to the *Psychopharmacology Bulletin* should contact:

Allen Raskin, Ph.D.
Editor-in-Chief
Psychopharmacology Bulletin
National Institute of Mental Health
5600 Fishers Lane Rm. 10C-14
Rockville, MD 20857

We respectfully ask you to adhere to the following guidelines when preparing a paper for the *Psychopharmacology Bulletin:*

1. Manuscript Format: Manuscripts should be typed double-spaced with ample margins, and submitted in triplicate. Do not split paragraphs from one page to another, even if this makes page lengths uneven. Also, do not hyphenate words at the end of a line, even if this makes uneven lines.

Title page should include each author's name, degree, and full address.

Papers should be written in *third* person, e.g., the investigators found, *Not*: I found, we found. Contents should be *substantive*, not indicative, e.g., the investigator used the gas chromatography method to determine the three molecular structures, *Not*: The author described the method for determining the structure of the drug.

2. Figures: Figures, charts, or graphs should be submitted as glossies (photographs printed on smooth shiny paper) or should be professionally prepared using black ink on white paper. Only one copy is needed. Indicate in the text where these figures and their legends should be placed.

3. References: References mentioned in the text should appear as full citations in the **References** following the text with *all* authors cited in the reference list, e.g., Simpson, G.M., Lee, L.H., Zubok, B, and Gardos. A rating scale for tardive dyskinesia. *Psychopharmacology (Berlin)*, 64(2):171-179, 1979.

If a work has two authors, always cite both names every time the reference occurs in the text, e.g. (Swanson & Cole 1974). If more than two authors, cite only the surname of the first author in the text followed by et al., e.g., Williams et al. 1963.

4. Abbreviations: Abbreviations should appear in parentheses after the first time they are mentioned in the paper, ie., Brief Psychiatric Rating Scale (BPRS).

Use generic names in referring to drugs; trade names may be given in parenthesis the first time a drug is mentioned only.

Journal titles should be abbreviated in the *References* according to the National Library of Medicine's Index Medicus.

5. Brief Reports: Authors wishing very rapid reporting of new work may submit manuscripts of up to five typed double-spaced pages for inclusion as Brief Reports. If accepted, these results would appear in the next issue of the *Bulletin*. In preparing a manuscript for publication as a Brief Report, please follow the format cited above.

DEPARTMENT OF
HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20857

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.H.S.
HHS 396

FOURTH CLASS
BOOK RATE

DHHS Publication No. (ADM) 82 - 173
Printed 1982

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20857